Synthesis and Reactions of α-Azido Alcohols

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Die vorliegende Arbeit beschäftigt sich mit der Untersuchung von α-Azidoalkoholen, welche über die Reaktion von aliphatischen sowie aromatischen Aldehyden mit HN_3 leicht zugänglich sind und die im Gleichgewicht mit den jeweiligen Ausgangsstoffen vorliegen. Bei Raumtemperatur stellt sich dieses Gleichgewicht sehr schnell ein und man erhält spezifische Konzentrationen an Eduktaldehyd, Stickstoffwasserstoffsäure und α-Azidoalkohol. Die Reaktion von Aldehyden mit HN_3 generiert dabei ein neues Chriralitätszentrum, wodurch die Umsetzung chiraler Aldehyde, wie z. B. von Zuckerderivaten, zwei anomere Produkte hervorbringt.[36]

Die erstmalig erfolgreichen Synthesen zur Erzeugung von 4-Brom-4-methylpentanal sowie 4-Azido-4-methylpentanal werden ebenfalls beschrieben. Letztere Verbindung reagiert dabei ebenso wenig *via* einer intramolekularen 1,3-dipolaren Cycloaddition zum entsprechenden 4,5-Dihydro-1,2,3,4-oxatriazol-Derivat wie das analoge 4-Azidobutanal, was im Gegensatz zu Literaturangaben steht.[49]

Des Weiteren werden einige interessante Reaktionen der α-Azidoalkohole untersucht. Die Oxidation mit Pyridiniumchlorochromat (PCC) bei –60°C führt zu Carbonylaziden. Die Photolyse bei –50°C generiert unter Stickstofffreisetzung Nitrene, welche mittels Wasserstoffwanderung und anschließender Tautomerisierung des resultierenden Intermediats zu Säureamiden umlagern. Die ebenfalls mögliche 1,2-Wanderung einer Gruppe R in α-Position führt dabei zu einem Intermediat, aus welchem sofort das entsprechende Formamid-Derivat entsteht. α-Azidoalkohole reagieren mit PBr_3 in einer sauberen Reaktion durch die Substitution der Hydroxylfunktion unter Bildung der jeweiligen 1-Azido-1-brom-Verbindung.

Stichworte: α-Azidoalkohole, Aldehyde, Stickstoffwasserstoffsäure, Azide, Gleichgewichtsreaktionen, Nucleophile Addition, Cycloaddition, Stickstoffheterocyclen, Oxidation, Photolyse.

Abstract

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In this work, α-azido alcohols which exist in equilibrium with the starting materials have been studied by the reactions of aliphatic and aromatic aldehydes with HN_3. In some cases the title compounds can be isolated from the mixture at low temperature. At room temperature, however, the equilibrium is fast and there are again specific concentrations of the aldehyde, hydrazoic acid, and the α-azido alcohol. The reaction of aldehydes with HN_3 creates a new chiral center and a chiral aldehyde, e.g. sugar derivatives, produces two anomeric products.[36]

The first procedures to prepare 4-bromo-4-methylpentanal and 4-azido-4-methylpentanal are also reported. The latter compound and also the parent 4-azidobutanal do not lead to 4,5-dihydro-1,2,3,4-oxatriazoles by intramolecular 1,3-dipolar cycloaddition, although it was claimed in the literature.[49]

Furthermore, some interesting reactions of the α-azido alcohols have been investigated. The oxidation of α-azido alcohols with pyridinium chlorochromate (PCC) at −60 ˚C leads to formation of carbonyl azides. The photolysis of α-azido alcohols at −50 ˚C generates nitrenes with liberation of dinitrogen, which lead to the formation of acid amides after the migration of hydrogen and subsequent tautomerism of the intermediate. 1,2-Migration of a group R in the α-position can produce an intermediate stage which is rapidly converted into formamide derivative. α-Azido alcohols react with PBr_3 to give 1-azido-1-bromo derivatives in a clean reaction by substitution of hydroxyl group at the α-position.

Keywords: α-Azido alcohols, Aldehydes, Hydrazoic acid, Azides, Equilibrium reactions, Nucleophilic addition, Cycloaddition, Nitrogen heterocycles, Oxidation, Photolysis.

Dedication

This thesis is dedicated to my parents
for their love, endless support
and encouragement.

TABLE OF CONTENTS

List of Symbols and Abbreviations

α	Alpha
β	Beta
δ	Chemical shift
$\tilde{\nu}$	Wavenumber
AcOH	Acetic acid
anal.	Analysis
aq	Aqueous
br	Broad
Brine	Saturated aqueous sodium chloride
Bu	Butyl
°C	Degree Celsius
^{13}C NMR	Carbon-13 nuclear magnetic resonance spectroscopy
calcd.	Calculated
$CaCl_2$	Calcium chloride
$CDCl_3$	Deuterated chloroform
$CHCl_3$	Chloroform
CH_2Cl_2	Methylene chloride
CCl_4	Carbon tetrachloride
cm^{-1}	Reciprocal centimeters
*c*Hex	Cyclohexyl
d	Doublet
dd	Doublet of doublets
ddd	Doublet of doublet of doublets
dt	Doublet of triplets
DMSO	Dimethyl sulfoxide
D_2O	Deuterated water
DMF	Dimethylformamide
DMAP	4-Dimethylaminopyridine
DDQ	2,3-Dichloro-5,6-dicyano-*p*-benzoquinone
Et	Ethyl
Et_2O	Diethyl ether
EtOAc	Ethyl acetate

EtOH	Ethanol
$Eu(fod)_3$	Tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium
g	Gram(s)
gHSQCAD	Gradient Heteronuclear Single Quantum Coherence
gHMBCAD	Gradient Heteronuclear multiple-bond correlation spectroscopy
HN_3	Hydrazoic acid
h	Hour(s)
HBr_g	Hydrogen bromide gas
HBr	Hydrobromic acid
H^+	Proton or protic acid
^1H NMR	Proton nuclear magnetic resonance spectroscopy
HR-MS	High resolution mass spectrometry
Hz	Hertz
IR	Infrared spectroscopy
J	Coupling constant
$KMnO_4$	Potassium permanganate
m	Multiplet
MHz	Mega Hertz
mL	Milliliter(s)
M^+	Molecule Ion
m/*z*	Mass/Charge
min	Minute(s)
MeOH	Methanol
mbar	Millibar
MAK	Maximum allowed concentration at workplace
M	Molar
Me	Methyl
mg	Milligram(s)
mmol	Millimole(s)
mol	Mole(s)
$molL^{-1}$	Mole per liter
Mp	Melting point
NMR	Nuclear magnetic resonance

PCC	Pyridinium chlorochromate
Ar	Aryl
ppm	Parts per million
Pr	Propyl
P_2O_5	Phosphorus pentoxide
PBr_3	Phosphorus tribromide
QN_3	Hexadecyltributylphosphonium azide
q	Quartet
qd	Quartet of doublets
qt	Quartet of triplets
RT	Room temperature
R	Alkyl group
s	Singlet
THF	Tetrahydrofuran
TLC	Thin-layer chromatography
TMS	Tetramethylsilane
t	Triplet
td	Triplet of doublets
THF	Tetrahydrofuran
OTs	Tosyloxy
TMGA	Tetramethylguanidinium azide
X	Halogen atom

1. INTRODUCTION AND TASK OF STUDY

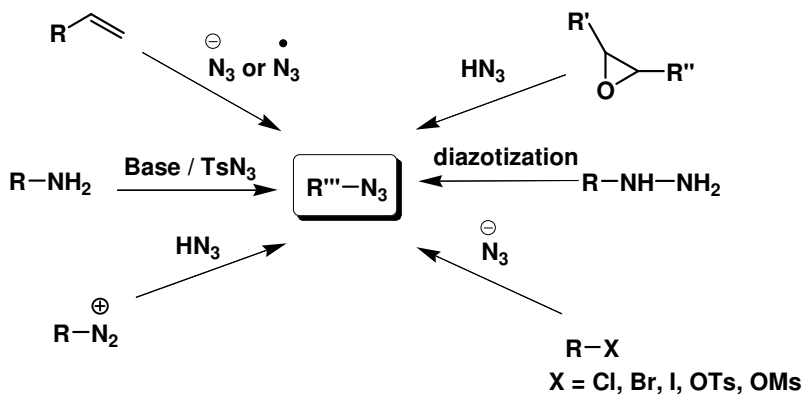
1.1. Introduction

1.1.1 Organic Azides

Organic Azides represent a unique substance class, which is able to undergo a multitude of reactions used for a variety of applications in industry.[1,2]

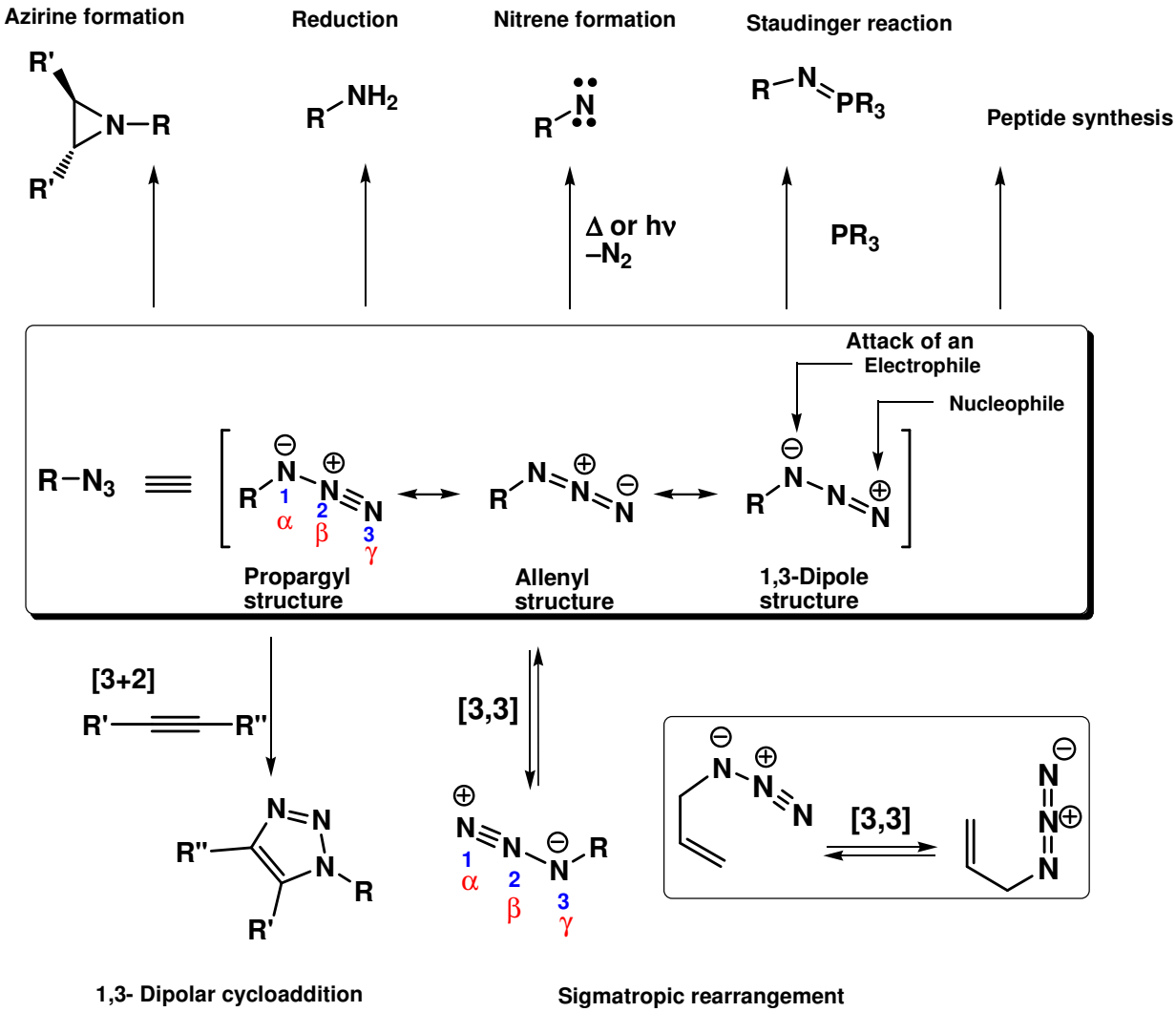
The first organic azide (phenyl azide) was synthesized by P. Grieß in 1864.[3,4] It followed the discovery of hydrogen azide and the Curtius rearrangement of acyl azides to the corresponding isocyanates by T. Curtius from 1890 to 1894.[5] The organic azides received considerable attention in the 1950s and 1960s with new applications in the chemistry of the acyl, aryl, and alkyl azides.[6,7] Organic azides are used for the synthesis of heterocycles (triazoles, tetrazoles, aziridines), as blowing agents, and functional groups in pharmaceuticals e.g. azidonucleosides for the treatment of AIDS.[8] In 1893, A. Michael described thermal reaction of azide with dimethyl but-2-ynedioate, which was later studied in detail by R. Huisgen.[9a] In 1961, R. Huisgen reported the Huisgen reaction, e.g. 1,3-dipolar [2+3] cycloaddition between an azide and a terminal or internal alkyne to give a 1,2,3-triazole.[9b] The same conversion was performed at room temperature using a Cu(I) catalyst by M. Meldal and K. B. Sharpless in 2002, and is one of the most popular reactions in the click chemistry.[10]

Organic azides can be prepared by numerous methods, e.g. by nucleophilic substitution using ionic azides,[2] addition reactions, [11,12] insertion of an N_2 group (diazo transfer),[13] insertion of a nitrogen atom (diazotization),[14] cleavage of triazines and analogous compounds, and rearrangement of azides (Scheme 1).



Scheme 1. Synthesis of Organic Azides

Hexadecyltributylphosphonium azide (QN_3) and tetramethylguanidinium azide (TMGA) as well as other reagents whose solubility is significantly higher in organic solvent as compared to the alkali metal azides (NaN_3 and LiN_3) can also be used to introduce the azide function. The low melting point of this reagent allows convenient usage as a (supercooled) melt. Thus, extremely rapid nucleophilic substitution reactions and isolation of unstable products are possible by simple re-condensation.[15]



Scheme 2. Reactions of Organic Azides

Organic azides are good intermediates for the synthesis of a variety of nitrogen containing compounds. In principle, they react with electrophiles (Lewis acids, acids, carbonium ions) at N-1 and nucleophiles (phosphanes, organometallic reagents) at N-3. The azido group can be kept intact or it can be reduced to amines. The decomposition and cleavage of nitrogen led to intermediate nitrenes[3a] (photochemically, thermally, or by use of a catalyst) which shows various interesting sequentional reactions.[16]

Organic azides can give Huisgen 1,3-dipolar or [3+2] cycloaddition products by reaction with strained alkenes (norborne, norbornadiene) and with alkynes (cyclooctyne).[9,10]

1.1.2. Hydrazoic Acid

Hydrazoic acid (HN_3), also known as hydrogen azide or azoimide,[17] was first isolated in 1890 by T. Curtius.[5a] It is a colorless, volatile and extremely explosive liquid at room temperature. It is highly toxic with a pungent smell and its vapors can cause violent headaches and act as a non-cumulative poison. Its aqueous solution dissolves many metals (e.g. zinc, iron) with liberation of hydrogen and formation of salts. Its heavy metal salts are explosive and readily interact with alkyl iodides. Azides of alkali metals (excluding lithium) or alkaline earth metals are not explosive, but decompose on heating to liberate N_2 gas.[18]

Hydrazoic acid is a weak acid (pK_a = 4.6-4.7) and forms poorly water soluble lead, silver and mercury(I) salts comparable to halogen acids. Dissolution in the strongest acids produces explosive salts containing the $H_2N_3^+$ ion.[18]

$$\overset{\oplus\ \ominus}{HN{=}N{=}N} + HSbCl_6 \longrightarrow [H_2N{=}\overset{+}{N}{=}N][SbCl_6^-]$$

Hydrazoic acid can be produced by acidification of an azide salt e.g sodium azide, lithium azide or barium azide.[19] The solution of sodium azide in water contains trace quantities of hydrazoic acid in equilibrium with the azide salt, and addition of a stronger acid converts it to hydrazoic acid. The pure acid can be obtained by fractional distillation.

$$NaN_{3(s)} + HCl_{(aq)} \longrightarrow HN_{3(aq)} + NaCl_{(aq)}$$

$$NaN_{3(s)} + H_2SO_{4(aq)} \longrightarrow HN_{3(aq)} + NaHSO_{4(aq)}$$

1.1.3. Explosive Nature of Organic Azides and Toxicology

Covalently bonded organic azides are thermally decomposable and are considered as an explosive class of compounds. Explosive reaction is expected for azido compounds having $(N_C + N_O)/N_N$ ratio of 3 or greater than 3, (N= number of atoms).[20]

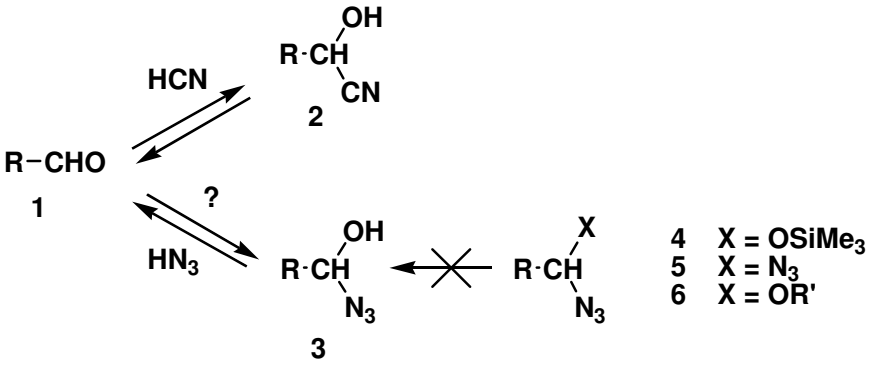
Organic compounds with high azide contents are very sensitive to friction and impact, causing explosions. Organic azides also show remarkably lower ignition temperatures in comparison to inorganic metal azides. Most of the organic azides decompose at approximately 180 °C. Some organic azides also show light sensitivity[21] and strong incompatibility with certain chemicals. Several examples have been published where azides exploded when they were brought in contact with sulfuric acid or other compounds.[7,22,23]

Dry sodium azide, its solution, and hydrazoic acid are extremely toxic and can be absorbed by inhalation, ingestion.[24,25] In the event of contact of the skin or mucous membranes with azides, the affected parts must be rinsed thoroughly with water.

The MAK value for sodium azide is 0.07 ppm; for hydrazoic acid 0.1 ppm. Even very small amounts of azides cause headache, irritation of the eyes and mucous membranes, heightened irritability and excitation, impairment of vision, shortness of breath, reduction of blood pressure, risk of collapse or fainting.

1.1.4. α-Azido Alcohols

The synthetically important cyanohydrins **2** prepared from aldehydes **1** and hydrogen cyanide are widely cited in literature,[26] but the synthesis of α-azido alcohols from aldehydes and hydrazoic acid was entirely unknown (Scheme 3).



Scheme 3. Reaction of Aldehydes with HCN and HN_3

The reaction of silylethers **4** with methanol gave aldehyde **1**[27] as the only product. The solvolysis of diazide **5** also gave **1** as the end product, and the azido alcohol was postulated to be a short lived intermediate.[28]

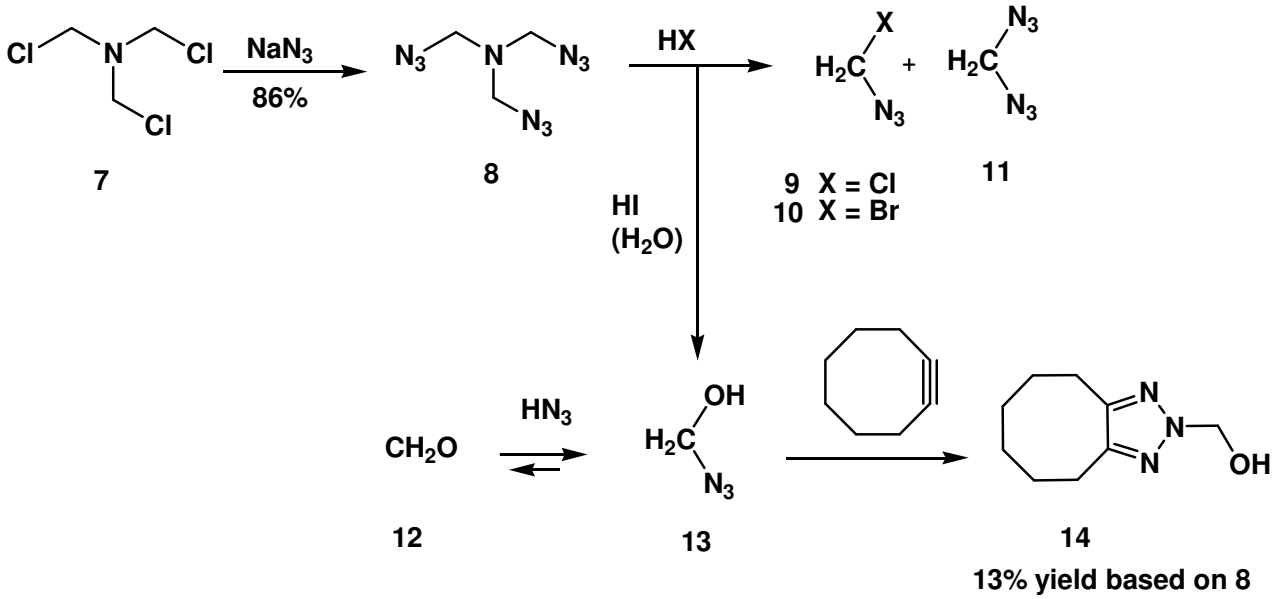
The compounds **4**[27,29] and **5**[30,31] as well as α-azido ether **6**[31,32] can be synthesized from precursor **1**, isolated and characterized, but no spectroscopic data are available for the

existence of α-azido alcohols. This seems to indicate that aldehydes do not react readily with hydrazoic acid.[32]

Recently, formation of azidomethanol (**13**) in situ was reported by the reaction of formaldehyde with sodium azide in the presence of acetic acid. This reaction was completed by copper(I)-catalyzed cycloaddition at terminal alkynes to give 1,2,3-triazoles.[33]

K. Banert et al. discovered the α-azido alcohols incidentally during the preparation of azidochloromethane (**9**), azidobromomethane (**10**) and diazide **11** by treating triazide **8** with anhydrous hydrogen halides (Scheme 4).[34, 36]

The desired products **9** and **10** were intermediates in the nucleophilic substitution of the corresponding dihalomethanes to generate **11** but could not be detected during these transformations.[34,35] Whereas **9** prepared from **8** was isolated as an explosive colorless liquid, **10** was less stable and thus characterized only in solution.[34,36] When **8** was reacted with hydrogen iodide in chloroform under apparently not completely anhydrous conditions, surprisingly azidomethanol (**13**) was produced, which was analyzed by NMR and IR spectroscopy.



Scheme 4. Attempted Synthesis of Azidoiodomethane

The structure of **13** was additionally confirmed by treatment with cyclooctyne[37] and isolation of a stable product **14**, which resulted from 1,3-dipolar cycloaddition followed by rearrangement. Solution of **13** in chloroform showed only small proportions of the cleavage products **12** and hydrazoic acid. Thus, it is suggested that the equilibrium between **12**/HN_3

and **13** favors the α-azido alcohol, which is easily available by mixing **12** and hydrazoic acid in chloroform.[36]

1.2. Task of the Study

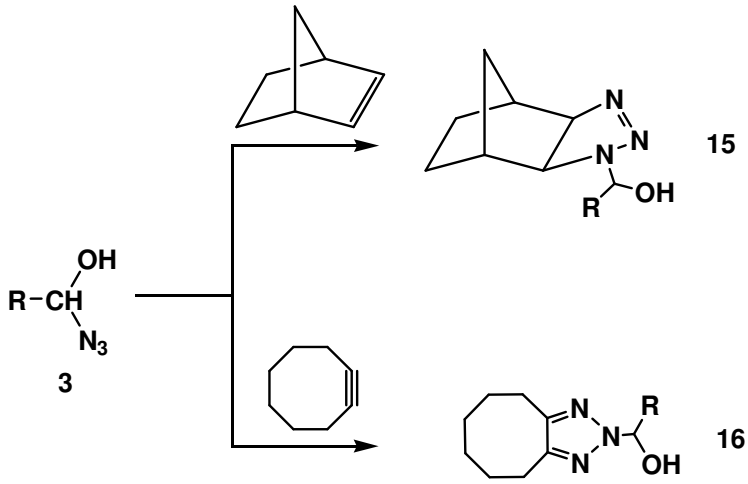
1.2.1. Synthesis of α-Azido Alcohols

In this study, the reactions of various aldehydes, e.g. formaldehyde, acetaldehyde, propionaldehyde, etc., with HN_3 to produce α-azido alcohols should be investigated. The reactivity of synthesized α-azido alcohols should be investigated.

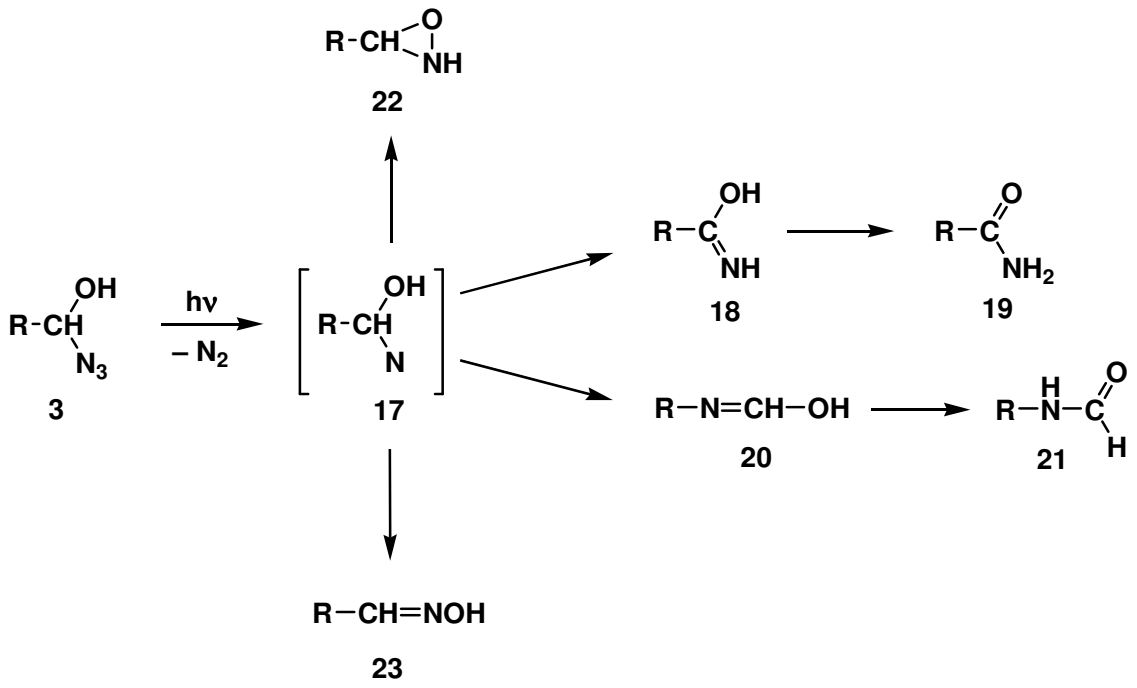
1.2.2. Reactions of α-Azido Alcohols

1.2.2.1. Due to Presence of Azido Group

α-Azido alcohols can undergo 1,3-dipolar cycloaddition, photolysis and Staudinger reaction due to the presence of an azido group. α-Azido alcohols can give 1,3-dipolar cycloaddition products with strained alkenes, e.g. norbornene and with alkynes, e.g. cyclooctyne (Scheme 5).



Scheme 5. Reaction of α-Azido Alcohols with Norbornene and Cyclooctyne

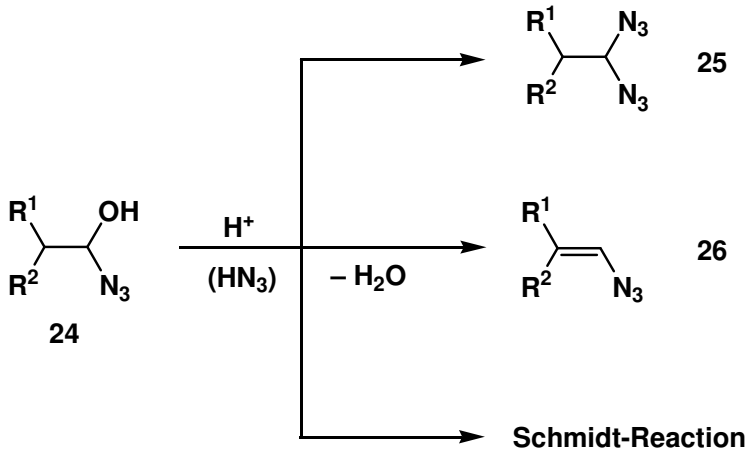


Scheme 6. Photolysis of α-Azido Alcohols

The photolysis of **3** can possibly lead to the formation of nitrene **17** after liberation of nitrogen gas. The nitrene **17** can further give different subsequent reactions indicated in Scheme 6. These reactions can yield oxaziridine **22** by insertion. Alternatively, after the migration of the hydrogen, the subsequent tautomerism of the intermediates **18** can produce acid amide **19**. 1,2-Migration of R can produce the intermediate stage **20** which is converted to formamide **21**. 1,2-Migration of the OH-group would transform **17** into oxime **23**.

1.2.2.2. Due to Presence of Hydroxyl Group

α-Azido alcohols can possibly undergo substitution reactions with other nucleophiles, etherification, esterification, dehydration, addition reactions and its oxidation under suitable reaction conditions can yield the corrosponding acyl azide.



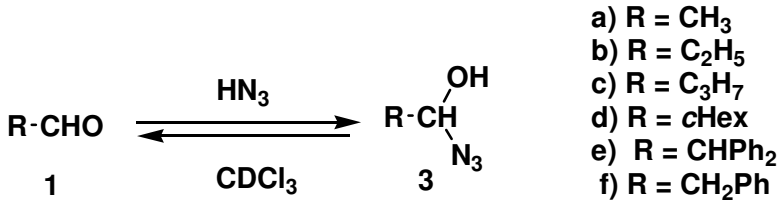
Scheme 7. Reaction of α-Azido Alcohols with Acids

The substrate of type **24** can perhaps give dehydration reaction (Scheme 7); it can lead to formation of diazides **25** or vinylazides **26** in the presence of acids as catalyst. More drastic conditions can lead to Schmidt reaction. Further reactions, e.g. reaction with phosphines and other phosphorus (III)-compounds, should also be studied.

2. RESULTS AND DISCUSSION

2.1. Synthesis of α-Azido Alcohols by Hydroazidation of Aldehydes

It was observed that aldehydes react with HN_3 to produce α-azido alcohols **3**, which exist in equilibrium with the starting materials. At low temperature, the title compounds can be isolated from the mixture by removing volatile starting materials and solvents. At room temperature, however, the equilibrium is fast and there are again specific concentrations of the aldehyde **1**, hydrazoic acid and α-azido alcohol **3**.



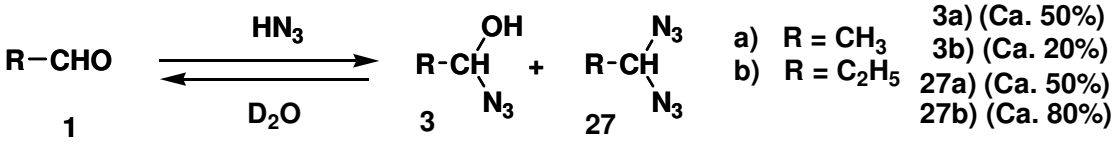
Scheme 8. Synthesis of α-Azido Alcohols from Aldehydes

The reaction of aldehydes **1** with HN_3 creates a new chiral center and a chiral aldehyde, e.g., sugar derivatives, produces two diastereomeric products ***like***, ***unlike*** in case of only two centers of chirality, and mixture of anomers in case of more than two centers of chirality. Presumably, the stereoisomers are formed because of the fast establishment of equilibrium under thermodynamic control.

2.1.1. α-Azido Alcohols from Aliphatic Aldehydes

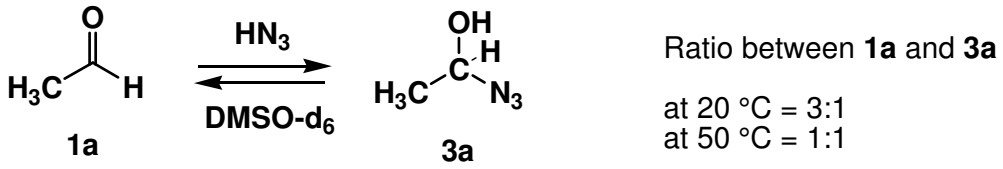
2.1.1.1. Synthesis of α-Azido Alcohols in D_2O

Aliphatic aldehydes (acetaldehyde, propionaldehyde) reacted with HN_3 solution in D_2O by bimolecular addition of HN_3 to the carbonyl group to produce α-azido alcohols **3** and 1,1-diazido alkanes **27**, which exist in equilibrium with the starting materials. It was not possible to isolate pure α-azido alcohol from the equilibrium mixture (Scheme 9).



Scheme 9. Reaction of Aldehydes with HN_3 in D_2O

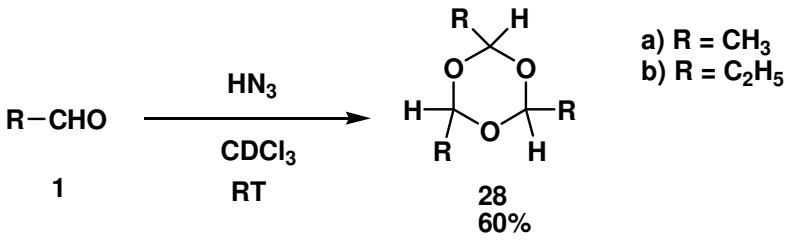
2.1.1.2. Synthesis of α-Azido Alcohols in DMSO-d_6



Scheme 10. Synthesis of α-Azido Alcohols in DMSO-d_6

Acetaldehyde (**1a**) and DMSO-d_6 were mixed with solution of HN_3 in CH_2Cl_2, the excess of HN_3, acetaldehyde (**1a**), and CH_2Cl_2 was distilled off under vacuum at –55 °C to –60 °C to obtain an equilibrium mixture containing α-azidoethanol (**3a**) in DMSO-d_6. The ratio between α-azidoethanol (**3a**) and acetaldehyde (**1a**) is ca. 3:1 at room temperature. It was not possible to calculate the exact amount of α-azidoethanol (**3a**), HN_3 and acetaldehyde in the equilibrium mixture due to presence of H_2O in DMSO-d_6. The equilibrium mixture in DMSO-d_6 has a higher concentration of α-azidoethanol (**3a**) as compared to those in $CDCl_3$ but it was not possible to isolate pure α-azidoethanol (**3a**) from the equilibrium mixture. The equilibrium mixture in DMSO-d_6 was heated to 50 °C and then cooled back to room temperature. The ratio between α-azidoethanol (**3a**) and acetaldehyde (**1a**) is ca. 1:1 at 50 °C. It was observed that the equilibrium mixture has a higher concentration of α-azidoethanol (**3a**) at room temperature and lower concentration at 50 °C due to the equilibrium, as it is shifted backwards at higher temperature. The further work on the measurement of equilibrium constants and their temperature dependence is being done by Dipl.-Chem. C. Berndt within his Ph.D project.

2.1.1.3. Side Reaction during the Synthesis of α-Azido Alcohols



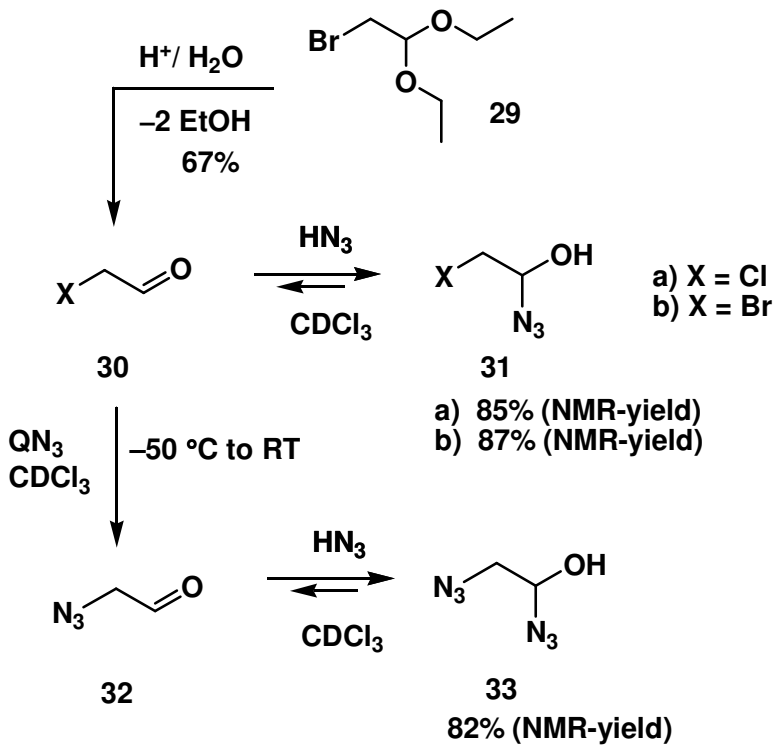
Scheme 11. Side Reaction during the Synthesis of α-Azido Alcohols

It was observed that acetaldehyde (**1a**) and propionaldehyde (**1b**) reacted with equimolar and higher quantity of HN_3 to produce of α-azidoethanol (**3a**) and α-azidopropanol (**3b**). The higher concentration of aldehyde and longer reaction time led to the formation of 2,4,6-trimethyl-1,3,5-trioxane (paraldehyde) (**28a**) and of 2,4,6-triethyl-1,3,5-trioxane (**28b**) which are commercially available compounds.

2.1.2. Reaction of Halogenated Aliphatic Aldehydes with HN_3

2.1.2.1. Reaction of Halogenated Acetaldehydes (30) with HN_3

Chloroacetaldehyde (**30a**) was prepared from 45% aqueous solution of chloroacetaldehyde by treatment with an equal mass of dry $CaCl_2$ followed by distillation ($Kp._{760\ Torr}$: 82 °C). Bromoacetaldehyde (**30b**) was prepared by acidic hydrolysis of bromoacetaldehyde diethyl acetal (**29**) using 0.1N sulfuric acid, according to M. J. McLean et al.'s procedure.[38]



Scheme 12. Reaction of Halogenated Acetaldehyde with HN_3

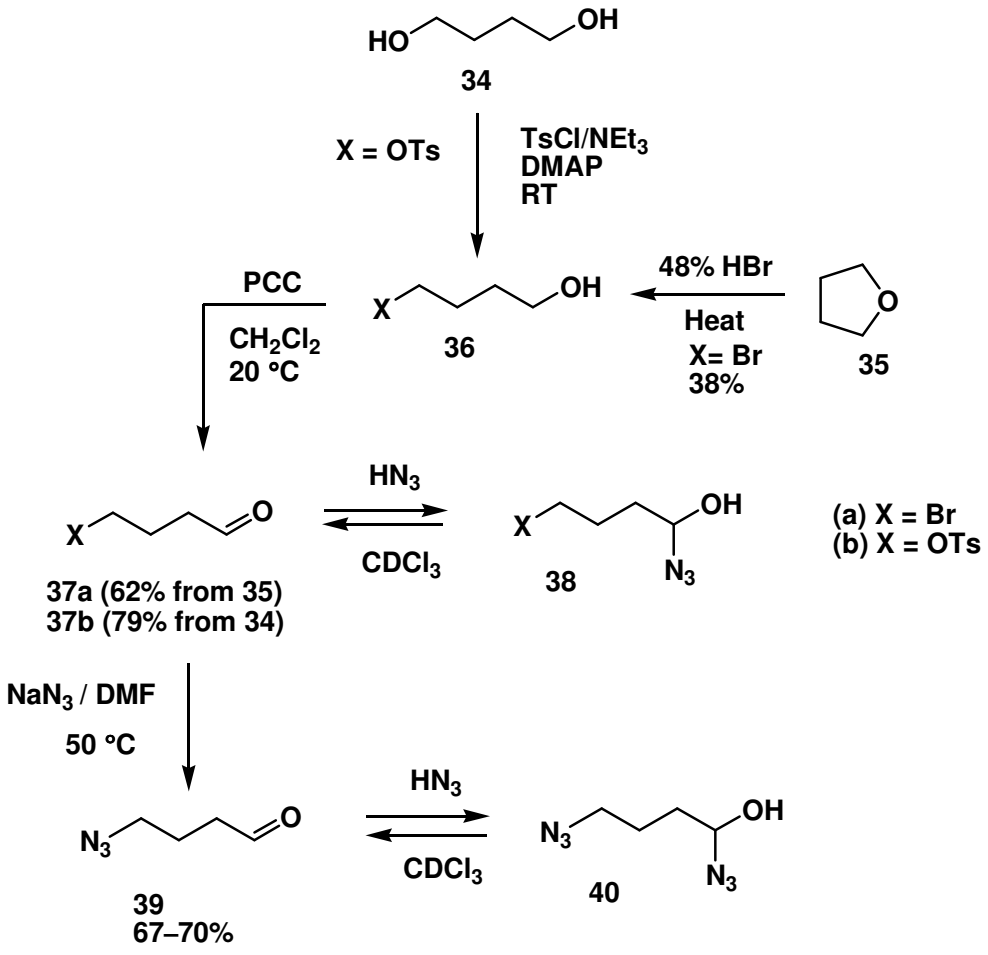
1-Azido-2-chloroethanol (**31a**) and 1-azido-2-bromoethanol (**31b**) were prepared by addition of HN_3 to chloroacetaldehyde (**30a**) and bromoacetaldehyde (**30b**), respectively. Hydrazoic acid is added only to the carbonyl group of chloro/bromoacetaldehyde and nucleophilic substitution of the chloro/bromo substituent at C-2 does not take place, which can be

confirmed by ^{13}C NMR signal for C-2 at δ = 46.8 ppm for **31a** and at δ = 35.9 ppm for **31b** (Scheme 12).

Azidoacetaldehyde (**32**) was prepared by treating chloroacetaldehyde (**30a**) or bromoacetaldehyde (**30b**) with hexadecyltributylphoshphonium azide (QN_3) in $CDCl_3$, followed by re-condensation under vacuum at −50 ˚C to room temperature. Pure azidoacetaldehyde (**32**) decomposes on standing at room temperature. Azidoacetaldehyde (**32**) was reacted with HN_3 to obtain 1,2-diazidoethanol (**33**), and C-2 resulted in a ^{13}C NMR signal with δ = 54.9 ppm.

2.1.2.2. Reaction of 4-Subsituted Butanals (37) with HN_3

4-Bromobutanal (**37a**) was prepared by reaction of THF (**35**) with 48% aq. HBr, followed by oxidation with PCC and further purification by flash chromatography to give 62% yield, utilitizing method described by E. Vedejs et al. in 1979.[39]



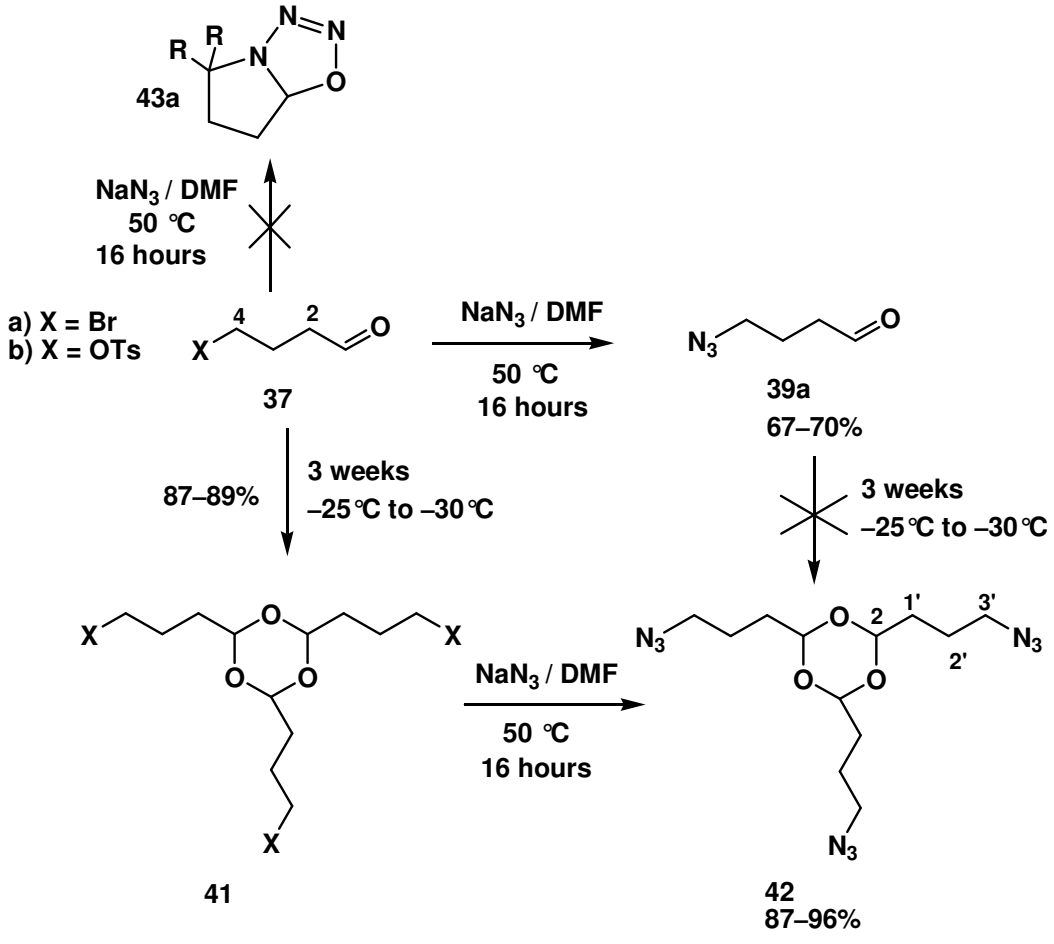
Scheme 13. Reaction of 4-Subsituted Butanals with HN_3

Using chemistry reported by Y. Wu, 4-oxobutyl 4-methylbenzenesulfonate (**37b**) was synthesized by tosylation of butane-1,4-diol (**34**)[40] with $TsCl/NEt_3$ and DMAP, followed by oxidation with PCC in CH_2Cl_2 with 79% yield. 1-Azido-4-bromobutan-1-ol (**38a**) and 4-Azido-4-hydroxybutyl 4-methylbenzenesulfonate (**38b**) were prepared by addition of HN_3 to 4-bromobutanal (**37a**) and 4-oxobutyl 4-methylbenzenesulfonate (**37b**), respectively.

Hydrazoic acid was added only to the carbonyl group of aldehydes and nucleophilic substitution of the substituents at C-4 does not take place, which was characterized by ^{13}C NMR signal for C-4 at δ = 34.5 ppm for **38a** and at δ = 69.4 ppm for **38b**. It was confirmed by comparing with ^{13}C NMR data for C-4 of compound **40** at δ = 50.6 ppm (Scheme 13).

2.1.2.3. Synthesis of Azido Aldehydes from Bromo Aldehydes

Compound **37a** was obtained by utilizing the procedure described in Scheme 13. Compound **37a** is unstable and attempts of distillation at atmospheric pressure led to the trimerization product **41a**.



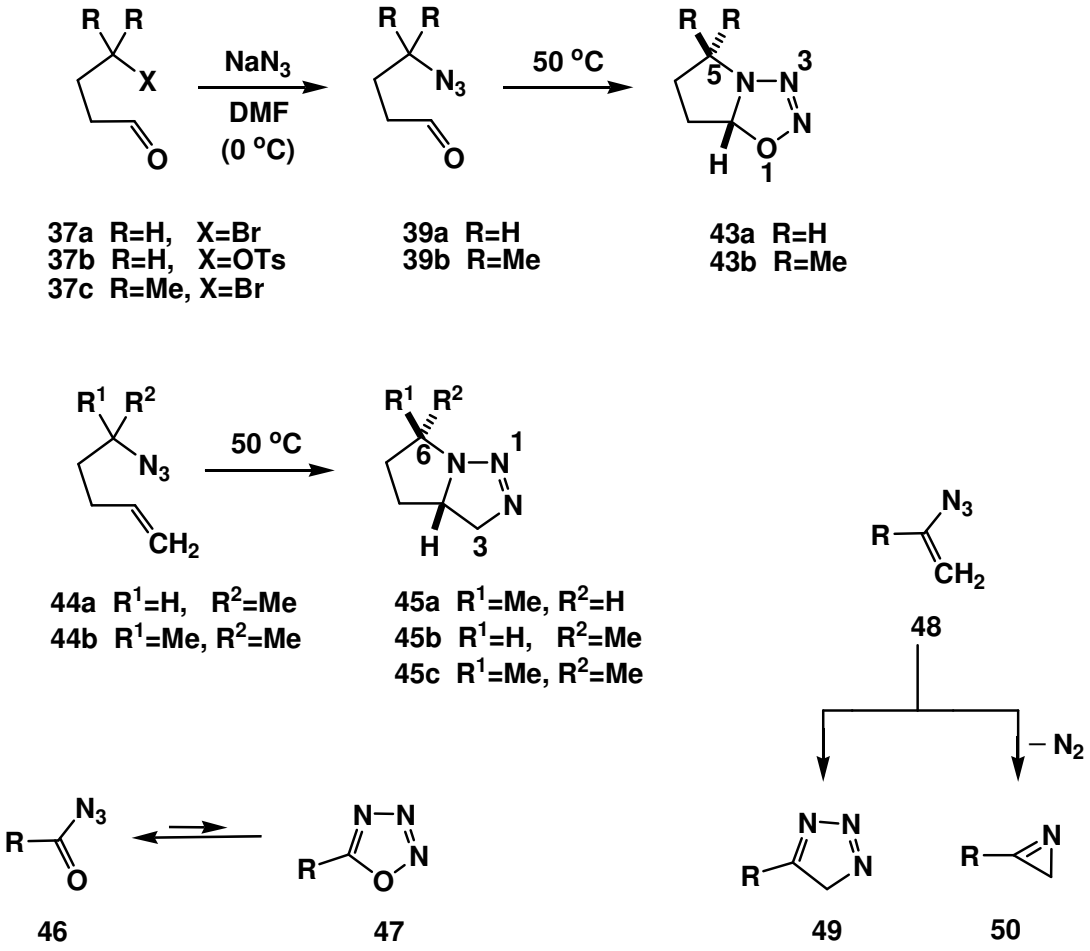
Scheme 14. Reactions of 4-Functionalized Butanals.

In 2002, Yuan Ma reported on the products **43a**,**b** prepared in good yields (85–89%) by treating the precursors **37a**,**b** or **37c**, respectively, with sodium azide in DMF at 50 °C (Scheme 15).[41] The formation of heterocycles **43a**,**b** was explained by a reaction sequence of nucleophilic substitution followed by intramolecular 1,3-dipolar cycloaddition. Thus, it was claimed that the reaction of **37a** with sodium azide at 0 °C led to the intermediate **39a**, which could be converted into **43a** on heating at 50 °C. Since compounds **43a**,**b** represent the first and only examples of 4,5-dihydro-1,2,3,4-oxatriazoles, the results reported by Yuan Ma were cited and reviewed repeatedly.[43] This literature results could not be repeated / confirmed but corrected due to the formation 4-azidobutanal.[49]

4-Azidobutanal (**39a**) was synthesized by treating **37a** or **37b** with sodium azide in DMF at 50 °C (Scheme 14). However, under these conditions and also on heating **39a** with or without sodium azide at 50 °C, no heterocyclic product **43** was formed. The same result was observed after prolonged heating at 80 °C; slow decomposition of **39a** was noticed at 90 °C. The bromide **37a** is known to be unstable. We found that the trimer **41a** was generated on heating of neat **37a**. In a clean reaction, storing **37a** for three weeks at −25 to −30 °C led to **41a** in 87 % yield. The analogous transformation of **37b** gave the heterocyclic product **41b** with 89 % yield. At 50 °C, but not at 0 °C or room temperature, **41a** or **41b** were converted into **42** in the presence of sodium azide in DMF. Each of the 1,3,5-trioxanes **41** or **42** was formed as a single diastereomer, most probably, with all-*cis* configuration, which is quite normal in the case of aldehyde trimerization.[42] The ^{1}H and ^{13}C NMR spectroscopic data, reported for **43** in 2002,[41] are identical with our data of **41a** but differ significantly from those of **42**. Thus, we assume that **41a** was taken erroneously for **43a** and something was perplexed with these compounds.[41]

2.1.2.4. Viability of 4,5-Dihydro-1,2,3,4-Oxatriazoles Reinvestigated

A great proportion of all organic compounds belong to the class of heterocycles, which include fundamental groups of natural products as well as biologically and pharmaceutically active substances. Especially, compounds bearing nitrogen and/or oxygen atoms in five-membered rings are highly important targets and the synthesis of the first examples of such a new heterocyclic system obviously deserves particular interest.



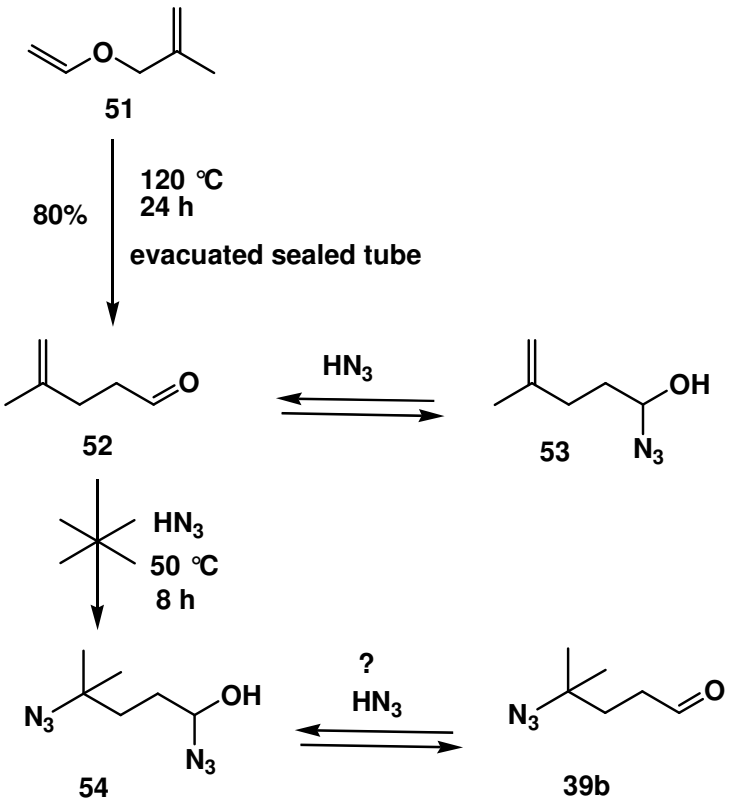
Scheme 15. Intramolecular cycloaddition and cyclization reactions of azides.

The well-known[44] transformation of **44a** and **44b** into **45a**,**b** and **45c**, respectively, seems to be similar to the formation of **43a**,**b** from **39a**,**b**. However, the question arises whether the carbonyl group of an aldehyde and an azido unit are thermodynamically more favorable than a non-aromatic 4,5-dihydro-1,2,3,4-oxatriazole including a weak O–N single bond. If azido and carbonyl group result in an aromatic conjugated system as shown in the case of acyl azides **46**, it is well-documented that open-chain **46** is thermodynamically more stable than aromatic 1,2,3,4-oxatriazole **47**.[43a,45] On the other hand, the ring closure of vinyl azides **48** to give 4*H*-1,2,3-triazoles **49**, which can tautomerize to produce aromatic 1,2,3-triazoles, may be an exothermic process. Nevertheless, the transformation **48** → **49** is rarely observed,[46,47a] because loss of dinitrogen and formation of 2*H*-azirines **50** proved to be a more general reaction of **48**.[47,48]

When we compared the NMR data given for **43a**,**b** by Yuan Ma[41] with those of **45a**–**c**,[44] we had to call in question the substructures of 4,5-dihydro-1,2,3,4-oxatriazoles. Whereas H-6 of **45a** resulted in a ^{1}H NMR signal at δ = 4.34 ppm,[44b] H-5 of **43a** was claimed to resonate at δ = 3.44 ppm.[41] However, even greater contradictions were found in the case of ^{13}C NMR data: C-6 of **45a** and **45b** showed signals in the range δ = 57–60 ppm, and the corresponding signal of **45c** was found at δ = 64.9 ppm,[44b] while only signals in the interval δ = 26–34 ppm could be assigned to C-5 of **43a**,**b** based on the data of Yuan Ma.[41] Furthermore, the folded structure of **45** led to CH_2 groups with diastereotopic protons (^{2}J = 16.5 Hz) and to diastereotopic methyl groups in the case of **45c**.[44b] This should also be true for **43a**,**b**. But no hints on diastereotopic protons or methyl groups were given, and **43b** was characterized by five instead of six ^{13}C NMR signals.[41] The NMR spectroscopic data of such heterocycles reported previously do not agree with those of similar substances and are incompatible with ^{13}C NMR spectroscopic chemical shifts calculated by quantum chemical methods, in collaboration with Prof. Dr. A. A. Auer, Max-Planck-Institut für Eisenforschung GmbH. These calculations show furthermore that the intramolecular cycloaddition of 4-azidobutanals to give the title compounds **43** is strongly endothermic and thus most probably not possible.[49]

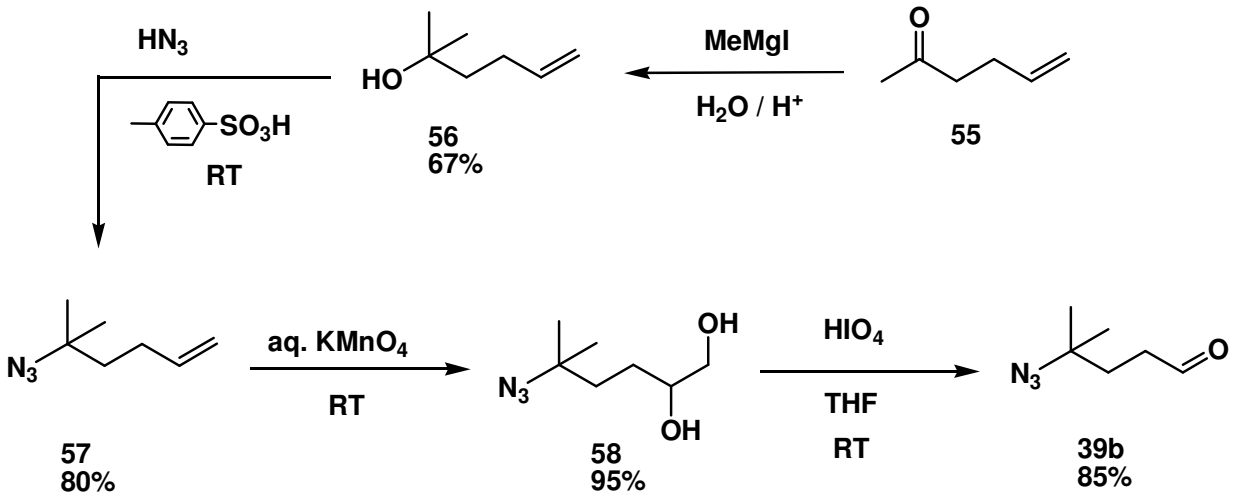
2.1.2.5. Synthesis of 4-Azido-4-methylpentanal (39b)

4-Methylpent-4-enal (**52**) was prepared by heating 2-methylprop-2-enyl vinyl ether (**51**) in an evacuated sealed tube at 120 °C for 24 h, and was purified by flash chromatography using CH_2Cl_2 as eluent with 80% yield, utilizing a known method by R. Baker et al.[50]



Scheme 16. Attempted Synthesis of 4-Azido-4-methylpentanal (39b)

4-Methylpent-4-enal (**52**) was treated with 2M HN_3 solution in $CDCl_3$ and the mixture was stirred at room temperature to obtain an equilibrium mixture containing only 1-azido-4-methylpent-4-en-1-ol (**53**). The equilibrium mixture was heated in an NMR tube at 50 °C for 8 hours. Hydrazoic acid was only added to the carbonyl group of the aldehyde and addition of HN_3 to the C,C double bond did not take place (Scheme 16).



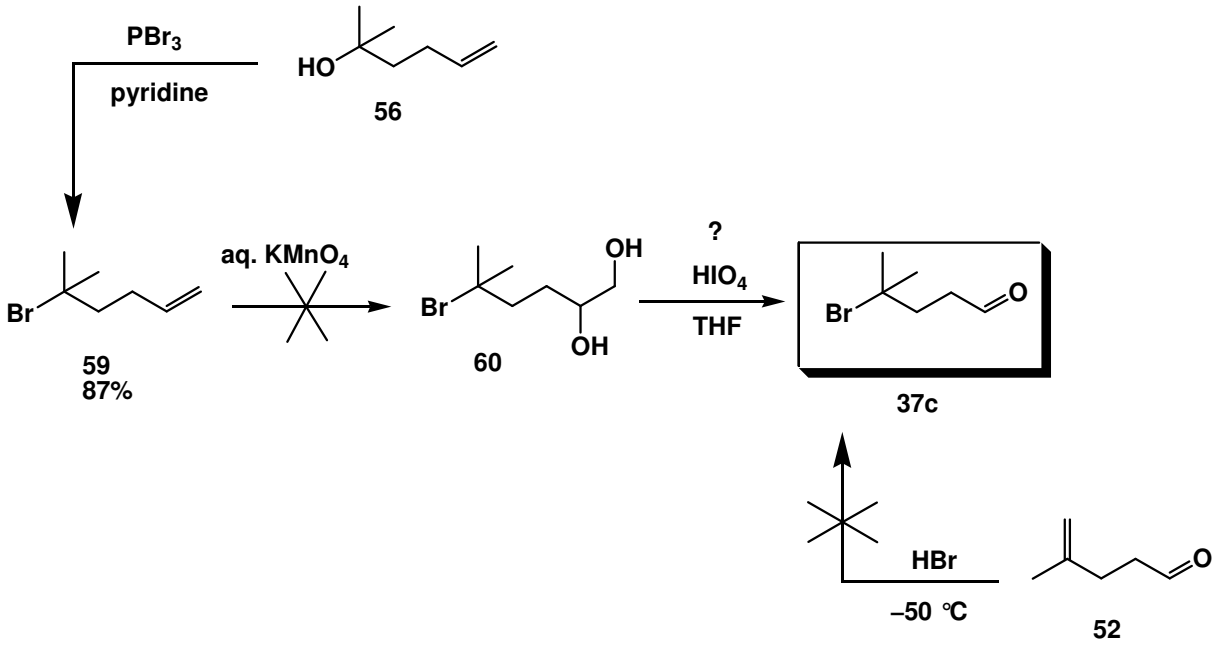
Scheme 17. Synthesis of 4-Azido-4-methylpentanal

A. L. Logothetis synthesized 5-azido-5-methylhex-1-ene (**57**) by reaction of 2-methylhex-5-en-2-ol (**56**) with HN_3 in the presence of H_2SO_4 and $CHCl_3$ as solvent at −5 °C to 0 °C with 41−46% yield.[44a] The above method was modified now to obtain **57** with 80% yield.

Finally, 4-azido-4-methylpentanal (**39b**) was successfully prepared with 81% yield in a two step reaction: by permanganate dihydroxylation of 5-azido-5-methylhex-1-ene (**57**) at 0 °C to give 5-azido-5-methylhexane-1,2-diol (**58**), followed by oxidative cleavage of **58** using periodic acid in THF to give **39b** as described in Scheme 17.

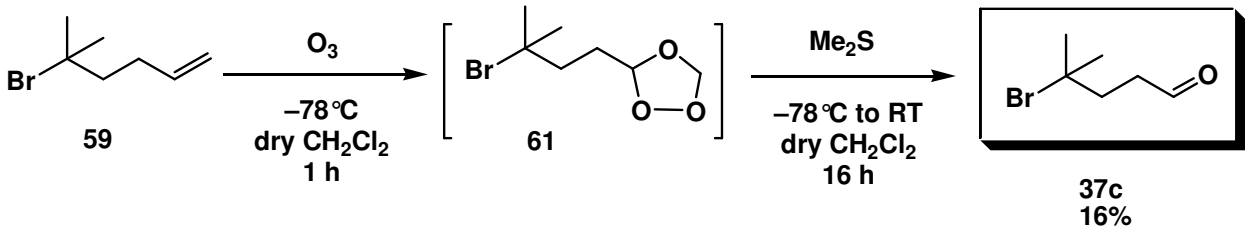
2.1.2.6. Synthesis of 4-Bromo-4-methylpentanal (37c)

Attempts were made to synthesize 4-bromo-4-methylpentanal (**37c**) by the reaction of 4-methylpent-4-enal (**52**) with hydrogen bromide (HBr_g) in $CDCl_3$ at −50 °C or with hydrobromic acid at 0 °C. Unfortunately, the product **37c** could not be obtained, which was probably highly unstable and decomposed at room temperature as well as at −50 °C to produce mixture of decomposition products in the presence of HBr.



Scheme 18. Attempted Synthesis of 4-Bromo-4-methylpentanal (37c)

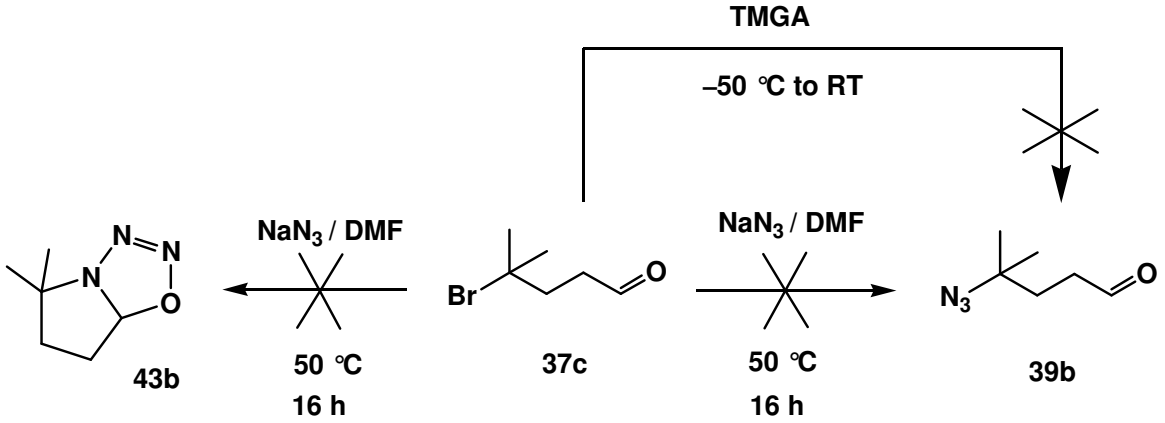
A second trial to synthesize **37c** was performed by the reaction of 5-bromo-5-methylhex-1-ene (**59**) with aq. $KMnO_4$ solution, followed by reaction with periodic acid to obtain 4-bromo-4-methylpentanal (**37c**). This also failed possibly due to sensitivity of **59** or **60** to water which led to the formation of a mixture of decomposition products (Scheme 18).



Scheme 19. Successful Synthesis of 4-Bromo-4-methylpentanal (37c)

Finally, 4-bromo-4-methylpentanal (**37c**) was successfully prepared with 16% yield by reaction of 5-bromo-5-methylhex-1-ene (**59**) with ozone at −78 °C followed by workup with dimethyl sulfide, and was further purified by flash chromatography on silica gel, eluting with CH_2Cl_2 (Scheme 19).

2.1.2.7. Reaction of 4-Bromo-4-methylpentanal (37c) with NaN_3 in DMF

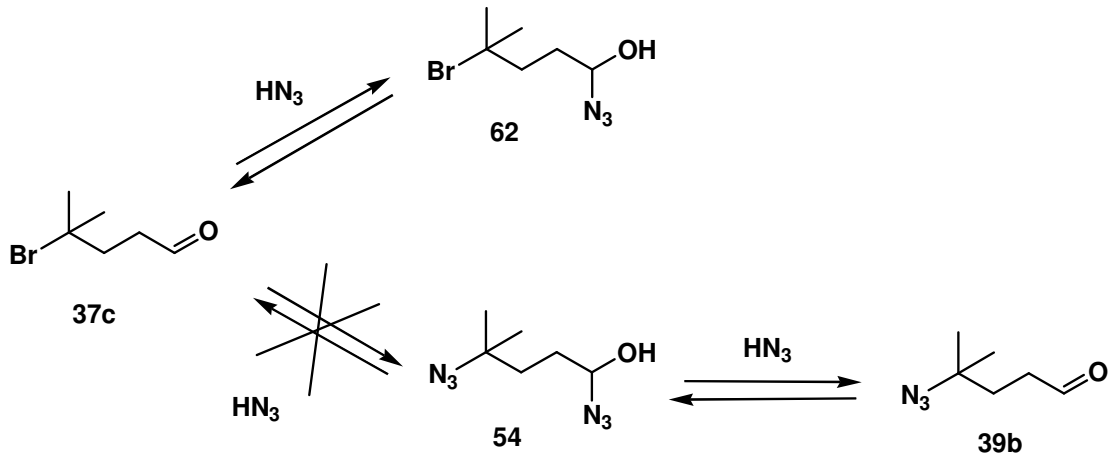


Scheme 20. Attempted Synthesis of 4-Azido-4-methylpentanal (39b) from 4-Bromo-4-methylpentanal (37c)

4-Bromo-4-methylpentanal (**37c**) was heated at 50 °C in DMF-d_7 with NaN_3 or reacted with TMGA at –50 °C to RT, but no substitution product **39b** and no nontrivial product **43b** was observed in both cases, rather 4-bromo-4-methylpentanal (**37c**) decomposed to produce undefined decomposition products (Scheme 20).

2.1.2.8. Reaction of 4-Bromo-4-methylpentanal (37c) with HN_3

1-Azido-4-bromo-4-methylpentan-1-ol (**62**) was prepared by addition of HN_3 to 4-bromo-4-methylpentanal (**37c**). 1,4-Diazido-4-methylpentan-1-ol (**54**) was not observed.



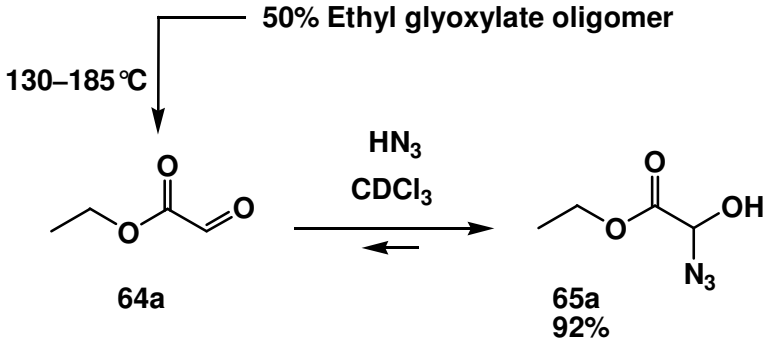
Scheme 21. Reaction of 4-Bromo-4-methylpentanal (37c) with HN_3

Hydrazoic acid was only added to the carbonyl group of aldehyde and nucleophilic substitution of the bromo substituent at C-4 did not take place, which was confirmed by ^{13}C NMR signal for C-4 at δ = 66.5 ppm for **62** and at δ = 61.2 ppm for **54**. Compound **54** was prepared for comparison from **39b** and HN_3 (Scheme 21).

2.1.3. α-Azido Alcohols from Electron-Deficient Aldehydes

2.1.3.1. Reaction of Ethyl Glyoxalate (64a) with HN_3

50% Ethyl glyoxylate oligomer in toluene was distilled at atmospheric pressure at 130−185 °C. After toluene was fractionated, pure ethyl glyoxylate (**64a**) was distilled at 48 °C and 30 Torr. The freshly prepared compound was directly used because ethyl glyoxylate (**64a**) oligomerizes readily on standing at room temperature as well as in freezer (−25 to −30 °C).



Scheme 22. Reaction of Ethyl Glyoxalate (64a) with HN_3

Ethyl glyoxalate (**64a**) was reacted with HN_3 at room temperature to produce the corresponding α-azido alcohol [ethyl 2-azido-2-hydroxyacetate (**65a**)] with higher yield as compared to other aliphatic aldehydes, as equilibrium was shifted to the addition product (Scheme 22). The excess of solvent and HN_3 were distilled off at −40 °C under vacuum to obtain ethyl 2-azido-2-hydroxyacetate (**65a**) as a colorless liquid. It was not possible to recondense **65a** and to remove starting materials completely (Figure 1).

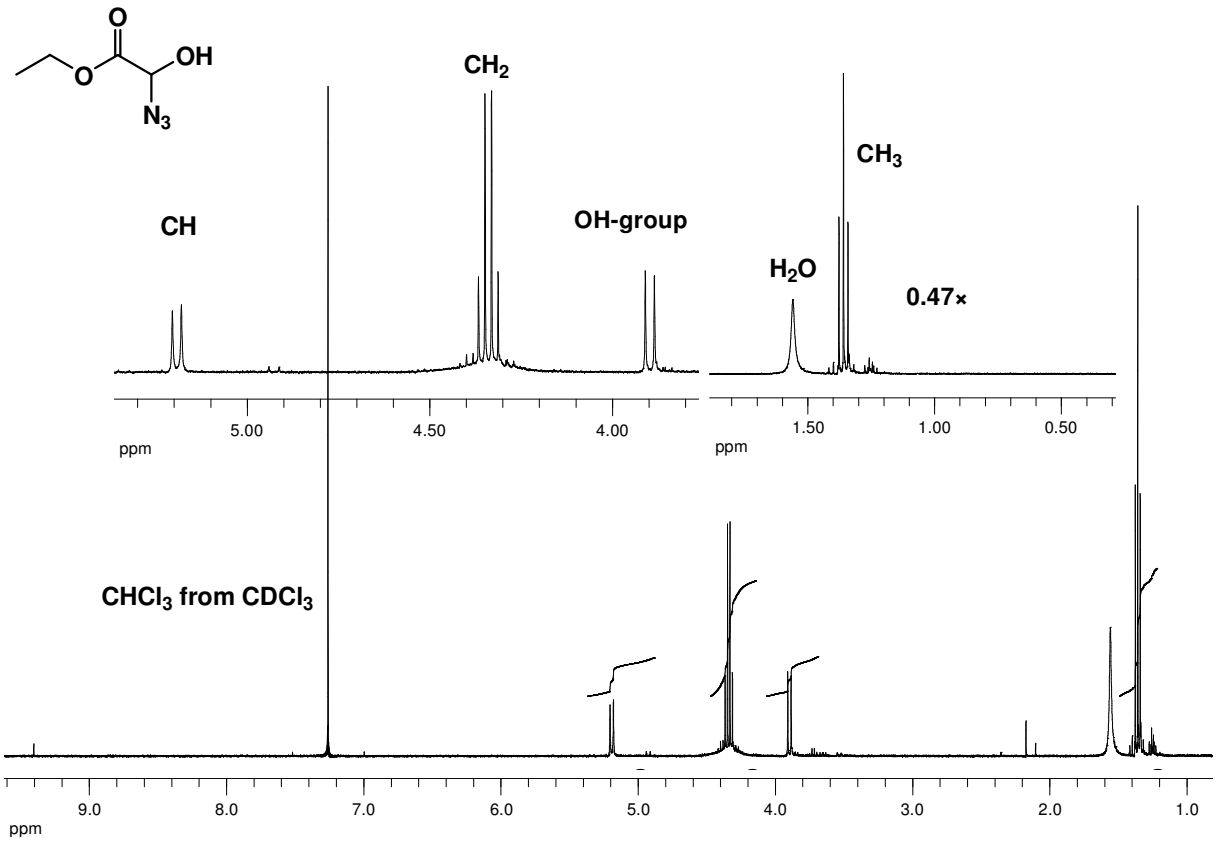
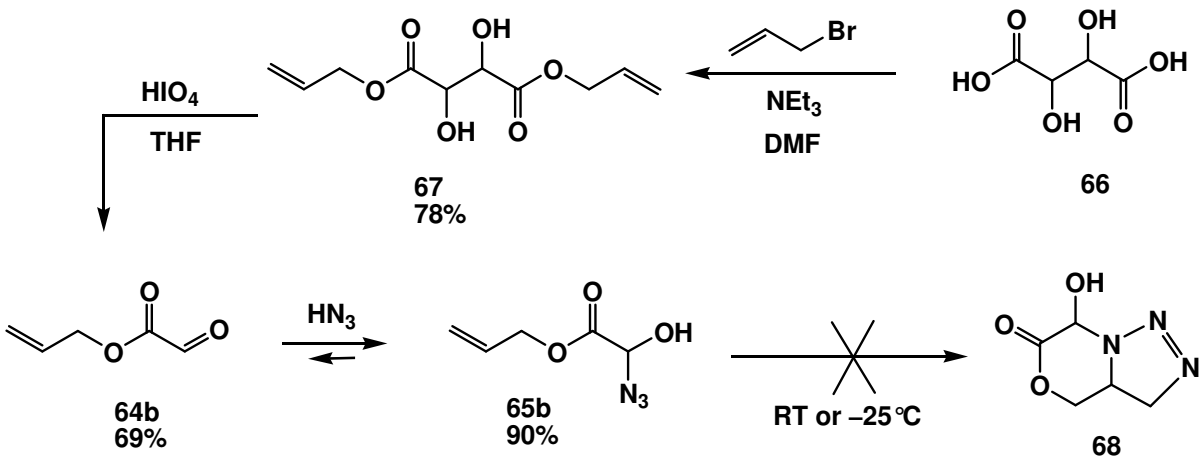


Figure 1. ^{1}H NMR Spectrum of Pure Ethyl 2-Azido-2-hydroxyacetate (**65a**) in $CDCl_3$ at Room Temperature.

2.1.3.2. Synthesis of Allyl 2-Azido-2-hydroxyacetate (65b)

Utilizing, a known procedure by R. N. Guthikonda et al., allyl 2-oxoacetate (**64b**) was prepared as a yellow liquid with 69% yield over two step reaction, and was used without any further purification.[51]

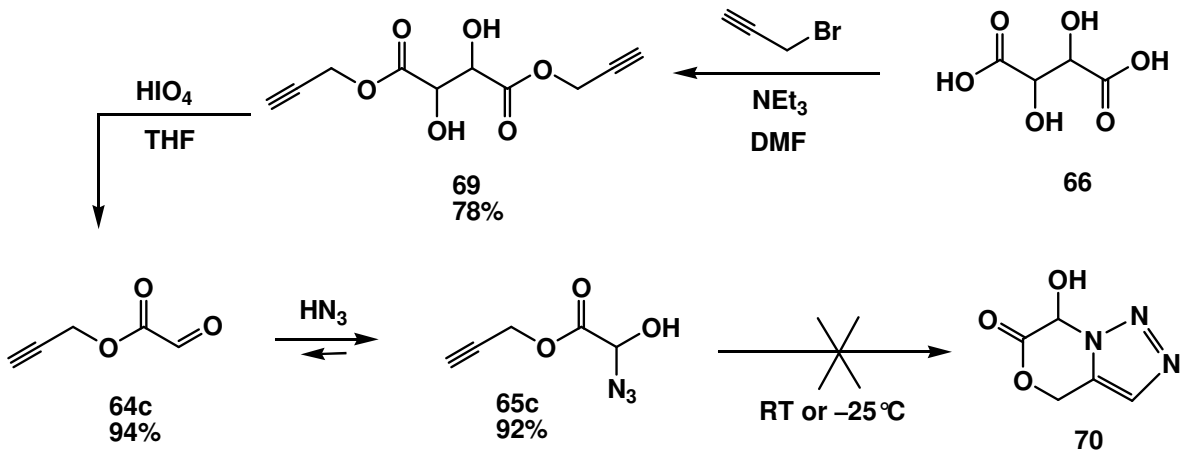


Scheme 23. Synthesis of Allyl 2-Azido-2-hydroxyacetate (65b)

Allyl 2-oxoacetate (**64b**) reacted with 2M HN_3 solution in $CDCl_3$ to obtain allyl 2-azido-2-hydroxyacetate (**65b**) as a light yellow liquid. It was not possible to recondense **65b** and to remove starting materials completely. So, it was proposed that allyl 2-azido-2-hydroxyacetate (**65b**) could undergo intramolecular 1,3-dipolar cycloaddition to produce 7-hydroxy-3a,4-dihydro-3*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazin-6(7*H*)-one (**68**), but product **68** was not observed after 4 weeks at room temperature as well as after one month at −25 °C (Scheme 23).

2.1.3.3. Synthesis of Prop-2-ynyl 2-Azido-2-hydroxyacetate (65c)

The known procedure, for the preparation of allyl 2-oxoacetate (**64b**) was repeated with minor amendments to prepare prop-2-ynyl 2-oxoacetate (**64c**) with 93% yield in a three step reaction. Purification was performed by flash chromatography.[51]

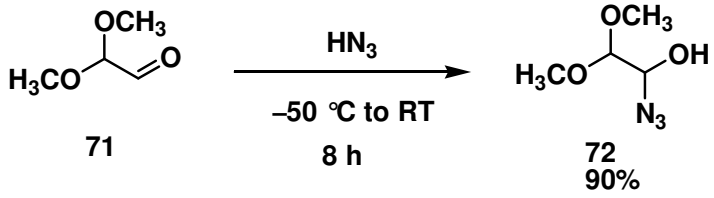


Scheme 24. Synthesis of Prop-2-ynyl 2-Azido-2-hydroxyacetate (65c)

Prop-2-ynyl 2-oxoacetate (**64c**) was reacted with 2M HN_3 solution in $CDCl_3$, followed by removal of solvent and HN_3 at −40 °C under vacuum to obtain prop-2-ynyl 2-azido-2-hydroxyacetate (**65c**) as a light yellow liquid. It was not possible to recondense **65c** and to remove starting materials completely. In the current work it was anticipated that prop-2-ynyl 2-azido-2-hydroxyacetate (**65c**) can undergo intramolecular 1,3-dipolar cycloaddition to produce 7-hydroxy-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazin-6(7*H*)-one (**70**), but the product **70** was not detected at −25 °C as well as at room temperature after 10 weeks (Scheme 24).

2.1.3.4. Reaction of 2,2-Dimethoxyacetaldehyde (71) with HN_3

2,2-Dimethoxyacetaldehyde (**71**) is commercially available as aqueous solution which was dried using an equal mass of dry $CaCl_2$ followed by distillation prior to use.

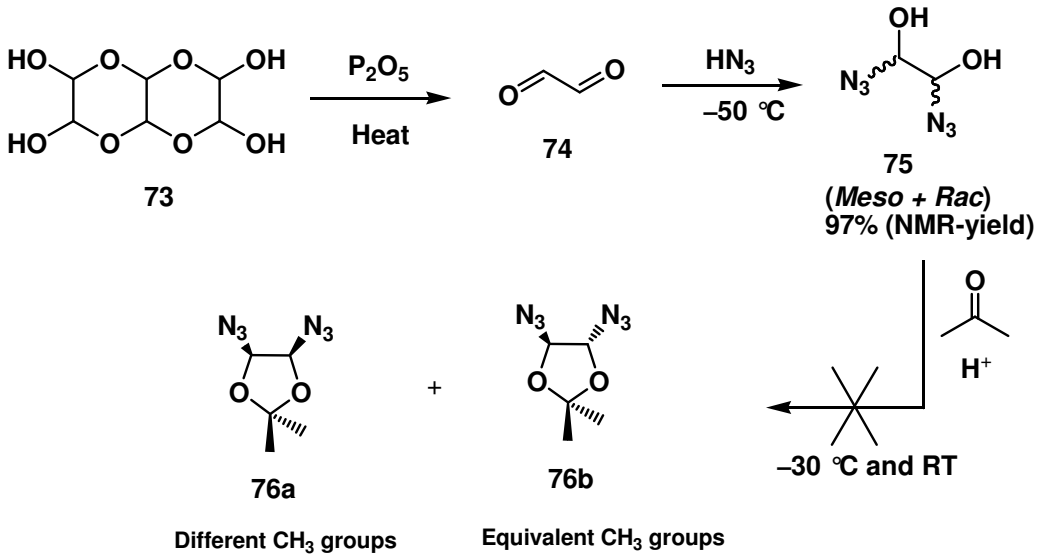


Scheme 25. Synthesis of 1-Azido-2,2-Dimethoxyethanol (72)

2,2-Dimethoxyacetaldehyde is an electron deficient aldehyde due to presence of two methoxy groups at C-2 which are electron withdrawing through inductive effect, hence carbonyl carbon is particularly electron deficient. 2,2-Dimethoxyacetaldehyde (**71**) was reacted with 2M HN_3 solution in $CDCl_3$ to obtain 1-azido-2,2-dimethoxyethanol (**72**) with 90% yield.

2.1.3.5. Reaction of Oxalaldehyde (74) with HN_3

Following a known procedure by C. Harries et al., oxalaldehyde gas (**74**) was produced and a dilute solution in $CDCl_3$ was obtained which polymerizes on standing at room temperature.[52]



Scheme 26. Reaction of Oxalaldehyde (74) with HN_3

Oxalaldehyde (**74**) reacts with HN_3 solution to give a mixture of *meso*- and *racem*-1,2-diazidoethane-1,2-diol (**75**), which can be identified by two signals in ^{13}C NMR spectrum. Reaction of 1,2-diazidoethane-1,2-diol (**75**) with acetone was not successful and 4,5-diazido-2,2-dimethyl-1,3-dioxolane (**76**) could neither be obtained at room temperature nor at –30 °C after several days (Scheme 26).

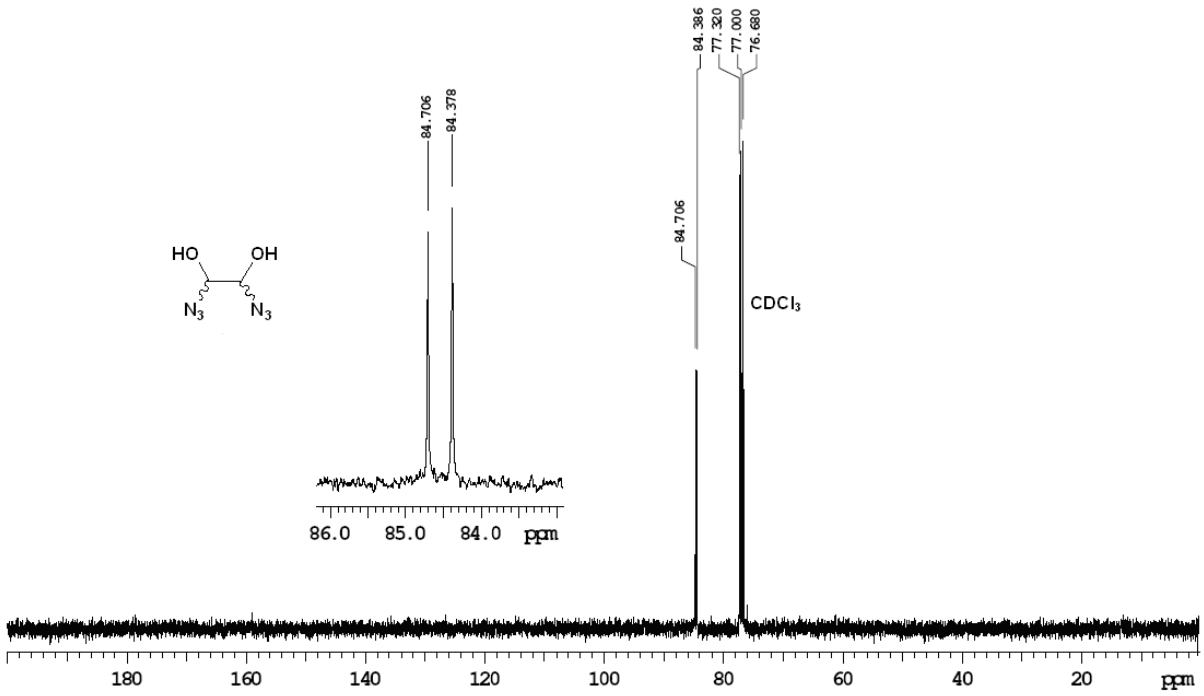
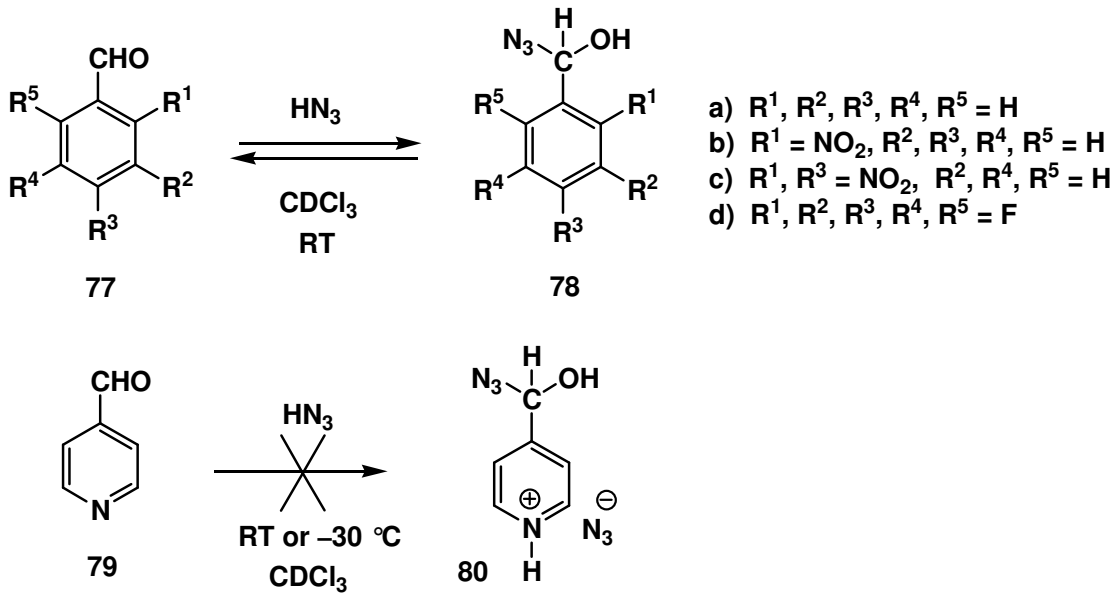


Figure 2. ^{13}C NMR Spectrum of Pure 1,2-Diazidoethane-1,2-Diol (**75**) in $CDCl_3$ at Room Temperature.

2.1.4. α-Azido Alcohols from Aromatic Aldehydes



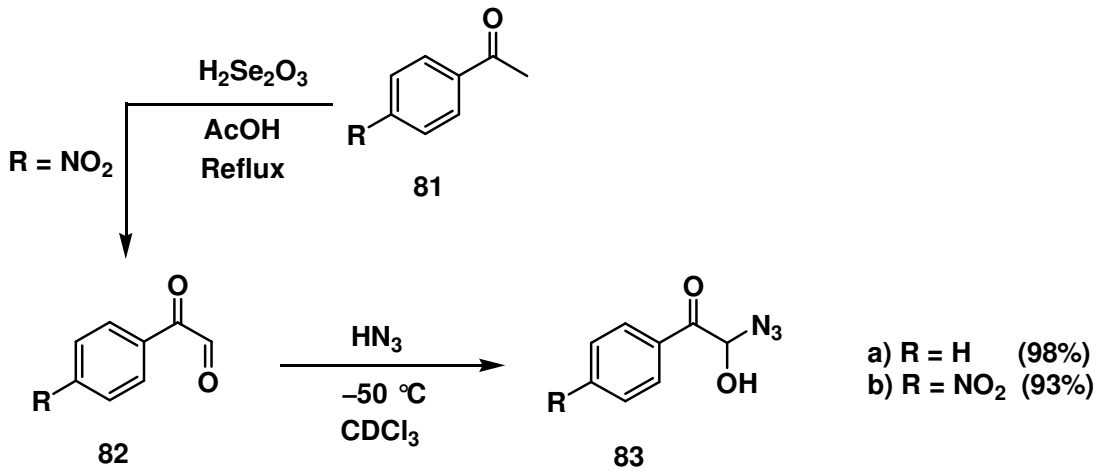
Scheme 27. α-Azido Alcohols from Aromatic Aldehydes

Aromatic aldehydes, e.g. benzaldehyde, did not noticeably react with 2M HN_3 solution but higher concentrations as 8–10M give α-azido alcohols.[36] Electron-deficient aromatic aldehydes like 2-nitrobenzaldehyde (**77b**) and 2,4-dinitrobenzaldehyde (**77c**) react with HN_3 to give α-azido alcohols [azido(2-nitrophenyl)methanol (**78b**), azido(2,4-dinitrophenyl)methanol (**78c**)] in a relatively higher proportion, which is probably stabilized due to the formation of intramolecular H-bondings between nitro and hydroxyl group of the α-azido alcohol. 2,3,4,5,6-Pentafluorobenzaldehyde (**77d**) reacted with HN_3 to give azido(perfluorophenyl)methanol (**78d**). Isonicotinaldehyde (**79**) did not react with HN_3 at –30 °C as well as at room temperature (Scheme 27).

2.1.5. Reaction of 2-Oxo-2-phenylacetaldehyde Derivatives (82) with HN_3

2-Oxo-2-phenylacetaldehyde (**82a**)[53] reacts with HN_3 to produce 2-azido-2-hydroxy-1-phenylethanone (**83a**) with a high yield of 98%. Presumably, equilibrium is shifted forward to α-azido alcohol due to the electron withdrawing group attached to the aldehydic group. 2-Azido-2-hydroxy-1-phenylethanone (**83a**) was recrystallized with chloroform/*n*-pentane to give light yellow crystals. The X-ray crystal structure measurement was not successful as the crystals were not stable enough at room temperature and decompose to produce aldehyde and HN_3.

Utilizing the chemistry reported by L. Steinbach et al.,[54] 2-(4-Nitroophenyl)-2-oxoacetaldehyde (**82b**) was prepared and reacted with 5M HN_3 solution in $CDCl_3$ to obtain 2-azido-1-(4-nitrophenyl)-2-hydroxyethanone (**83b**) as yellow oily liquid with 93% yield (Scheme 28).



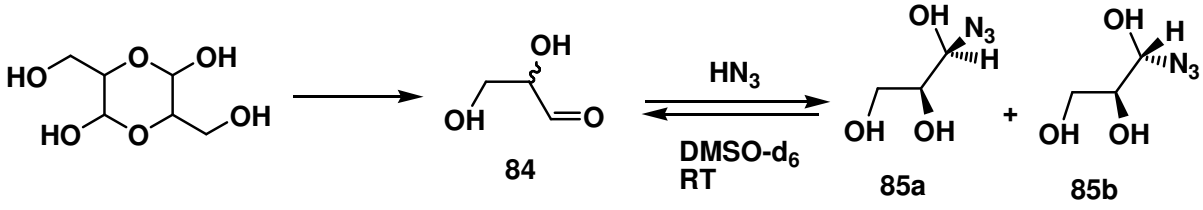
Scheme 28. Reaction of 2-Oxo-2-phenylacetaldehyde Derivatives (82) with HN_3

2.1.6. α-Azido Alcohols from Sugar Derivatives

The reaction of aldehydes with HN_3 creates a new chiral center. The chiral aldehydes, e.g. sugar derivatives, produce two diastereomeric products ***like*** and ***unlike*** in case of two centers of chirality and a mixture of anomers for more than two centers of chirality. It can be shown that the stereoisomers are formed because of the fast establishment of equilibrium which is under thermodynamic control.

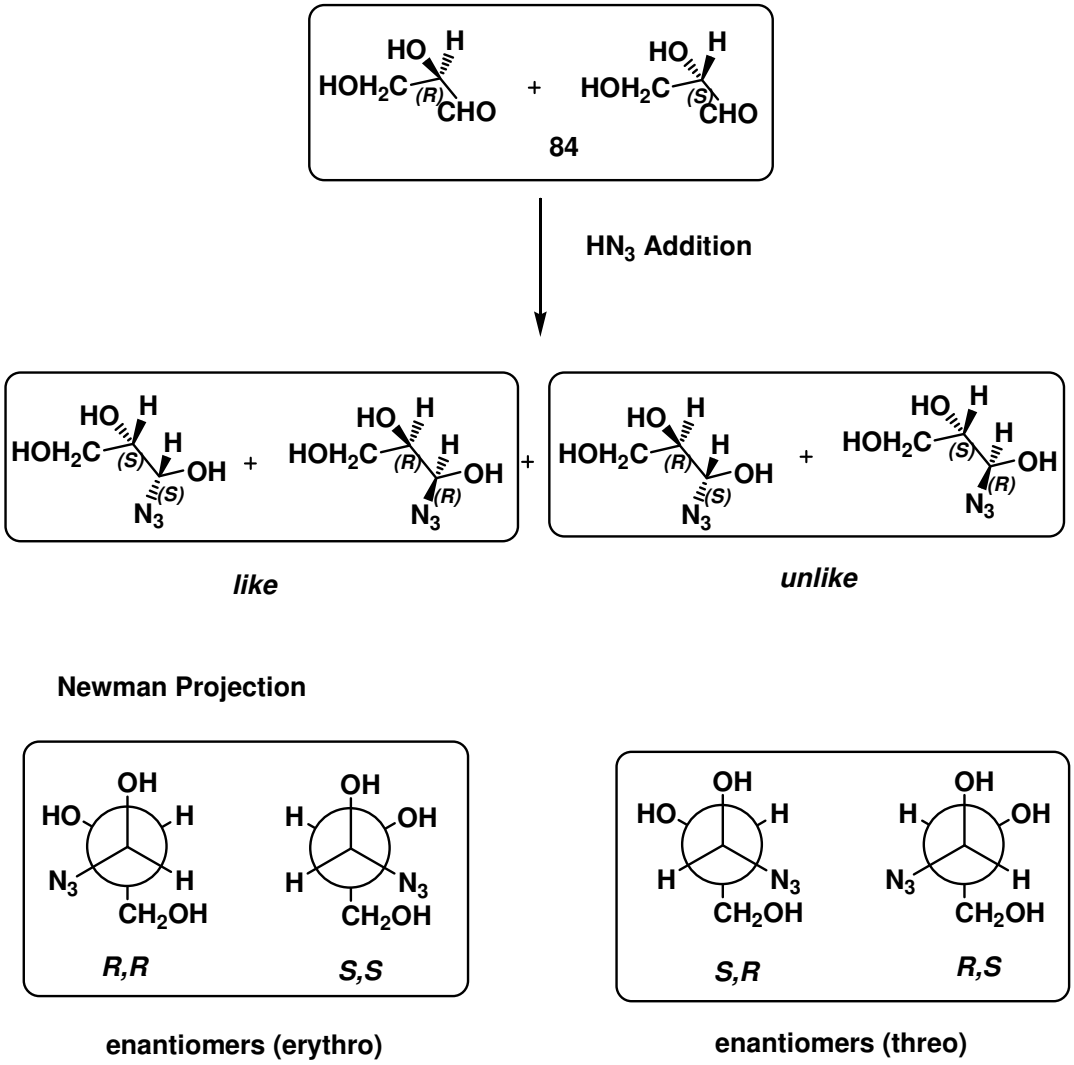
2.1.6.1. Reaction of *dl*-Glyceraldehyde (84) with HN_3

dl-Glyceraldehyde (**84**) (from *dl*-glyceraldehyde dimer) was reacted with HN_3 to produce two diastereomeric products (1*R*,2*S*)-1-azidopropane-1,2,3-triol (**85a**) and (1*S*,2*S*)-1-azidopropane-1,2,3-triol (**85b**) as well as the corresponding enantiomers (Scheme 29a).



Scheme 29a. Reaction of *dl*-Glyceraldehyde with HN_3

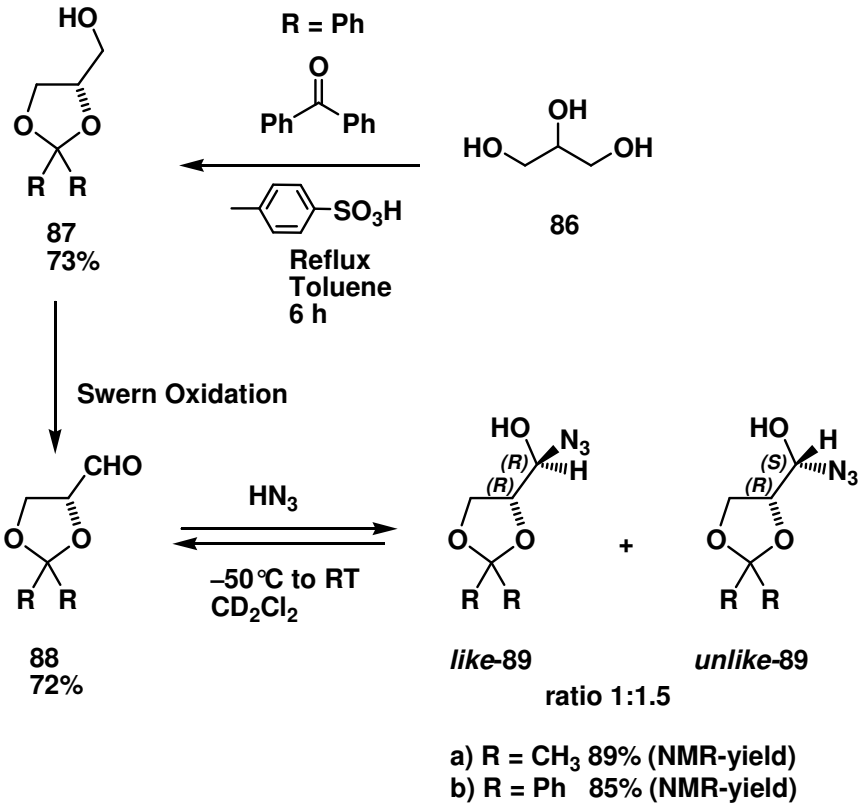
dl-Glyceraldehyde (**84**) (racemic mixture) reacted with HN_3 to produce four possible isomers (two like product and two unlike products) and two diastereomeric pairs of enantiomers. Due to the isochronic chemical shifts of the enantiomers, the ^{13}C NMR spectrum showed only two sets of signals of the diastereomeric products, and a complicated ^{1}H NMR spectrum (Scheme 29b).



Scheme 29b. Stereochemistry of 1-Azidopropane-1,2,3-triol (85)

2.1.6.2. Reaction of (*R*)-2,2-Dimethyl and 2,2-Diphenyl-1,3-dioxolane-4-carbaldehyde (88) with HN_3

(*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (**88a**) reacted with HN_3 to produce (*R*)-azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (***like*-89a**) and (*S*)-azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (***unlike*-89a**) (Scheme 30). The ^{13}C NMR spectrum showed two sets of signals, and a complicated ^{1}H NMR spectrum indicated the formation of two diastereomeric products (Figure 3).



Scheme 30. Reaction of (*R*)-2,2-Dimethyl and 2,2-Diphenyl-1,3-dioxolane-4-carbaldehyde (88) with HN_3

2,2-Diphenyl-1,3-dioxolane-4-carbaldehyde (**88b**) was obtained by following a known method by M. Sax et al.[55] This compound reacted with HN_3 to produce two diastereomeric products ***like*-89b** and ***unlike*-89b** (Scheme 30). The ^{13}C NMR spectrum also showed two sets of signals, and a complicated ^{1}H NMR spectrum.

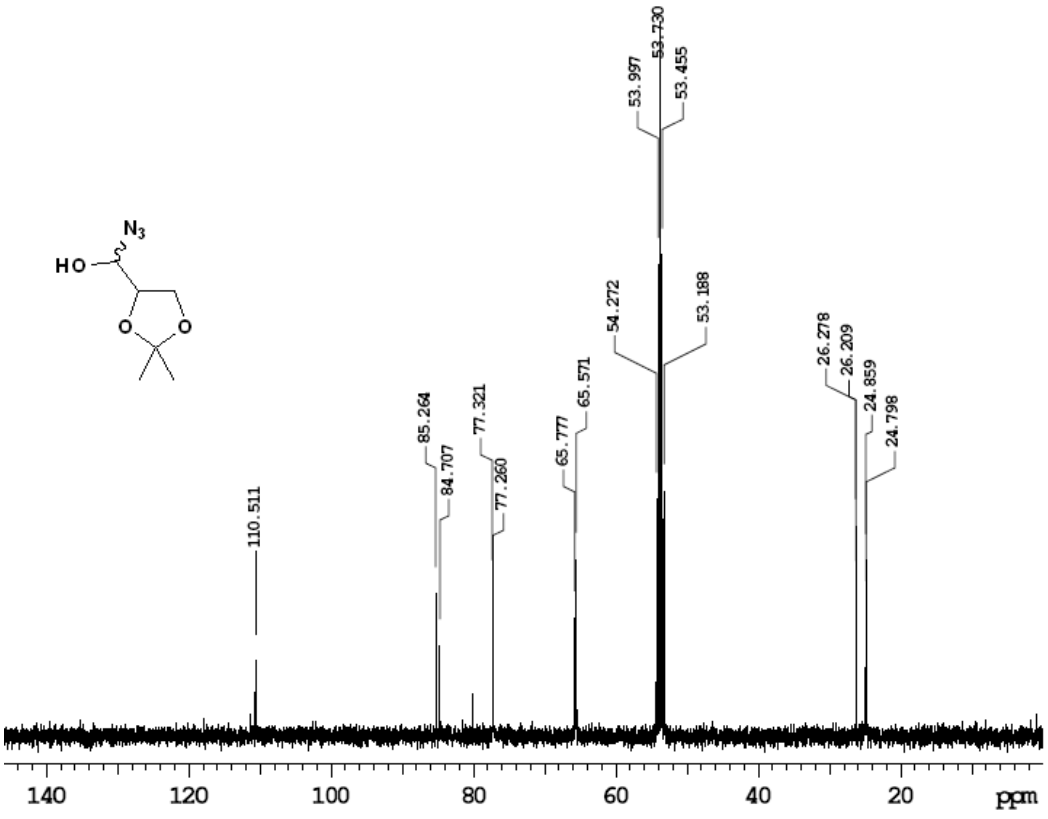
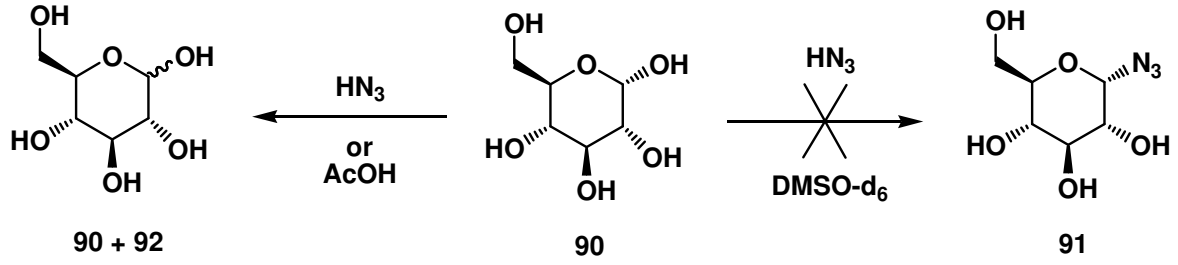


Figure 3. ^{13}C NMR Spectrum of (*R*)-Azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (*like*-**89a**) and (*S*)-Azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (*unlike*-**89a**)

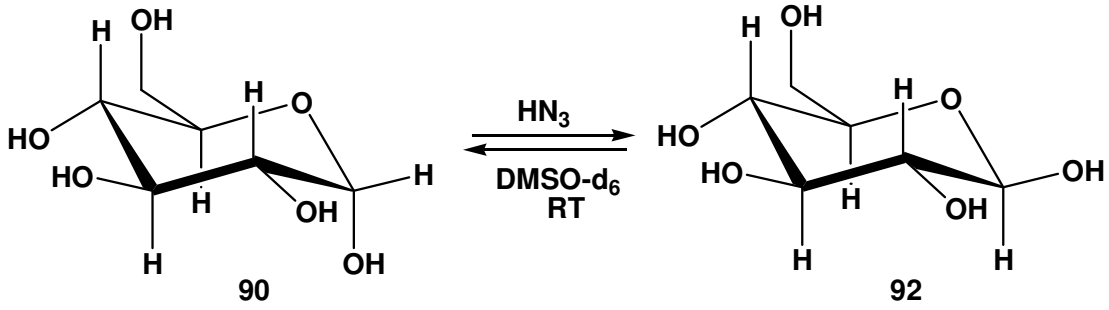
2.1.6.3. Reaction of α-D-Glucose (90) with HN_3



Scheme 31a. Reaction of α-D-Glucose (90) with HN_3

The reaction of aldehydes with HN_3 emerges a new chiral center to produce mixture of two anomers. We proposed that glucose may also react with HN_3 to produce (2*S*,3*R*,4*S*,5*S*,6*R*)-2-azido-6-(hydroxymethyl)-tetrahydro-2H-pyran-3,4,5-triol (**91**)[56] but only α and β anomeric forms of glucose were observed in the presence of HN_3 due to mutarotation which was further

confirmed by reaction of glucose with CH_3COOH in DMSO-d_6 by ^1H NMR experiment (Scheme 31a). Mutarotation was discovered by Dubrunfaut in 1846, when he noticed that the specific rotation of aqueous sugar solution changes with time (Scheme 31b).[57]

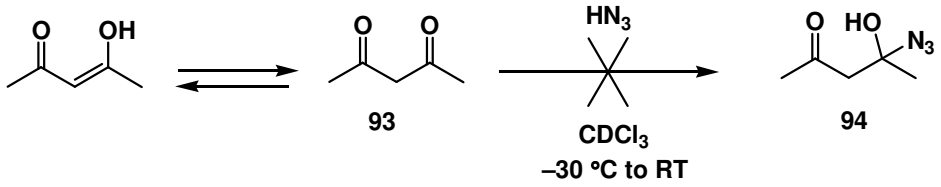


Scheme 31b

2.2. α-Azido Alcohols from Ketones

2.2.1. Reaction of Pentane-2,4-dione (93) with HN_3

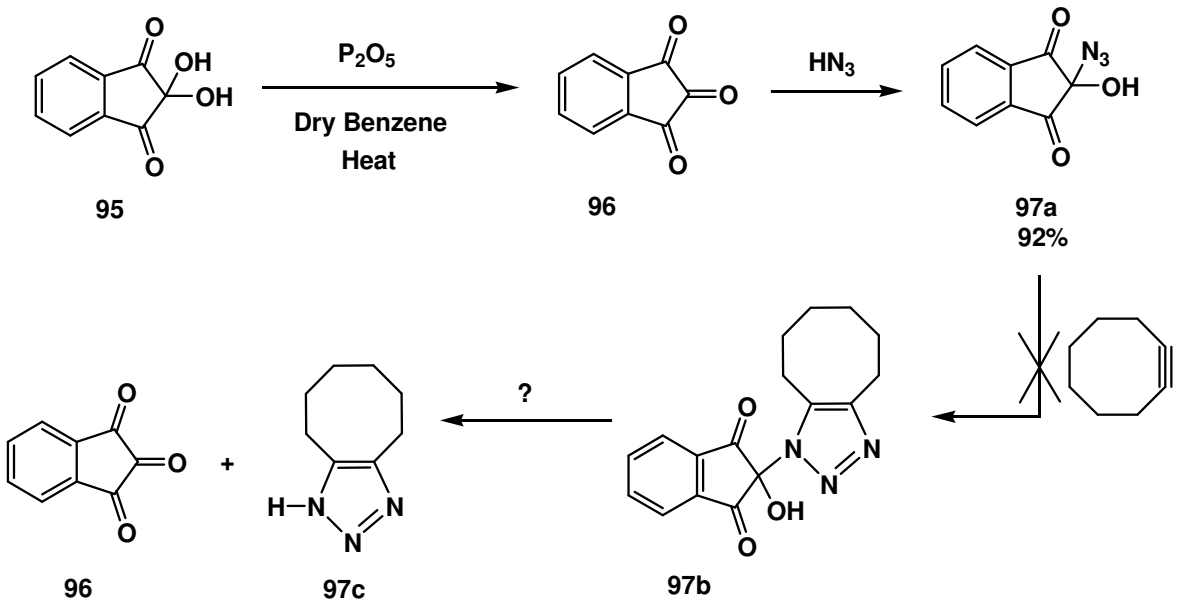
Pentane-2,4-dione (**93**) was treated with HN_3, but no 4-azido-4-hydroxypentan-2-one (**94**) was observed at room temperature as well as at −30 °C after several days (Scheme 32).



Scheme 32 Reaction of Pentane-2,4-dione (93) with HN_3

2.2.2. Reaction of Indane-1,2,3-trione (96) with HN_3

By following a known method by G. B. Gill et al., indane-1,2,3-trione (**96**)[58] was prepared. This compound reacted readily with HN_3 at room temperature to produce 2-azido-2-hydroxyindane-1,3-dione (**97a**) as orange crystals which were further reacted with cyclooctyne to obtain 2-(4,5,6,7,8,9-hexahydrocycloocta[*d*][1,2,3]triazol-1-yl)-2-hydroxy-2*H*-indene-1,3-dione (**97b**). Unfortunately, product **97b** was not obtained, since it was probably unstable and dissects into **96** and **97c** (Scheme 33).



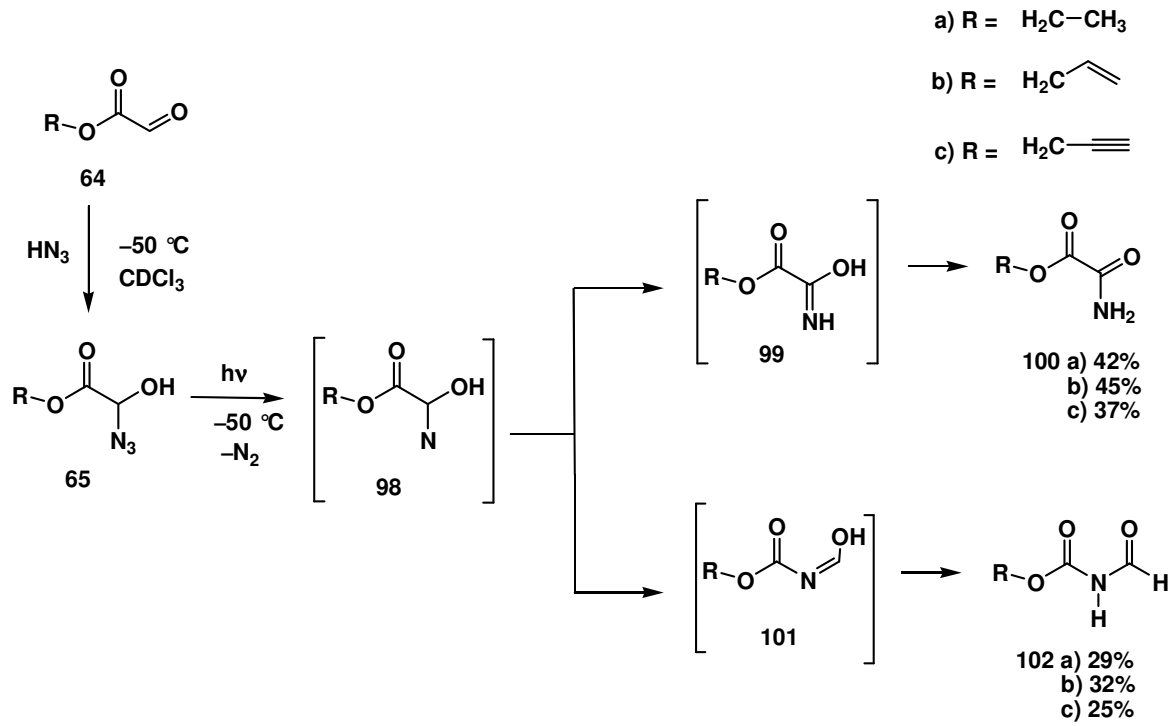
Scheme 33. Reaction of Indane-1,2,3-trione (96) with HN_3

2.3. Reactions of α-Azido Alcohols

2.3.1. Photolysis of α-Azido Alcohols

2.3.1.1. Photolysis of α-Azido Alcohols from Ethyl Glyoxalate Derivatives

Ethyl glyoxalate (**64a**) reacted with HN_3 at room temperature to produce the corresponding α-azido alcohol [ethyl 2-azido-2-hydroxyacetate (**65a**)] with higher yield as compared to other aliphatic aldehydes, as equilibrium was shifted to the addition product. On photolysis at −50 °C for 8 hours, **65a** was completely converted to ethyl 2-amino-2-oxoacetate (**100a**) (42% yield) and ethyl formylcarbamate (**102a**)[59] (29% yield). The photolysis of **65a** induced the generation of nitrene **98a** with the liberation of nitrogen gas. The nitrene **98a** led to the formation of ethyl 2-amino-2-oxoacetate (**100a**) after the migration of hydrogen and subsequent tautomerization of the intermediate **99**. 1,2-Migration of the ethoxycarbonyl group can produce the intermediate stage **101** which was rapidly converted to ethyl formylcarbamate (**102**) (Scheme 34).

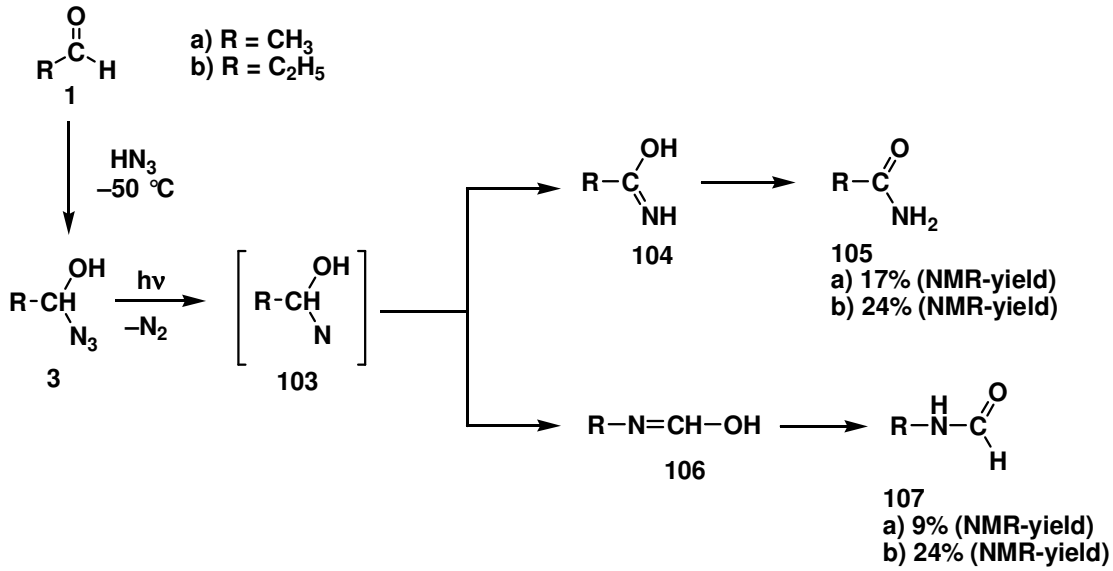


Scheme 34. Photolysis of α-Azido Alcohols from Ethyl Glyoxalate Derivatives

Allyl 2-oxoacetate (**64b**) and prop-2-ynyl 2-oxoacetate (**64c**) reacted with HN_3 at room temperature to produce the corresponding α-azido alcohols [allyl 2-azido-2-hydroxyacetate (**65b**) and prop-2-ynyl 2-azido-2-hydroxyacetate (**65c**)], respectively in higher yield as compared to other aliphatic aldehydes, as equilibrium was shifted to the addition product. On

photolysis at −50 °C for 8 hours, **65b** was completely converted to allyl 2-amino-2-oxoacetate (**100b**) with 45% yield and allyl formylcarbamate (**102b**) with 32% yield. On photolysis at −50 °C for 10 hours, **65c** was converted to prop-2-ynyl 2-amino-2-oxoacetate (**100c**) with 37% yield and prop-2-ynyl formylcarbamate (**102c**) with 25% yield. Compound **100b** was reported by I. Kawamato et al. as starting material for the synthesis of penem antibiotic in 1987.[60]

2.3.1.2. Photolysis of α-Azido Alcohols from Aliphatic Aldehydes



Scheme 34. Photolysis of α-Azido Alcohols from Aliphatic Aldehydes

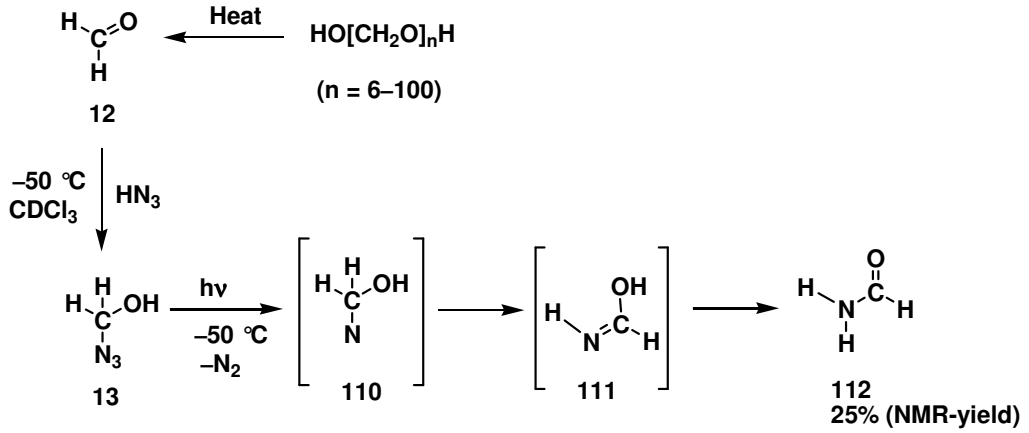
1-Azidoethanol (**3a)** was photolysed at −50 °C for 8 hours to produce acetamide (**105a**) (17% NMR-yield), and *N*-methylformamide (*E* and *Z*-rotamer) (**105b**) (9% NMR-yield) which are commercially available compounds.

1-Azidopropan-1-ol (**3b)** was photolysed at −50 °C for 8 hours to produce propionamide (**105b**) (24% NMR-yield), and *N*-ethylformamide (*E* and *Z*-rotamer) (**107b**) (24% NMR-yield) which are also commercially available compounds (Scheme 34).

2.3.1.3. Photolysis of Azidomethanol (13)

Formaldehyde gas (**12**)[61] was passed through 5M HN_3 solution in $CDCl_3$ at −50 °C and the excess of solvent and HN_3 was distilled off at −50 °C under vacuum to obtain pure azidomethanol (**13**), which was carefully resolved with cold $CDCl_3$ keeping the temperature at −50 °C. Azidomethanol (**13**) was prepared by another method by Y. H. Joo in 2007 (see

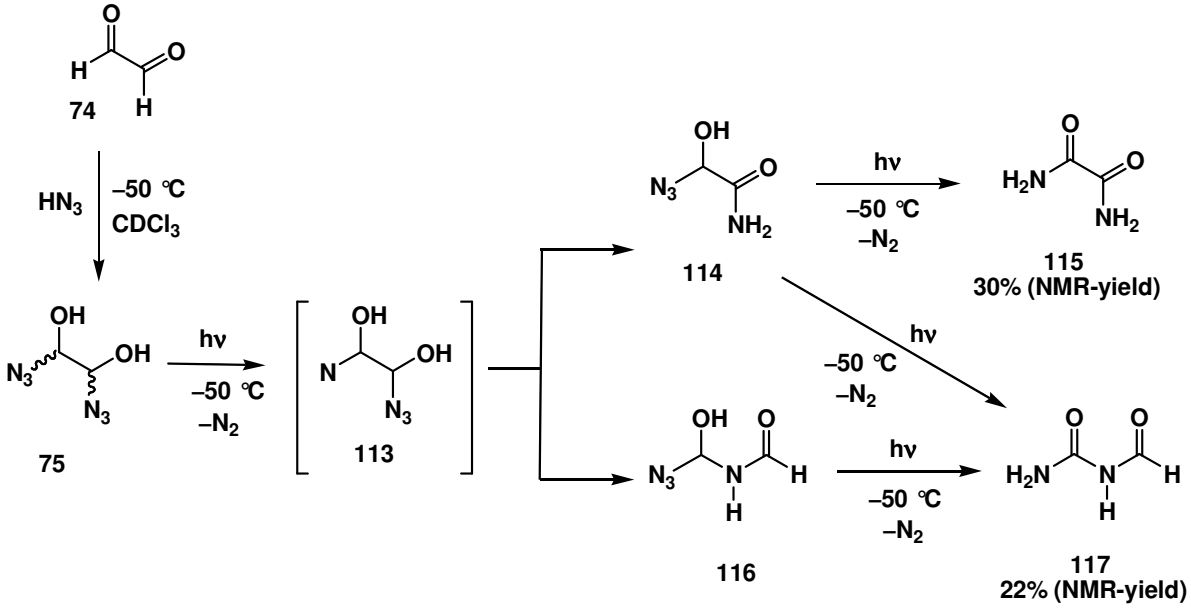
Scheme 4).[62] Later in 2008, J. Kalisiak et al., reported generation of azidomethanol (**13**) in situ from protonated formaldehyde and sodium azide.[33]



Scheme 35. Photolysis of Azidomethanol (13)

On photolysis at −50 °C and −90 °C, azidomethanol (**13**) led to formamide (**112**) with 25% yield (Scheme 35). G. Maier et al., described the isomerization of matrix isolated formamide and IR-spectroscopic detection of formimidic acid.[63]

2.3.1.4. Photolysis of 1,2-Diazidoethane-1,2-diol (75)



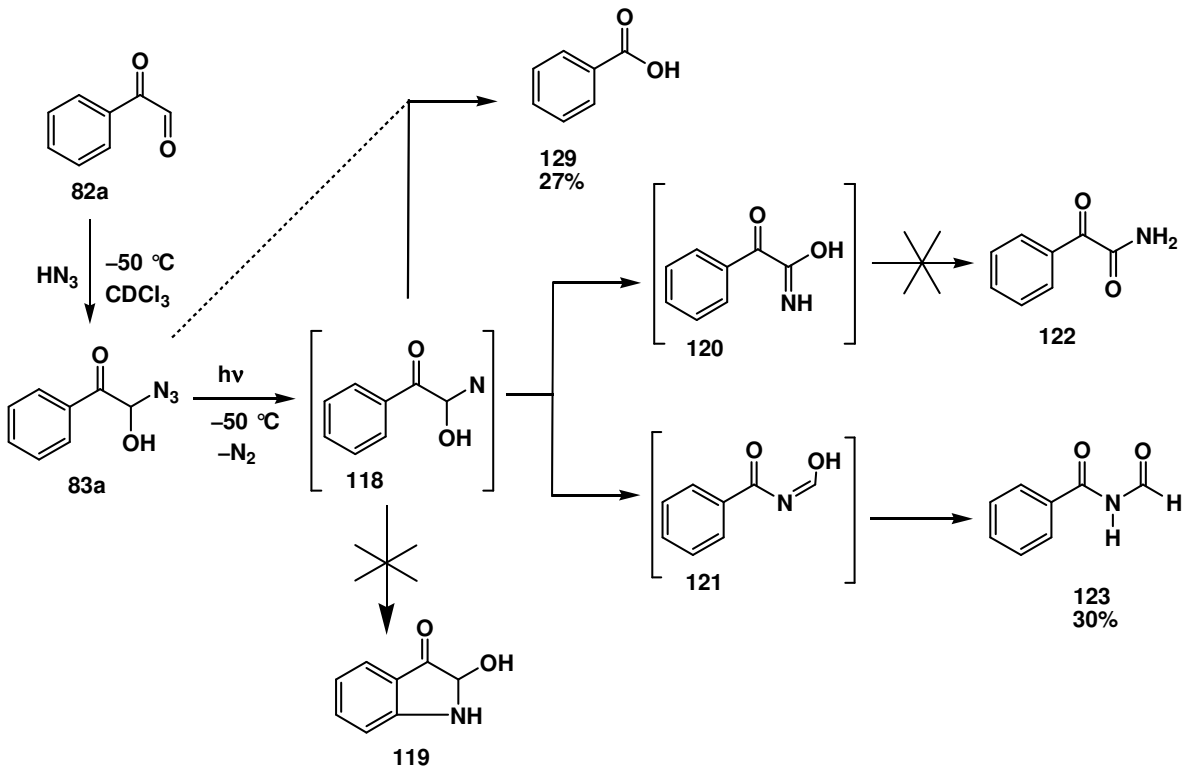
Scheme 36. Photolysis at 1,2-Diazidoethane-1,2-diol

On photolysis at −50 °C for 6 hours, 1,2-diazidoethane-1,2-diol (**75**) was converted to oxalamide (**115**) (30% NMR-yield) and *N*-carbamoylformamide (**117**) (22% NMR-yield),

which was confirmed by comparing NMR-data of commercially available compounds **115** and **117** (Scheme 36).

2.3.1.5. Photolysis of 2-Azido-2-hydroxy-1-phenylethanone (83a)

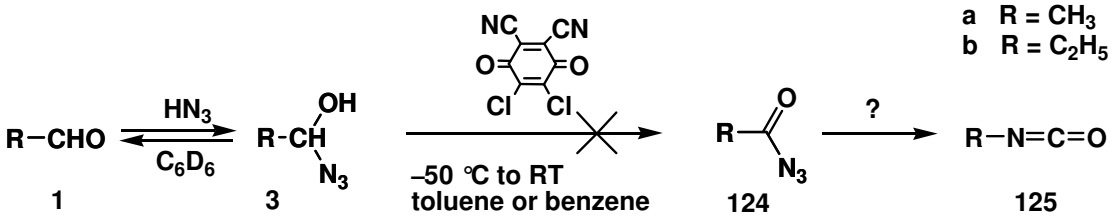
On photolysis at −50 °C, 2-azido-2-hydroxy-1-phenylethanone (**83a**) gave the corresponding formamide derivative *N*-formylbenzamide (**123**) with 30% yield and benzoic acid (**129**) with 27% yield which is probably formed by loss water from **120** to give a cyano-derivative which might further react with H_2O and undergo a substitution reaction to **129** by loss of HCN. But compounds 2-hydroxyindolin-3-one (**119**) and 2-oxo-2-phenylacetamide (**122**) were not observed (Scheme 37).



Scheme 37. Photolysis of 2-Azido-2-hydroxy-1-phenylethanone (83a)

2.3.2. Oxidation of α-Azido Alcohols

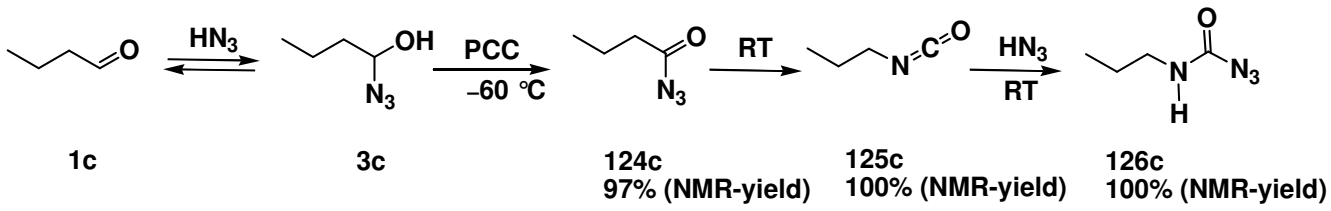
Attempts were made to oxidize α-azido alcohols **3** with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), but no reaction was observed, at −50 °C in toluene as well as at room temperature in benzene (Scheme 38).



Scheme 38. Attempted Oxidation of α-Azido Alcohol 3

2.3.2.1. Reaction of α-Azidobutanol (3c) with PCC

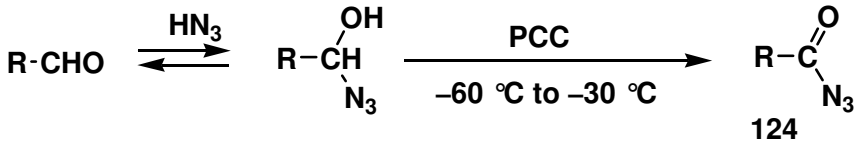
α-Azidobutanol (**3c**) was oxidized with pyridinium chlorochromate (PCC) at −60 °C to produce butyryl azide (**124c**),[64] which was completely transformed into 1-isocyanatopropane (**125c**) on standing at room temperature after 4 hours. The compound **125c** was reacted with HN_3 to produce propylcarbamoyl azide **126c**[65] after 16 hours at room temperature (Scheme 39).



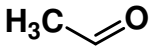
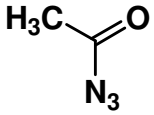
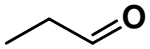
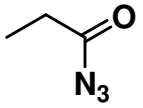
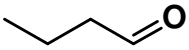
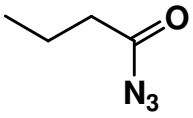
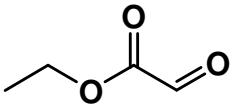
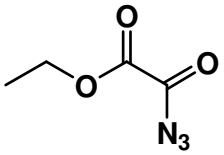
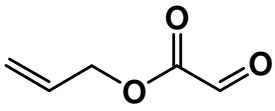
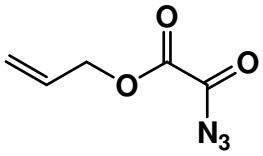
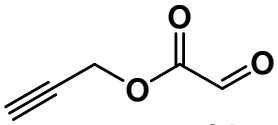
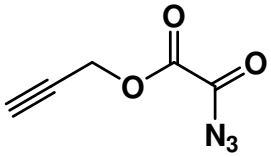
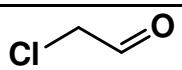
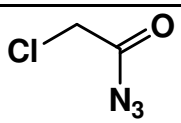
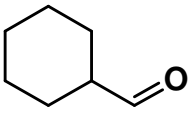
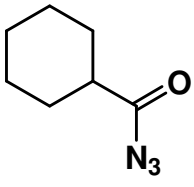
Scheme 39a. Oxidation of α-Azidobutanol (3c)

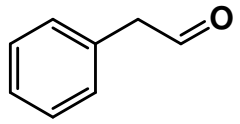
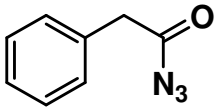
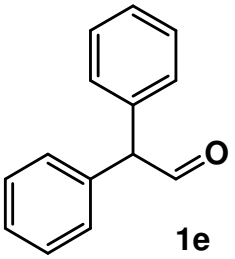
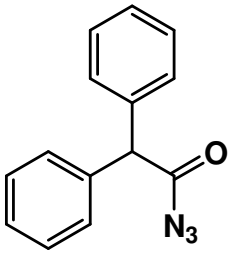
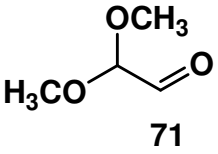
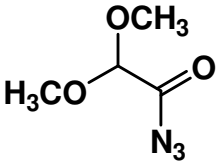
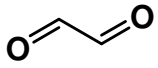
Q. Fan et al. reported on the transformation of 2-azido-1-hydroxy-containing compounds to nitriles with one carbon less than the starting materials by oxidation with pyridinium chlorochromate (PCC).[66]

Table 1. Oxidation of α-Azido Alcohol

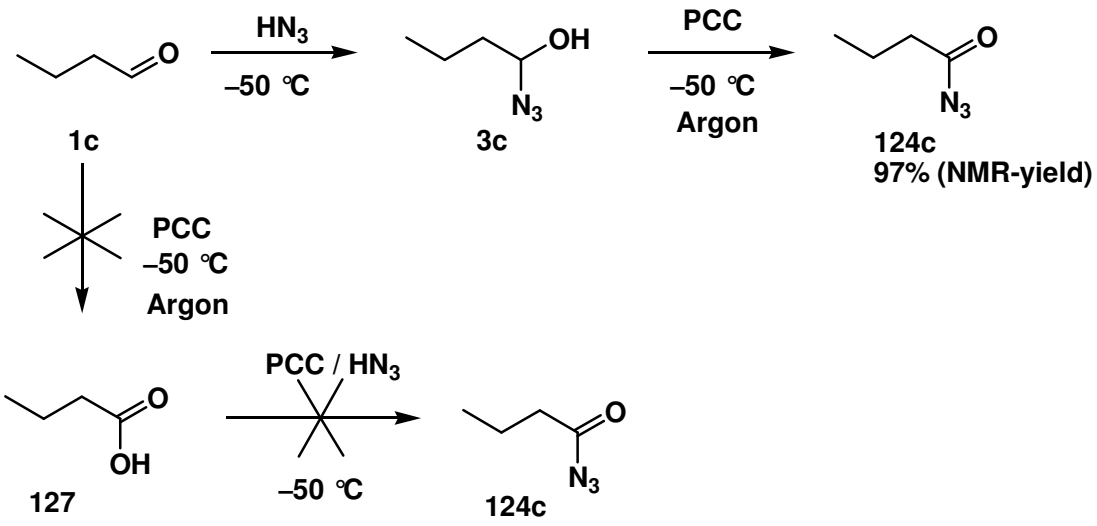


124

Aldehyde	Temperature	Product	Yield (%) Based on Aldehyde
 **1a**	–50 °C	 **124a**[67]	82.9% (NMR-yield)
 **1b**	–50 °C	 **124b**[67]	85.6% (NMR-yield)
 **1c**	–50 °C	 **124c**[64]	97% (NMR-yield)
 **64a**	–50 °C	 **124d**[68]	85.6%
 **64b**	–50 °C	 **124e**	87%
 **64c**	–50 °C	 **124f**	85.9%
 **30a**	–50 °C	 **124g**[67]	85%
 **1d**	–50 °C	 **124h**	89%

 **1f**	−50 °C to −30 °C	 **124i**[64]	89%
 **1e**	−50 °C to −30 °C	 **124j**[69]	87%
 **71**	−50 °C	 **124k**	88%
 **74**	−50 °C	 **124l**[70]	82%

2.3.2.2. Reaction of Butyric Acid (127) with HN_3 and PCC

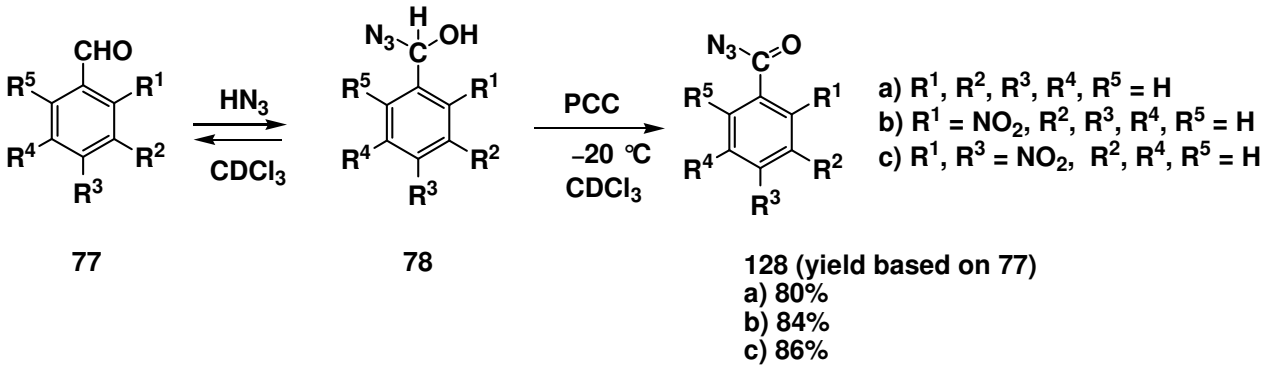


Scheme 39b. Reaction of Butyric Acid (127) with HN_3 and PCC

A control experiment was performed by treating butyric acid (**127**) with HN_3 and PCC, in order to investigate the mechanism of the reaction. We proposed that aldehyde might be first oxidized to carboxylic acid which could further be converted to carbonyl azide in the presence of HN_3 and pyridinium chlorochromate, but no reaction was observed at −60 °C after 6 hours as well as after 7 days at −30 °C (Scheme 39b).

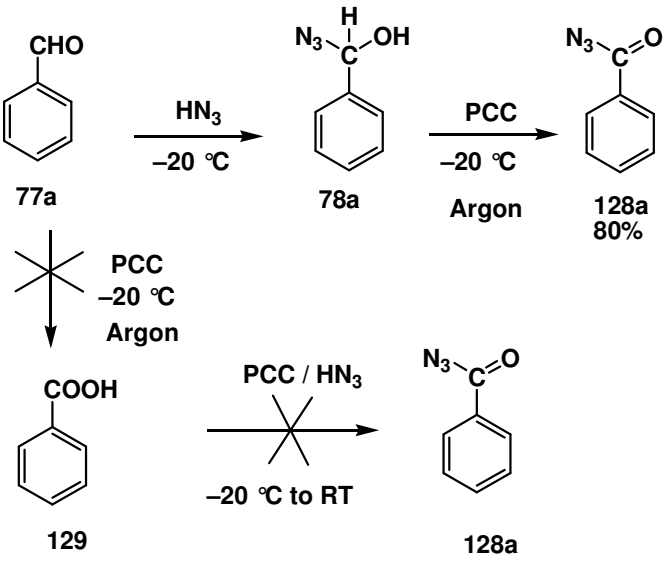
2.3.2.3. Oxidation of α-Azido Alcohols from Aromatic Aldehydes

α-Azido alcohols of aromatic aldehydes were oxidized with pyridinium chlorochromate (PCC) at −20 °C to give aroyl azides (Scheme 40a).



Scheme 40a. Oxidation of α-Azido Alcohols from Aromatic Aldehydes

The mechanism of reaction was investigated through a control experiment.

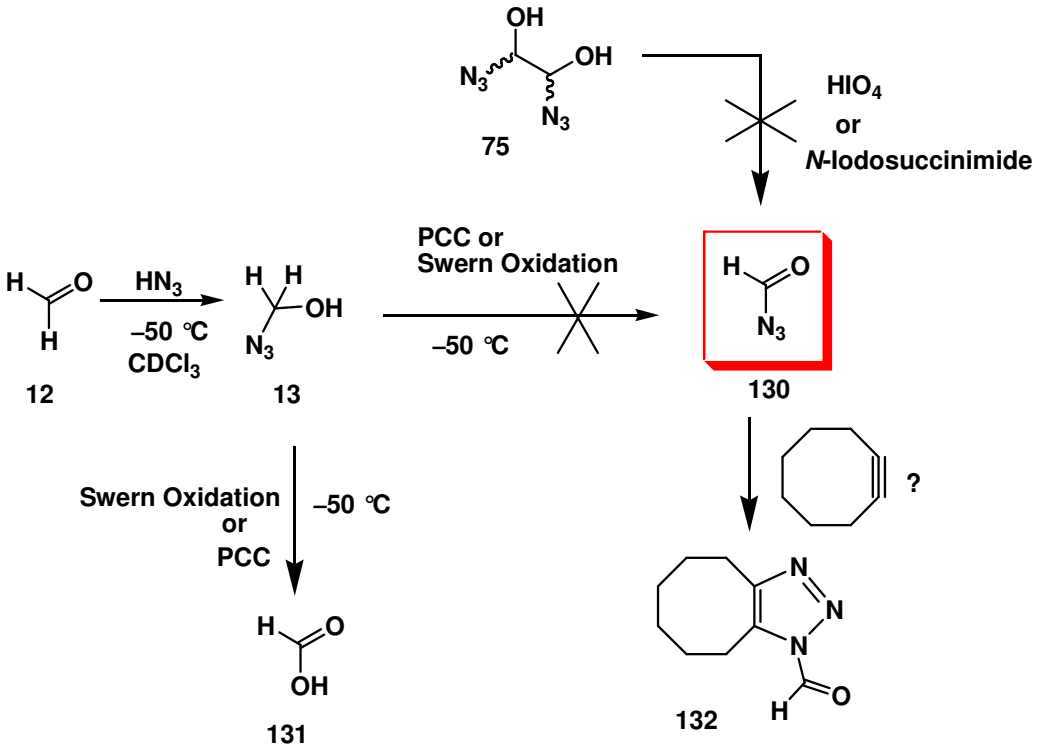


Scheme 40b. Control Experiment

We anticipated that benzaldehyde (**77a**) might first be oxidized to benzoic acid **(129)** which was further converted to benzoyl azide (**128a**) in the presence of HN_3 and pyridinium chlorochromate, but no reaction was observed after treating benzoic acid (**129**) with HN_3 and PCC at −20 °C after 6 hours as well as after 1 day at RT (Scheme 40b).

2.3.2.4. Attempted Synthesis of Formyl Azide (28)

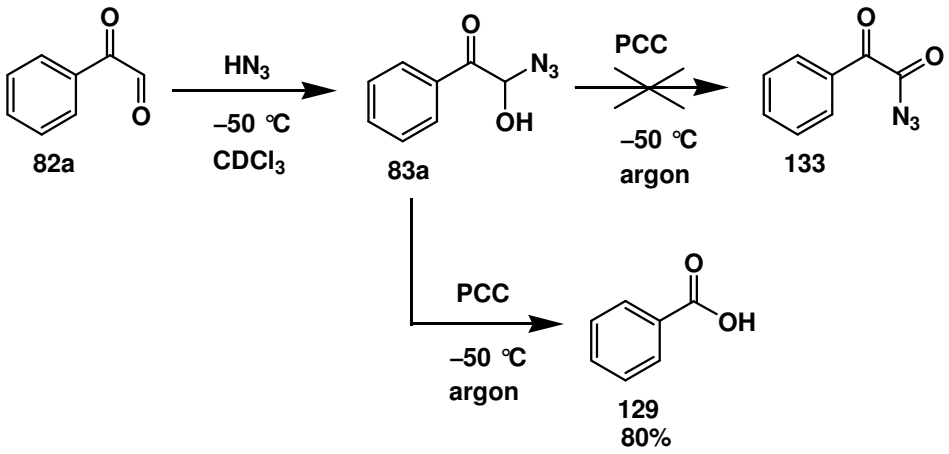
Attempts were made to oxidize azidomethanol (**109**)[62] at −50 °C using pyridinium chlorochromate under argon, as well as the reaction of 1,2-diazidoethane-1,2-diol (**75**) with periodic acid or *N*-iodosuccinimide to obtain unknown and most probably very unstable formyl azide (**130**). But NMR data showed that only formic acid (**131**) was generated in the first case, which was further confirmed by reaction with cyclooctyne. The 4,5,6,7,8,9-hexahydrocycloocta[*d*][1,2,3]triazole-1-carbaldehyde (**132**) was not observed (Scheme 41). Up to now, short-lived formyl azide (**130**) was described only in theoretical calculations.[45d,71]



Scheme 41. Attempted Synthesis of Formyl Azide (130)

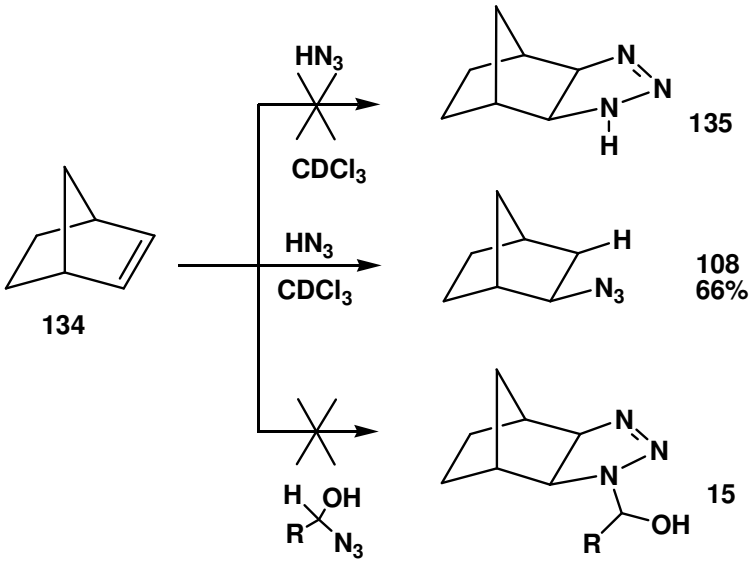
2.3.2.5. Oxidation of 2-Azido-2-hydroxy-1-phenylethanone (83a)

Attempts were made to oxidize 2-azido-2-hydroxy-1-phenylethanone (**82b**) at −50 °C using pyridinium chlorochromate under argon to obtain 2-oxo-2-phenylacetyl azide (**133**) but NMR data showed only the formation of benzoic acid (**129**) (Scheme 42).



Scheme 42. Attempted Oxidation of 2-Azido-2-hydroxy-1-phenylethanone (83a)

2.3.3. Reaction of α-Azido Alcohols with Norbornene (134) and its Derivatives

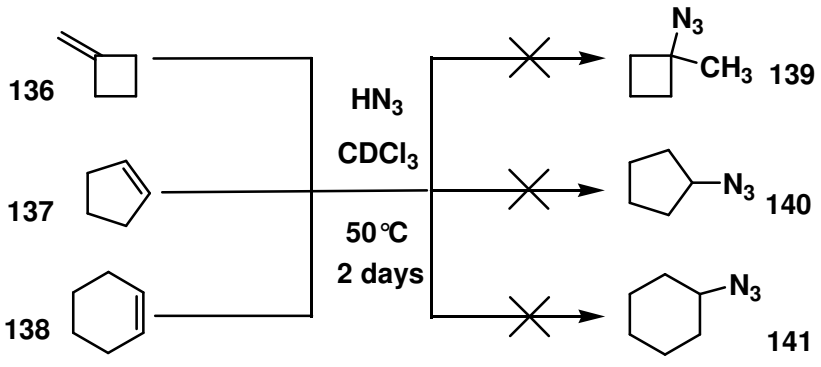


Scheme 43. Reaction of α-Azido Alcohols with Norbornene (134)

Attempts were made to prepare trapping products of α-azido alcohols. Norbornene (**134**) was reacted with covalent azides to produce cycloaddition products,[44b] but it was observed that its reaction with hydrazoic acid was more rapid and led to only *exo*-2-azidobicyclo[2.2.1]heptanes (**108**) by simple electrophilic addition of hydrazoic acid to the double bond (Scheme 43).[72a]

2.3.3.1. Reaction of Strained Alkenes with HN_3

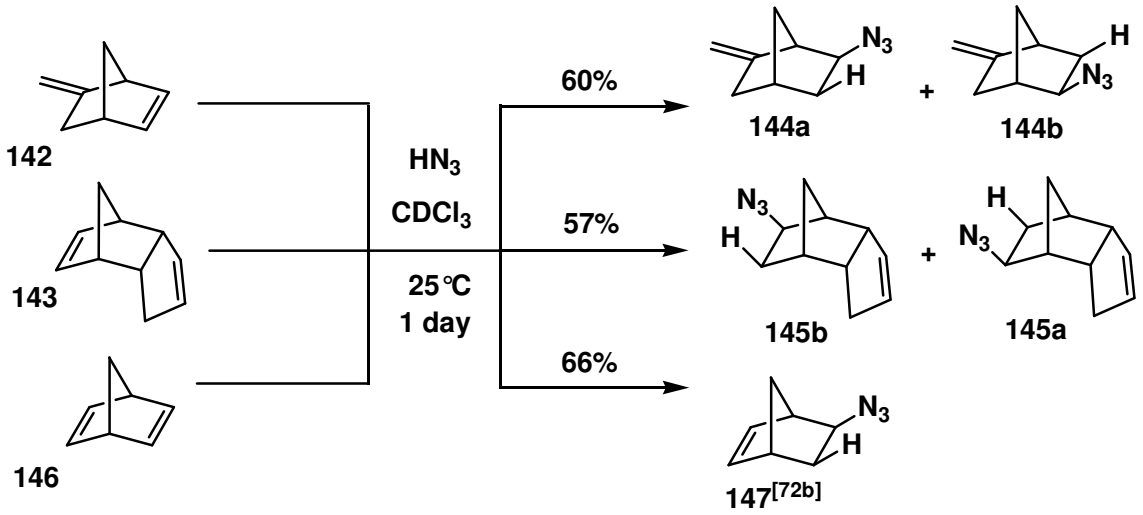
Methylenecyclobutane (**136**), cyclopentene (**137**) and cyclohexene (**138**) were reacted with 2M HN_3 solution. No reaction was observed at room temperature as well as at 50 °C after two days (Scheme 44).



Scheme 44. Attempted Reaction of Strained Alkenes with HN_3

2.3.3.2. Reaction of Norbornene Derivatives with HN_3

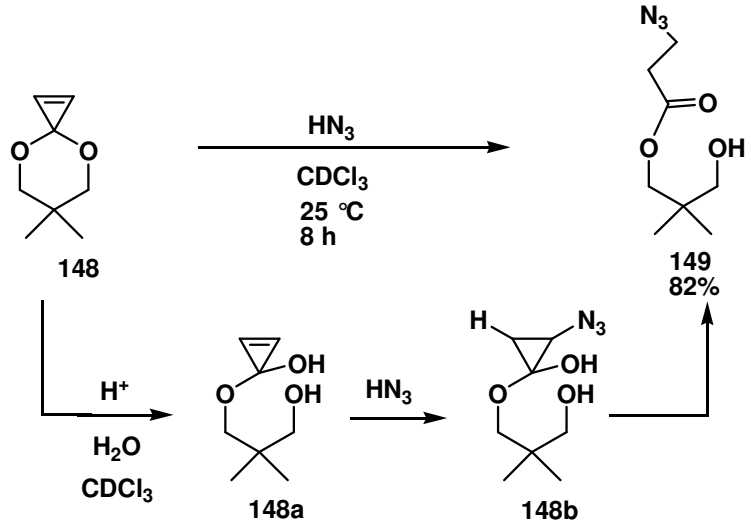
Norbornene derivatives, e.g. 5-methylene-2-norbornene (**142**), 1,3-cyclopentadiene dimer (**143**), and 2,5-norbornadiene (**146**)[72b] reacted with hydrazoic acid to produce *exo*-2-azido compounds by simple electrophilic addition of hydrazoic acid to the double bond (Scheme 45).



Scheme 45. Reaction of Norbornene Derivatives with HN_3

2.3.3.3. Reaction of 6,6-Dimethyl-4,8-dioxaspiro[2.5]oct-1-ene (148) with HN_3

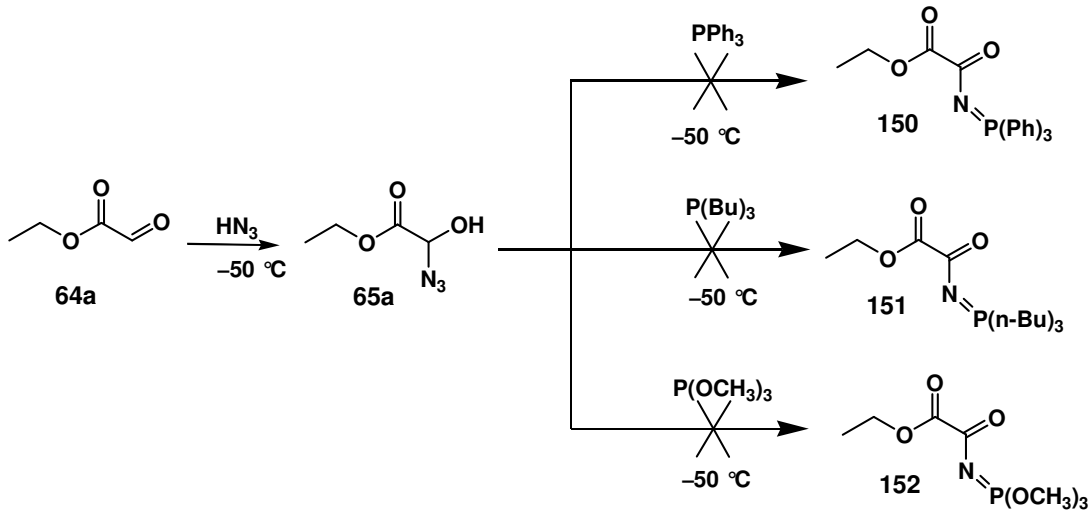
6,6-Dimethyl-4,8-dioxaspiro[2.5]oct-1-ene (**148**) reacted with 2M HN_3 solution in $CDCl_3$ at room temperature for one day to give 3-hydroxy-2,2-dimethylpropyl 3-azidopropanoate (**149**) as light yellow liquid with 82% yield.



Scheme 46. Reaction of 6,6-Dimethyl-4,8-dioxaspiro[2.5]oct-1-ene (148) with HN_3

The formation of **149** can be explained by ring opening of the cyclic ketal in the presence of HN_3, followed by electrophilic addition of HN_3 to the double bond and migration of hydrogen (Scheme 46).

2.3.4. Staudinger Reaction of α-Azido Alcohols

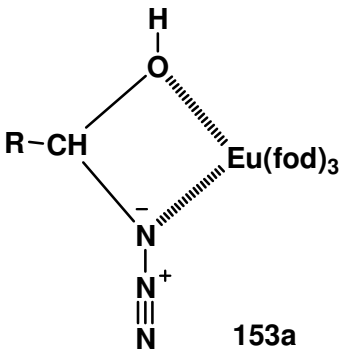


Scheme 47. Staudinger Reaction of α-Azido Alcohols

Triphenylphosphine, tributylphosphine and trimethyl phosphate were reacted with ethyl 2-azido-2-hydroxyacetate (**65a**) at −50 °C under argon. A mixture of several compounds was observed but no Staudinger product was achieved (Scheme 47).

2.3.5. Europium Shift Reagent Experiments

In order to assign the protons of α-azido alcohols in the ^1H NMR spectrum, a europium shift experiment was carried out. It was based on the formation of complex **153a** between the free electron pairs at the nitrogen atom of the azido group and the hydroxyl group of the α-azido alcohol with the shift reagent [Tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium], ($Eu(fod)_3$).

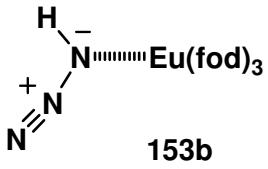


153a

The change in downfield chemical shift increases with the increase in the concentration of shift reagent and with the stability of the complexes.[73]

Europium shift experiment was carried out in $CDCl_3$ as solvent and Tetramethylsilane (TMS δ = 0.00 ppm) as internal standard. We proposed that the change in chemical shifts depends on [n(Eu(fod)$_3$: n(α-azido alcohol)], and a straight line could be obtained by plotting a graph between change in chemical shift and [n (Eu(fod)$_3$: n (α-azido alcohol)].

Unfortunately only a very small change in the chemical shift was observed, because Eu(fod)$_3$ probably reacted with HN_3 to produce a complex **153b** which shifted the equilibrium backwards, thereby causing a decrease in the concentration of α-azido alcohol.

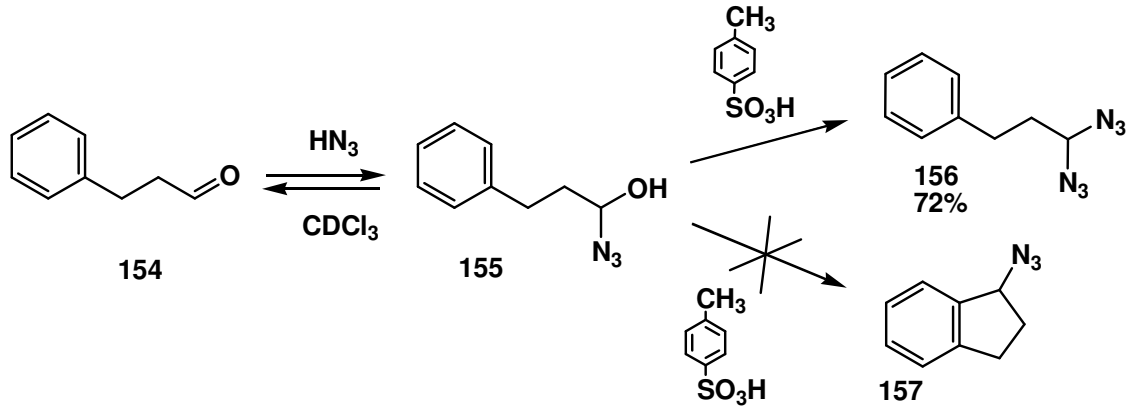


153b

2.3.6. Reaction of α-Azido Alcohols with HN_3 in the Presence of *p*-Toluenesulfonic Acid

2.3.6.1. Reaction of 1-Azido-3-phenylpropan-1-ol (155) with HN_3 in the Presence of *p*-Toluenesulfonic Acid

3-Phenylpropanal (**154**) was treated with HN_3 to give 1-azido-3-phenylpropan-1-ol (**155**) but ring closure to produce 1-azido-2,3-dihydro-1*H*-indene (**157**)[72a] was not possible. In the presence of *p*-toluenesulfonic acid, formation of 1,1-diazido,3-phenylpropane (**156**) was observed (Scheme 48).

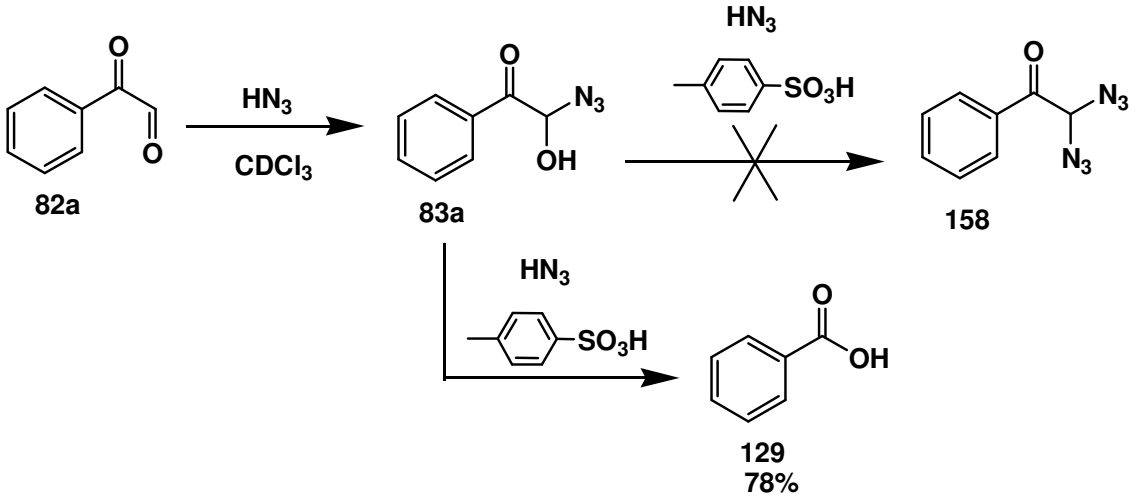


154 **155** **156** 72% **157**

Scheme 48. Reaction of 1-Azido-3-phenylpropan-1-ol (155) with HN_3 in the Presence of *p*-Toluenesulfonic Acid

2.3.6.2. Reaction of 2-Azido-2-hydroxy-1-phenylethanone (83a) with HN_3 and *p*-Toluenesulfonic Acid

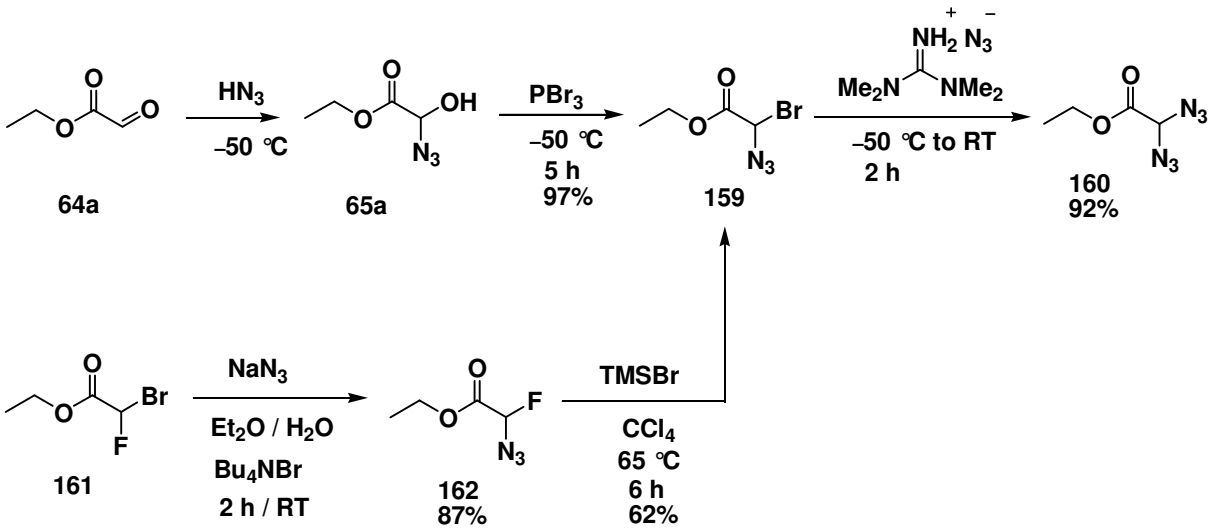
2-Azido-2-hydroxy-1-phenylethanone (**83a**) was reacted with 4-methylbenzenesulfonic acid and HN_3 to produce 2,2-diazido-1-phenylethanone (**158**) at room temperature but diazide **158** could not be obtained. NMR data showed only the formation of benzoic acid (**129**) (Scheme 49).



Scheme 49. Reaction of 2-Azido-2-hydroxy-1-phenylethanone (83a) with HN_3 and *p*-Toluenesulfonic Acid

2.3.7. Reaction of α-Azido Alcohols with PBr_3

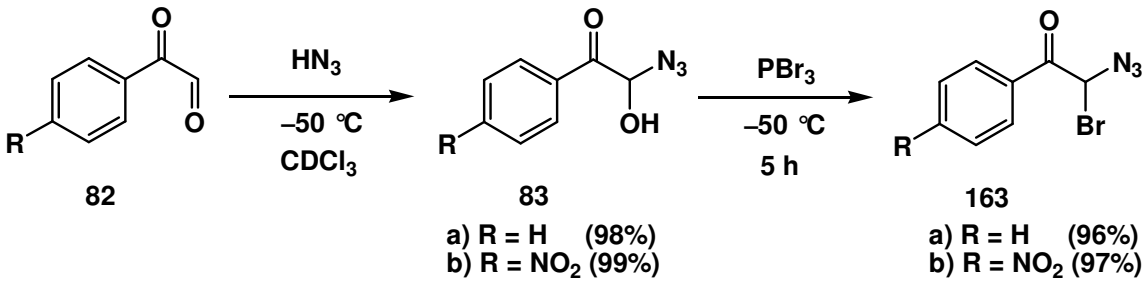
2.3.7.1. Reaction of Ethyl 2-Azido-2-hydroxyacetate (65a) with PBr_3



Scheme 50. Reaction of Ethyl 2-Azido-2-hydroxyacetate (65a) with PBr_3

2-Azido-2-hydroxyacetate (**65a**) reacts with PBr_3 at −50 °C to −30 °C for 5 hours to give ethyl 2-azido-2-bromoacetate (**159**)[74] in a clean reaction by substitution of hydroxyl group at the *alpha* position. The compound **159** was further reacted with TMGA (*N*,*N*,*N*',*N*'-tetramethylguanidinium azide) at −50 °C to room temperature for 2 hours to get ethyl 2,2-diazidoacetate (**160**)[74] (Scheme 50). Compound **159** was prepared from **161** via **162** for comparative study using a known method by Y. Takeuchi et al.[74]

2.3.7.2. Reaction of 2-Azido-2-hydroxy-1-phenylethanone (83) with PBr_3

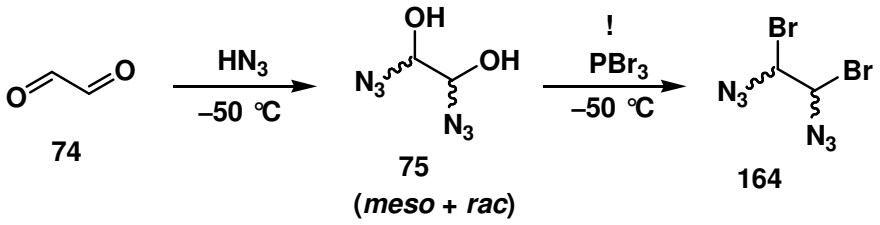


Scheme 51. Reaction of 2-Azido-2-hydroxy-1-phenylethanone Derivatives with PBr_3

2-Azido-2-hydroxy-1-phenylethanone (**83a**) and 2-azido-2-hydroxy-1-(4-nitrophenyl)ethanone (**83b**) were reacted with PBr_3 at −50 °C to −30 °C for 5 hours to give 2-azido-2-bromo-1-phenylethanone (**163a**) and 2-azido-2-bromo-1-(4-nitrophenyl)ethanone (**163b**), respectively in a clean reaction by substitution of the hydroxyl group at the *alpha* position (Scheme 51).

2.3.7.3. Reaction of 1,2-Diazidoethane-1,2-diol (75) with PBr_3

Attempts to prepare 1,2-diazido-1,2-dibromoethane (**164**) led to an explosion, which was presumably due to the formation of $P(N_3)_3$ (Scheme 52).

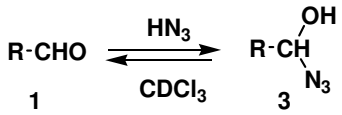


Scheme 52. Reaction of 1,2-Diazidoethane-1,2-diol (75) with PBr_3

3. SUMMARY AND OUTLOOK

3.1. Summary

The objective of this work was to investigate the reactions of aldehydes with HN_3 to give α-azido alcohols. For this purpose, reactions of a variety of aldehydes, aliphatic, aromatic and sugar derivatives were carried out. α-Azido alcohols existed in equilibrium with the starting materials, which could be removed from the mixture at low temperature in some cases. At room temperature, however, the equilibrium was fast and there were again specific concentrations of the aldehyde, hydrazoic acid, and the α-azido alcohol.

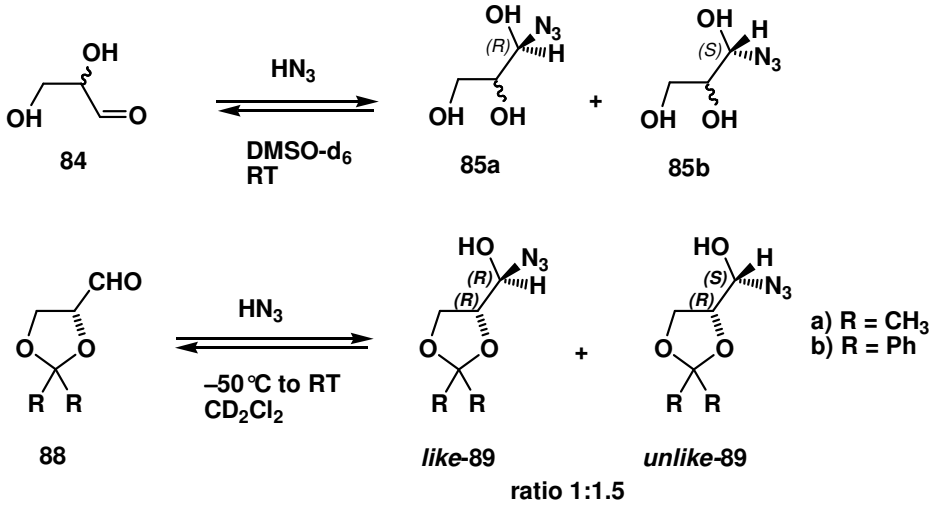


3a) R = CH_3
3b) R = C_2H_5
3c) R = C_3H_7
3d) R = *c*Hex
13) R = H
65a) R = CO_2Et
65b) R = $CO_2CH_2CH{=}CH_2$
65c) R = $CO_2CH_2C{\equiv}CH$
72) R = $CH(OMe)_2$
31a) R = CH_2Cl
31b) R = CH_2Br
33) R = CH_2N_3
38a) R = $(CH2)_3Br$
38b) R = $(CH2)_3OTs$
40) R = $(CH_2)_3N_3$
53) R = $CH_2CH_2C(Me){=}CH_2$
54) R = $CH_2CH_2CMe_2N_3$
62) R = $CH_2CH_2CMe_2Br$
3e) R = $CHPh_2$
3f) R = CH_2Ph
83a) R = C_6H_5CO
83b) R = C_6H_3-4- NO_2CO
128b) R = C_6H_4-2-NO_2
128c) R = C_6H_3-2,4-$(NO_2)_2$
155) R = $(CH_2)_3Ph$

Scheme 53. Synthesis of α-Azido Alcohols from Aldehydes

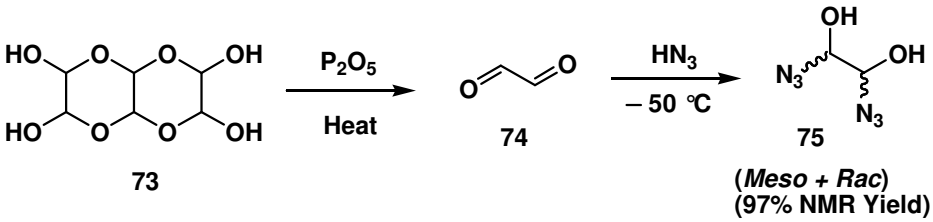
It was observed that acetaldehyde (**1a**) and propionaldehyde (**1b**) react with equimolar and higher quantities of HN_3 and produce the corresponding α-azido alcohols, while the higher concentration of aldehyde and longer reaction time led to the trimerization of the aldehyde.

The reaction of aldehydes with HN_3 created a new chiral center and a chiral aldehyde, e.g. sugar derivatives, produced two diastereomeric products (anomers) which could be characterized by ^{13}C-NMR.



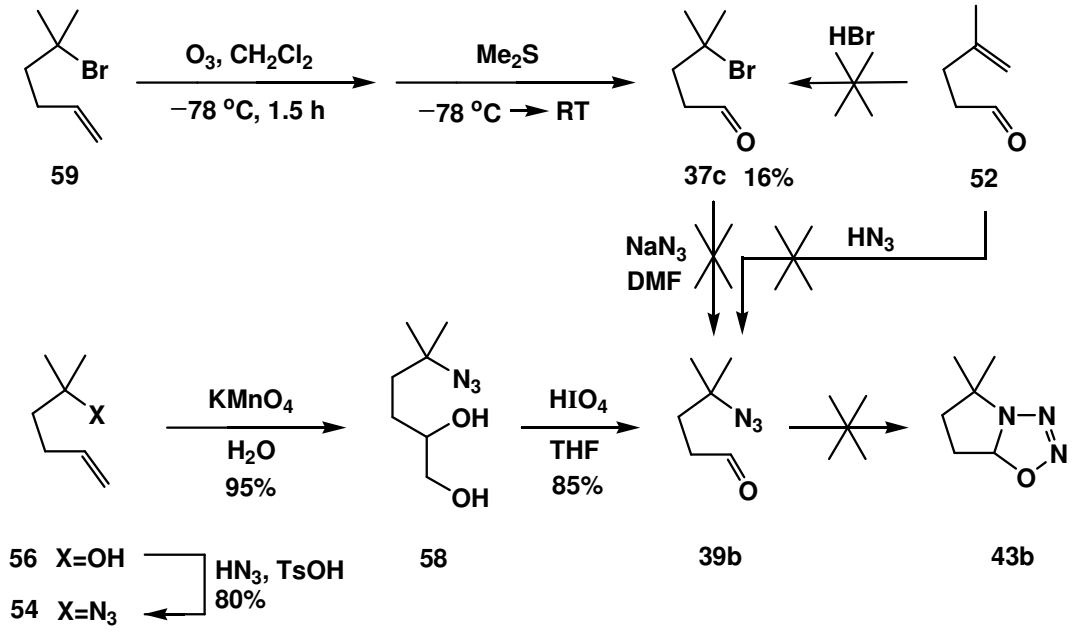
Scheme 54. Reaction of Sugar Derivatives with HN_3

Oxalaldehyde (**74**) reacts with HN_3 solution to give a mixture of *meso*- and *racem*-1,2-diazidoethane-1,2-diol (**75**), which can be identified by two sets of signal in ^{13}C-NMR spectrum.



Scheme 55. Reaction of Oxalaldehyde (74) with HN_3

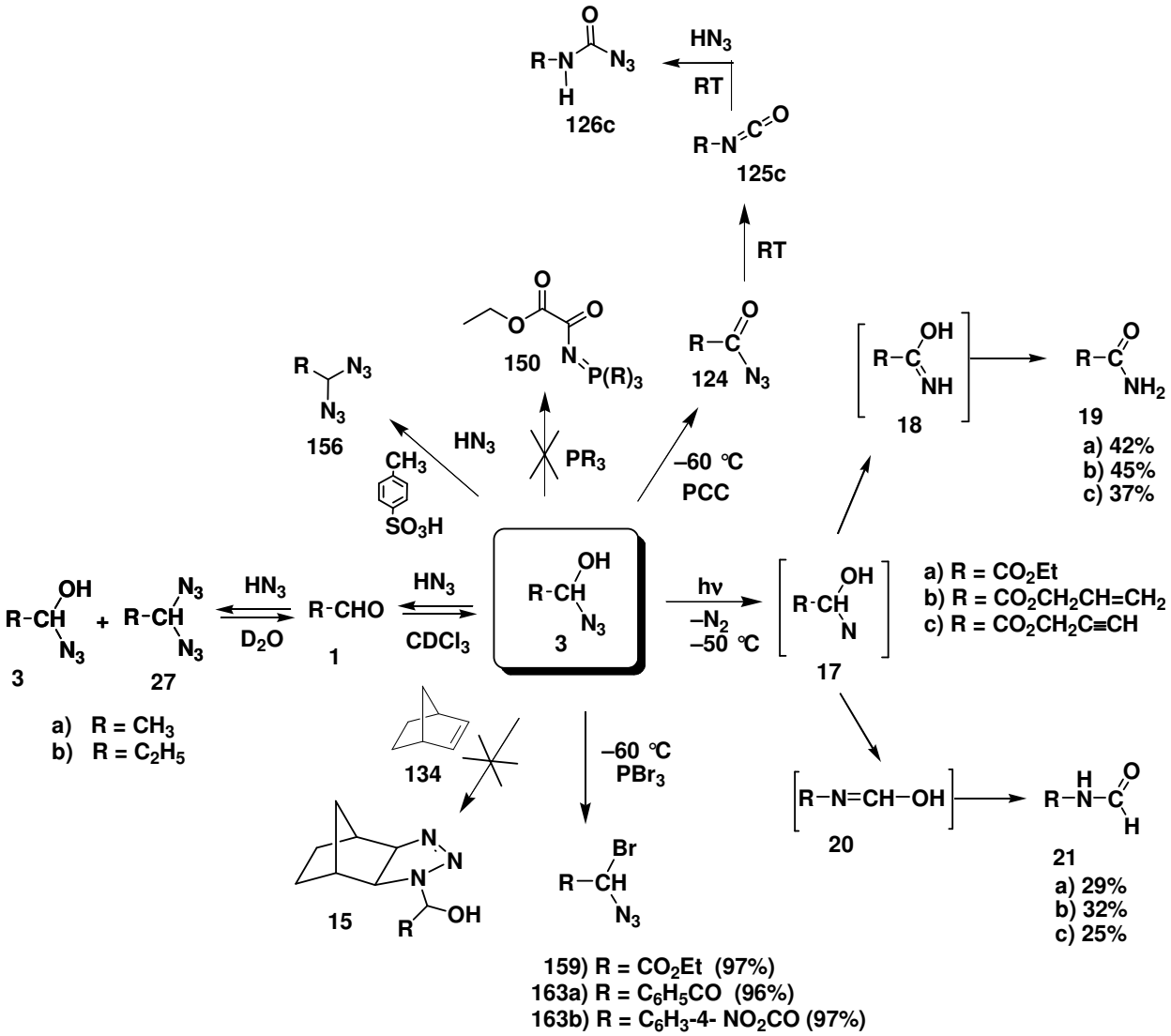
Furthermore, 4-bromo-4-methylpentanal and 4-azido-4-methylpentanal were prepared. 4-Azidobutanal derivatives did not lead to 4,5-dihydro-1,2,3,4-oxatriazoles by intramolecular 1,3-dipolar cycloaddition, although it was claimed in the literature.



Scheme 56. Synthesis of Bromide 37c and Azide 39b.

1-Azido-2-chloroethanol (**31a**), 1-azido-2-bromoethanol (**31b**), 1-azido-4-bromobutan-1-ol (**38a**) and 4-Azido-4-hydroxybutyl 4-methylbenzenesulfonate (**38b**) were prepared by addition of HN_3 to chloroacetaldehyde (**30a**) and bromoacetaldehyde (**30b**), 4-bromobutanal (**37a**) and 4-oxobutyl 4-methylbenzenesulfonate (**37b**), respectively. Hydrazoic acid is added only to the carbonyl group of chloro/bromoacetaldehyde and nucleophilic substitution of the chloro/bromo substituent at C-2 or C-4 does not take place, which can be confirmed by ^{13}C-NMR signals.

Aliphatic aldehydes (acetaldehyde, propionaldehyde) reacted with HN_3 solution in D_2O by bimolecular addition of HN_3 to the carbonyl group to produce α-azido alcohols **3** and 1,1-diazido alkanes **27**. Furthermore, some interesting reactions of the title compounds were investigated.



Scheme 57. Reactions of α-Azido Alcohols

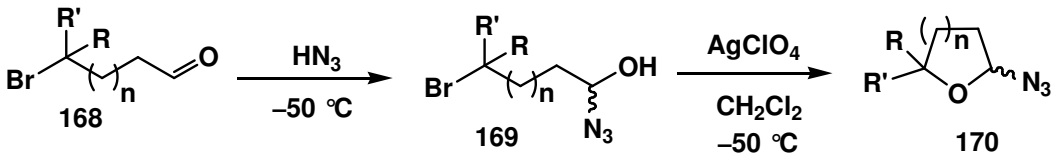
The oxidation of α-azido alcohols with pyridinium chlorochromate (PCC) at −60 °C (for aliphatic aldehydes) and −20 ˚C (aromatic aldehydes) led to formation of carbonyl azides. The photolysis of α-azido alcohols generated nitrenes with liberation of dinitrogen, which led to the formation of acid amides after the migration of hydrogen and subsequent tautomerism of the intermediate. 1,2-Migration of a group R in the α-position produced an intermediate stage which is rapidly converted into formamide derivative.

α-Azido alcohols reacted with PBr_3 to give 1-azido-1-bromo derivatives in a clean reaction by substitution of hydroxyl group at the α-position.

3.2. OUTLOOK

The hydroxyl group of α-azido alcohol can undergo substitution reaction with other reagents. It may give etherification or esterification reactions.

Reaction of α-azido alcohol from aldehydes (sugar derivatives), would be of interest for the synthesis of biologically important compounds.



Scheme 58. Reactions of α-Azido Alcohols

Although we have investigated only a few reactions of α-azido alcohols so far, we presume that these new compounds will enrich the multifarious chemistry of organic azides.

4. EXPERIMENTAL PART

4.1.1. Instrumentation

Melting points were measured on a BOETIUS apparatus from PENTAKON Company, Dresden. Melting points were not corrected.

IR spectra were measured using a FT-IR apparatus of type BRUKER IFS 28. The dissolved samples in $CDCl_3$ or CCl_4 were recorded at room temperature in the wave number ($\tilde{\nu}$) range from 400–4000 cm^{-1}. In some cases, only the main functional groups were reported.

NMR spectra were measured on a wide-band FT-spectrometer UNITY INOVA 400 from VARIAN Company. ^{1}H NMR spectra were measured at 400 MHz and ^{13}C NMR on 100 MHz. All measurements were performed at room temperature if not otherwise mentioned. Internal standard was TMS (δ = 0 ppm) or solvent signals recalculated relative to TMS. The multiplicities of ^{13}C NMR signals were determined without coupling constant value with help of gated spectra and/or DEPT 135 experiments. Mulplicity of the signals is given as follows: br. = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.

Photolysis experiments were carried out with a 150 W mercury high pressure burner TQ 150 from the quartz lamp Company Hanau. The irradiation was performed in a quartz glass device. The cooling of lamp shaft and photolysis of sample was done by means of ethanol using a cryostat of company LAUDA at desired temperature.

Mass spectrometry HR-MS spectra were obtained with a Mariner system 5229 spectrometer (Applied Biosystems).

Quantitative elemental analyses were measured on VARIO EL ELEMENTAR from the ANALYSENSYSTEM GmbH (Hanau).

4.1.2. Working Procedures and Conditions

Flash column chromatography was performed using silica gel (0.04–0.063 mm) from the FLUKA Company as stationary phase. The used solvents are mentioned in the experimental section.

Thin layer chromatography (TLC) was carried out on POLYGRAM SIL G/UV254 ready foils from the MACHEREY-NAGEL company.

All reactions were performed in oven-dried glassware. The solvents were distilled before use. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl prior to use. Other solvents and reagents, purchased from commercial sources were used directly or after distillation. Commercially available starting materials were purchased from ALDRICH, ACROS, or MERCK Company.

4.1.3. Synthesis of Hydrazoic acid Solution in Organic Solvents

Hydrazoic acid solution (8 ml, 2M, 16 mmol) was prepared by addition of concentrated H_2SO_4 (96 %, 2.8 ml, 50 mmol) to a solution of sodium azide (2.6 g, 40 mmol) in 8 ml $CDCl_3$ and 3 ml H_2O.[82] The organic layer was dried over $MgSO_4$ and was standardized by titrating against 0.1M NaOH solution.

4.1.4. Safety Instructions

Care must be taken in handling azides, which are explosive. Particularly, neat azides can lead to heavy explosions upon friction, impact, or heating. Hydrazoic acid is a colorless, toxic, volatile and highly explosive liquid. It is a weak acid like acetic acid very irritating to mucosa. Exposure to HN_3 causes palpitation, headache, feeling of pressure in the nose and hypertension. It should never be handled in pure form but always in solution; highly concentrated solution may lead to an explosion. Therefore, a safe concentration is 2 mol L^{-1}.

4.2. Synthesis of α-Azido Alcohols by Hydroazidation of Aldehydes

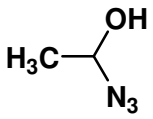
General Procedure

To the solution of hydrazoic acid in $CDCl_3$ was added aldehyde **1** at 0 °C or 25 °C. The mixture was stirred additionally for 2 h, so that the equilibrium was established. The isolation of pure α-azido alcohols **3** or at least removal of hydrazoic acid from **3** was performed by cooling the equilibrium mixture to –50 to –65 °C, followed by removal of all volatile compounds under vacuum (10^{-3} mbar). The remaining oil or solid was α-azido alcohol **3** or a mixture of aldehyde **1** and α-azido alcohol **3**. Precooled solvents ($CDCl_3$, CD_2Cl_2) were added at –50 °C and the solutions were transferred into a precooled NMR tube, which was further used for NMR spectroscopic measurement at low temperature.

4.2.1. Synthesis of α-Azidoethanol (3a)

Acetaldehyde (**1a**) (78 mg, 1.77 mmol, 0.1 ml) was mixed with the solution of HN_3 (6 ml, 2M, 12 mmol) and using the general procedure, α-azidoethanol (**3a**) in $CDCl_3$ was obtained.

α-Azidoethanol (3a): Colorless liquid. – **^{1}H NMR** ($CDCl_3$): δ = 1.37 (d, ^3J = 5.6 Hz, 3H), 3.99 (br, 1H, OH), 5.03 (q, ^3J = 5.7 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 22.1 (q, CH_3), 82.7 (d, CH).

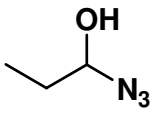


3a

4.2.2. Synthesis of α-Azidopropanol (3b)

Propionaldehyde (**1b**) (81 mg, 0.1 ml, 1.39 mmol) was mixed with a solution of HN_3 in $CDCl_3$ (6 ml, 2M, 12 mmol) at room temperature and utilizing the general procedure, α-azidopropanol (**3b**) solution in $CDCl_3$ was obtained.

α-Azidopropanol (3b): Colorless liquid. – **^{1}H NMR** ($CDCl_3$): δ = 0.80 (t, ^3J = 7.2 Hz, 3H), 1.49 (m, 2H, diastereotopic protons), 4.66 (t, ^3J = 5.8 Hz, 1H), OH-signal was covered by other signals. –**^{13}C NMR** ($CDCl_3$): δ = 8.6 (q, CH_3), 29.4 (t, CH_2), 87.3 (d, CH).

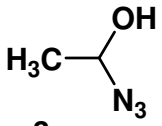


3b

4.2.3. Synthesis of α-Azidoethanol (3a) in D_2O

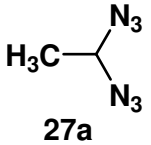
Acetaldehyde (**1a**) (78 mg, 1.77 mmol, 0.1 ml) and D_2O (2 ml) were mixed with a solution of 2M HN_3 in CH_2Cl_2 (6 ml, 12 mmol). The excess of HN_3, acetaldehyde (**1a**) and CH_2Cl_2 was distilled off under vacuum (10^{-3} mbar) at −55 °C to −60 °C to obtain an equilibrium mixture containing α-azidoethanol (**3a**) and 1,1-diazidoethane (**27a**) in D_2O. The ratio between α-azidoethanol (**3a**) and 1,1-diazidoethane (**27a**) was ca. 1:1 at room temperature, according to ^{1}H NMR integration. It was not possible to isolate pure α-azidoethanol (**3a**) from the mixture. CH_2Cl_2 was used as an internal standard for ^{13}C NMR measurement (δ = 53.2 ppm).

α-Azidoethanol (3a): ^{1}H NMR (D_2O): δ = 1.21 (d, ^3J = 5.6 Hz, 3H), 5.13 (q, ^3J = 5.2 Hz, 1H). The OH-signal was covered by other signals. – **^{13}C NMR** (D_2O): δ = 22.4 (q, CH_3), 87.4 (d, CH).



3a

1,1-Diazidoethane (27a): ^{1}H NMR (D_2O): δ = 1.25 (d, ^3J = 6.0 Hz, 3H), 5.08 (q, ^3J = 5.8 Hz, 1H). – **^{13}C NMR** (D_2O): δ = 20.6 (q, CH_3), 81.9 (d, CH).

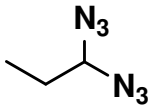


27a

4.2.4. Synthesis of α-Azidopropanol (27b) in D_2O

Propionaldehyde (**1b**) (78 mg, 1.34 mmol, 0.1 ml) and D_2O (2 ml) were mixed with solution of 2M HN_3 in CH_2Cl_2 (6 ml, 12 mmol), and stirred at room temperature for 2 h. The excess of HN_3, propionaldehyde and CH_2Cl_2 was distilled off under vacuum (10^{-3} mbar) at −55 °C to −60 °C to attain an equilibrium mixture containing α-azidopropanol (**3b**) and 1,1-diazidopropane (**27b**)[30b] as a major product in D_2O. CH_2Cl_2 was used as an internal standard for ^{13}C NMR measurement (δ = 53.2 ppm).

1,1-Diazidopropane (27b): Colorless explosive liquid. – **^{1}H NMR** (D_2O): δ = 0.81 (t, ^3J = 7.2 Hz, 3H), 1.53 (qd, ^3J = 7.2 Hz, ^3J = 6.2 Hz, 2H), 4.83 (t, ^3J = 6.0 Hz, 1H). – **^{13}C NMR** (D_2O): δ = 7.4 (q, CH_3), 28.0 (t, CH_2), 86.5 (d, CH).



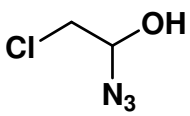
27b

4.3. Reaction of Halogenated Aliphatic Aldehydes with HN_3

4.3.1. Synthesis of 1-Azido-2-chloroethanol (31a)

45% Aqueous solution of chloroacetaldehyde (**30a**) was treated with equal mass of dry $CaCl_2$ and stirred at room temperature for 10 minutes. The mixture was distilled ($Kp._{760\ Torr}$: 82 °C) to yield chloroacetaldehyde (**30a**) as a colorless liquid. Chloroacetaldehyde (**30a**) (78.5 mg, 1 mmol) was mixed with a solution of 5M HN_3 in $CDCl_3$ (10 mmol, 2 ml), and stirred at room temperature for 10 minutes to obtain an equilibrium mixture containing 1-azido-2-chloroethanol (**31a**) in $CDCl_3$. The ratio between 1-azido-2-chloroethanol (**31a**) and chloroacetaldehyde (**30a**) is ca. 5:1 at room temperature due to ^1H NMR integration.

1-Azido-2-chloroethanol (31a): Colorless liquid, 85% NMR-yield.– **^1H NMR** ($CDCl_3$): δ = 3.56 (d, ^3J = 4.0 Hz, 2H), 5.14 (t, ^3J = 4.4 Hz, 1H). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 46.8 (t, CH_2), 83.4 (d, CH).

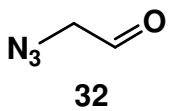


31a

4.3.2. Synthesis of Azidoacetaldehyde (32)

To a stirred solution of chloroacetaldehyde (**30a**) (1 g, 12.7 mmol) or bromoacetaldehyde (**30b**) (1.6 g, 12.7 mmol) in $CDCl_3$ (12 ml), hexadecyltributylphoshphonium azide (QN_3) (6.7 g, 12.8 mmol) was added. The mixture was stirred for 5−10 minutes. Azidoacetaldehyde (**32**) solution in $CDCl_3$ was isolated from the mixture by recondensation under vacuum (10^{-3} mbar) at −50 °C to room temperature. Pure azidoacetaldehyde (**32**) decomposes on standing at room temperature.

Azidoacetaldehyde (32): Colorless explosive liquid. – **^1H NMR** ($CDCl_3$): δ = 4.04 (s, 2H), 9.69 (s, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 58.2 (t, CH_2), 195.1 (d, CH). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 1736 cm^{-1} (C=O), 2098 cm^{-1} (N_3).



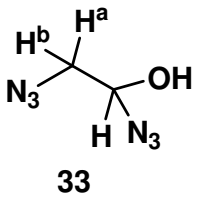
32

4.3.3. Synthesis of 1,2-Diazidoethanol (33)

Azidoacetaldehyde (**32**) (200 mg, 2.3 mmol) was mixed with a solution of 4M HN_3 (0.6 ml, 2.4 mmol) in $CDCl_3$ and stirred at room temperature for 10 minutes to obtain an equilibrium

mixture containing 1,2-diazidoethanol (**33**) in $CDCl_3$. The ratio between 1,2-diazidoethanol (**33**) and azidoacetaldehyde (**32**) is ca. 5:1 at room temperature due to ^1H NMR integration.

1,2-Diazidoethanol (33): Colorless liquid, 82% NMR-yield.– **^{1}H NMR** ($CDCl_3$): δ = 3.31 (dd, ^2J = 12.6 Hz, ^3J = 4.2 Hz, 1H, H^a), 3.39 (dd, ^2J = 12.8 Hz, ^3J = 4.4 Hz, 1H, H^b), 5.06 (t, ^3J = 4.2 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 54.9 (t, CH_2), 83.4 (d, CH).

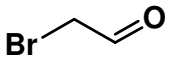


33

4.3.4. Synthesis of 1-Azido-2-bromoethanol (31b) in $CDCl_3$

Equal volumes of bromoacetaldehyde diethyl acetal (**29**) and 0.1N sulfuric acid were heated gently under reflux for 1 hr. and then allowed to cool. The pale yellow solution was carefully distilled at atmospheric pressure over 3–4 h and the fractions boiling between 75–80 °C were collected. To this colorless solution, 1N sodium hydroxide was added drop wise under stirring, until the pH of the turbid mixture was 7.0. Bromoacetaldehyde (**30b**) was extracted from the mixture by shaking with 3 volumes of $CHCl_3$. The organic layer was collected, dried over magnesium sulfate, filtered and partially evaporated under vacuum to give a mixture of bromoacetaldehyde (**30b**) and $CHCl_3$.[38] Bromoacetaldehyde (**30b**) is a toxic volatile compound with pungent smell. That is why $CHCl_3$ was removed only prior to use.

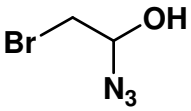
Bromoacetaldehyde (30b): Pale yellow liquid. – **^{1}H NMR** ($CDCl_3$): δ = 3.84 (d, ^3J = 2.4 Hz, 2H), 9.54 (t, ^3J = 2.4 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 34.65 (t, CH_2), 191.9 (d, CH).



30b

Bromoacetaldehyde (**30b**) (121.9 mg, 1 mmol) was mixed with a solution of 5M HN_3 in $CDCl_3$ (2 ml, 10 mmol), and stirred at room temperature for 10 minutes to obtain an equilibrium mixture containing 1-azido-2-bromoethanol (**31b**). The ratio between 1-azido-2-bromoethanol (**31b**) and bromoacetaldehyde (**30b**) is ca. 5:1 at room temperature due to ^1H NMR integration.

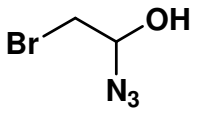
1-Azido-2-bromoethanol (31b): Light yellow liquid, 87% NMR-yield.– **^{1}H NMR** ($CDCl_3$): δ = 3.45 (m, 2H, diastereotopic protons), 3.61 (d, ^3J = 9.2 Hz, OH), 5.12 (dt, ^3J = 9.2 Hz, ^3J = 4.4 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 35.9 (t, CH_2), 82.7 (d, CH).



31b

4.3.5. Synthesis of 1-Azido-2-bromoethanol in DMSO-d_6 (31b)

Bromoacetaldehyde (**30b**) (121.9 mg, 1 mmol) and DMSO-d_6 (2 ml) were mixed with a solution of 5M HN_3 in $CHCl_3$ (2 ml, 10 mmol), and stirred at room temperature for 10 minutes to obtain an equilibrium mixture containing 1-azido-2-bromoethanol (**31b**). The excess of HN_3, bromoacetaldehyde (**30b**) and $CHCl_3$ was distilled off under vacuum at −30 °C to −20 °C to obtain 1-azido-2-bromoethanol (**31b**) in DMSO-d_6.

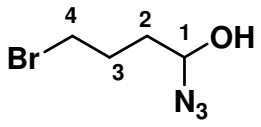


31b

1-Azido-2-bromoethanol (31b): Light yellow Liquid, 87% NMR-yield.– **^{1}H NMR** (DMSO-d_6): δ = 3.31 (d, ^3J = 5.2 Hz, OH), 3.49 (dd, ^2J = 10.4 Hz, ^3J = 5.2, 1H, diastereotopic proton), 3.52 (dd, ^2J = 10.4 Hz, ^3J = 5.2, 1H, diastereotopic proton), 5.14 (t, ^3J = 4.8 Hz, 1H). – **^{13}C NMR** (DMSO-d_6): δ = 36.7 (t, CH_2), 84.2 (d, CH).

4.3.6. Synthesis of 1-Azido-4-bromobutan-1-ol (38a)

4-Bromobutanal (**37a**) (0.37 g, 2.5 mmol) was mixed with 5M HN_3 solution in $CDCl_3$ (3 ml, 15 mmol). The mixture was stirred at room temperature to acquire an equilibrium mixture containing 1-azido-4-bromobutan-1-ol (**38a**). It was not possible to isolate pure 1-azido-4-bromobutan-1-ol (**38a**) from the equilibrium mixture.



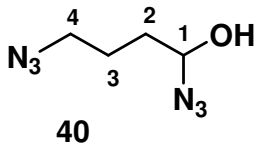
38a

1-Azido-4-bromobutan-1-ol (38a): **^{1}H NMR** ($CDCl_3$): δ = 1.72−1.78 (m, 2H, H-3, diastereotopic protons), 1.86−1.96 (m, 2H, H-2, diastereotopic protons), 3.39 (t, J = 6.8 Hz, 2H, H-4), 4.90 (t, J = 5.8 Hz, 1H, H-1). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 27.4 (t, CH_2), 32.9 (t, CH_2), 34.5 (t, CH_2), 85.2 (d, CH).

4.3.7. Synthesis of 1,4-Diazidobutan-1-ol (40)

4-Azidobutanal (**39**) (0.27 g, 2.5 mmol) was mixed with 5M HN_3 solution in $CDCl_3$ (3 ml, 15 mmol). The mixture was stirred at room temperature to obtain an equilibrium mixture containing 1,4-diazidobutan-1-ol (**40**). It was not possible to isolate pure 1,4-diazidobutan-1-ol (**40**) from the equilibrium mixture.

1,4-Diazidobutan-1-ol (40): **^{1}H NMR** ($CDCl_3$): δ = 1.64 (m, 4H, H-2, H-3, diastereotopic protons), 3.27 (m, 2H, H-4), 4.85 (t, *J* = 5.6 Hz, 1H, H-1). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 23.7 (t, CH_2), 33.1 (t, CH_2), 50.6 (t, CH_2), 85.4 (d, CH).

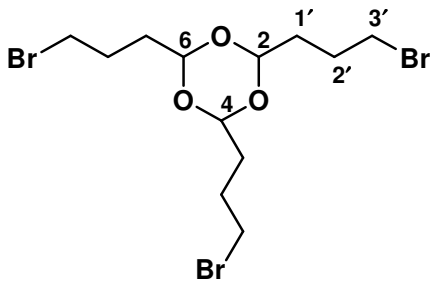


40

4.3.8. Synthesis of 2,4,6-Tris(3-bromopropyl)-1,3,5-trioxane (41a)

4-Bromobutanal (**37a**)[39,41] was stored in the freezer at −25 °C to −30 °C. After 3 weeks **37a** was completely transformed into **41a.** Compound **41a** was purified by recondensation at 40 °C under high vacuum. Attempts to recondensate **41a** at 100 °C led to **37a** due to cleavage of the cyclic acetal.

2,4,6-Tris(3-bromopropyl)-1,3,5-trioxane (41a):
Colorless oil, 87% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.79–1.84 (m, 6H, diastereotopic protons, H-1′), 1.96–2.03 (m, 6H, diastereotopic protons, H-2′), 3.43 (t, ^3J = 6.6 Hz, 6H, H-3′), 4.92 (t, ^3J = 5.2 Hz, 3H, H-2, H-4, H-6). – **^{13}C NMR** ($CDCl_3$): δ = 26.6 (t, CH_2), 32.7 (t, CH_2), 33.3 (t, CH_2), 100.3 (d, CH). – **IR** (CCl_4): $\tilde{\nu}$ = 2966 cm^{-1}, 2833 cm^{-1} (CH_2), 1077 cm^{-1} (HC–O–CH), 564 cm^{-1} (CH_2–Br). – **Anal. Calcd (%) for $C_{12}H_{21}O_3Br_3$** (453.01): C, 31.81; H, 4.67. **Found:** C, 31.13; H; 4.74.

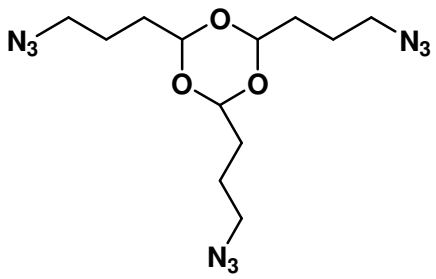


41a

4.3.9. Synthesis of 2,4,6-Tris(3-azidopropyl)-1,3,5-trioxane (42)

A mixture of 2,4,6-tris(3-bromopropyl)-1,3,5-trioxane (**41a**) (0.88 g, 1.94 mmol) and sodium azide (130 mg, 2 mmol) in DMF (5 ml) was stirred overnight at 50 °C. The reaction mixture was diluted with ether/hexane (1:1, 25 ml), washed twice with water and twice with brine, dried over $MgSO_4$, and the solvent was distilled off under vacuum to yield 2,4,6-tris(3-azidopropyl)-1,3,5-trioxane (**42**) as colorless liquid (0.62 g, 1.85 mmol, 96%).
The compound (**42**) was purified by short path recondensation at 25 °C under high vacuum. No reaction was observed by repeating treatment of **41a** with sodium azide at 0 °C or at room temperature.

2,4,6-Tris(3-azidopropyl)-1,3,5-trioxane (42): Colorless liquid, 96% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.66–1.77 (m, 12H, diastereotopic protons), 3.29 (t, 6H, *J* = 6.6 Hz), 4.90 (t, *J* = 4.4 Hz, 3H). – **^{13}C NMR** ($CDCl_3$): δ = 22.8 (t, CH_2), 31.2 (t, CH_2), 51.1 (t, CH_2), 100.5 (d, CH). – **IR** (CCl_4): $\tilde{\nu}$ = 2933 cm^{-1}, 2864 cm^{-1} (CH_2), 2095 cm^{-1} (N_3).



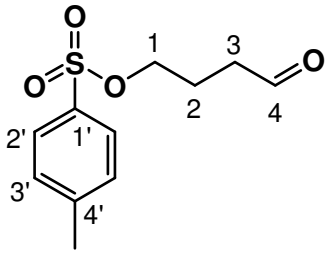
42

4.3.10. Synthesis of 4-Oxobutyl 4-Methylbenzenesulfonate (37b)

By following a known procedure, 4-hydroxybutyl 4-methylbenzenesulfonate (**36b**) was prepared, and was used without any further purification.[40]

To the stirred mixture of pyridinium chlorochromate (PCC, 2.5 g, 11.59 mmol) in CH_2Cl_2 (20 ml), under nitrogen at 0 °C, was added 4-hydroxybutyl 4-methylbenzenesulfonate (**36b**) (2 g, 8.18 mmol) over several minutes. After one hour the mixture was diluted with pentane (10 ml) and the solvent was decanted off. The black residue was extracted twice with pentane (10 ml). The combined pentane extracts were filtered through a short plug of silica gel, using pentane as eluant, yielding 4-oxobutyl 4-methylbenzenesulfonate (**37b**), as colorless oil (1.56 g, 6.46 mmol, 79%).

4-Oxobutyl 4-Methylbenzenesulfonate (37b): Colorless oil, 79% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.95 (m, 2H), 2.44 (s, 3H, CH_3), 2.55 (m, 2H), 4.05 (t, ^3J = 6.0 Hz, 2H, H-1), 7.34 (m, 2H, Ar), 7.75 (m, 2H, Ar), 9.70 (s, 1H, CHO). – **^{13}C NMR** ($CDCl_3$): δ = 21.41 (t, CH_2), 21.6 (q, CH_3), 39.5 (t, CH_2), 69.3 (t, CH_2), 127.8 (d, CH, Ar), 129.8 (d, CH, Ar), 132.7 (s, C, Ar), 144.9 (s, C, Ar), 200.4 (d, C=O). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 2745 cm^{-1} (H–C=O), 1713 cm^{-1} (C=O), 1599 cm^{-1} (Ar), 1495 cm^{-1} (Ar), 1178 cm^{-1} (C–O).

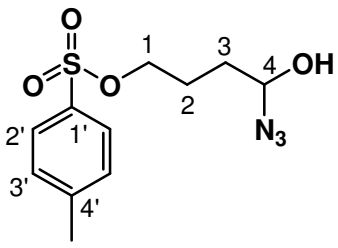


37b

4.3.11. Synthesis of 4-Azido-4-hydroxybutyl 4-Methylbenzenesulfonate (38b)

4-Oxobutyl 4-methylbenzenesulfonate (**37b**) (242.29 mg, 1.0 mmol) was mixed with 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol). The mixture was stirred at room temperature to obtain an

equilibrium mixture containing 4-azido-4-hydroxybutyl 4-methylbenzenesulfonate (**38b**). It was not possible to isolate pure 4-azido-4-hydroxybutyl 4-methylbenzenesulfonate (**38b**) from the equilibrium mixture at room temperature.



38b

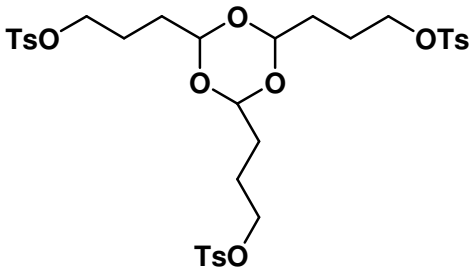
4-Azido-4-hydroxybutyl 4-Methylbenzenesulfonate (38b): ^{1}H NMR ($CDCl_3$): δ = 1.63 (m, 2H, diastereotopic protons), 1.72 (m, 2H, diastereotopic protons), 2.42 (s, 3H, CH_3), 4.01 (t, ^{3}J = 6.4 Hz, 2H, H-1), 4.84 (t, ^{3}J = 5.6 Hz, 1H, H-4), 7.33 (m, 2H, Ar), 7.71 (m, 2H, Ar). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 21.14 (t, CH_2), 21.3 (q, CH_3), 32.07 (t, CH_2), 69.4 (t, CH_2), 85.2 (d, CH), 127.5 (d, CH, Ar), 129.8 (d, CH, Ar), 131.9 (s, C, Ar), 145.2 (s, C, Ar).

4.3.12. Synthesis of 3,3',3''-(1,3,5-Trioxane-2,4,6-triyl)tris(propane-3,1-diyl) Tris(4-methylbenzenesulfonate) (41b)

4-Oxobutyl 4-methylbenzenesulfonate (**37b**) was stored in the freezer at −25 °C to −30 °C. After 3 weeks **37b** was completely transformed to 3,3',3''-(1,3,5-trioxane-2,4,6-triyl)tris(propane-3,1-diyl) tris(4-methylbenzenesulfonate) (**41b**).

Compound **41b** was purified by removing the starting material at 40 °C under high vacuum. Attempts to recondensate **41b** at 100 °C led to cleavage of cyclic acetal to produce **37b**.

K. Arimitsu et al. reported 2,4,6-tris(2-tosyloxyethyl)-1,3,5-trioxane as an acid amplifier, in autocatalytic decomposition of acid proliferation reaction in polymer films.[75]



41b

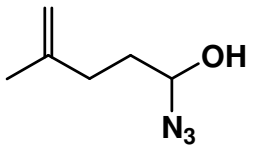
3,3',3''-(1,3,5-Trioxane-2,4,6-triyl)tris(propane-3,1-diyl) Tris(4-methylbenzenesulfonate) (41b): Colorless oil, 89% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.64 (m, 6H), 1.70 (m, 6H), 2.45 (s, 9H), 4.02 (t, ^{3}J = 6.0 Hz, 6H), 4.78 (t, ^{3}J = 5.2 Hz, 3H), 7.33 (m, 6H, Ar), 7.77 (m, 6H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 21.6 (q, CH_3), 30.0 (t, CH_2), 39.5 (t, CH_2), 70.0 (t, CH_2), 100.0 (d, CH), 127.8 (d, CH, Ar), 129.8 (d, CH, Ar), 132.9 (s, C, Ar), 144.7 (s, C, Ar). – **IR** (CCl_4): $\tilde{\nu}$ = 2966 cm^{-1}, 2833 cm^{-1} (CH_2), 1597 cm^{-1} (Ar), 1498 cm^{-1} (Ar), 1178 cm^{-1} (C–O),

942 cm^{-1} (HC–O–CH). – **Anal. Calcd (%) for $C_{33}H_{42}O_{12}S_3$** (726.87): C, 54.53; H, 5.82; O, 26.41; S, 13.23. **Found:** C, 54.42; H, 5.79; S, 13.14.

4.3.13. Synthesis of 1-Azido-4-methylpent-4-en-1-ol (53)

4-Methylpent-4-enal (**52**) was prepared by a known method,[50] and was purified by flash chromatography using CH_2Cl_2 as eluant. 4-Methylpent-4-enal (**52**) (98.14 mg, 1 mmol) was mixed with 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol). The mixture was stirred at room temperature to obtain an equilibrium mixture containing 1-azido-4-methylpent-4-en-1-ol (**53**).

1-Azido-4-methylpent-4-en-1-ol (53): ^{1}H NMR ($CDCl_3$): δ = 1.70 (s, 3H), 1.75 (m, 2H, diastereotopic protons), 2.09 (t, *J* = 8.0 Hz, 2H), 4.70 (m, 2H), 4.87 (t, ^3J = 5.6 Hz, 1H). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 21.9 (q, CH_3), 32.2 (t, CH_2), 33.8 (t, CH_2), 85.9 (d, CH), 110.3 (t, CH_2), 143.6 (s, C).



53

4.4. Synthesis of 4-Azido-4-methylpentanal (39b)

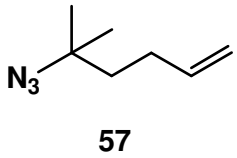
4.4.1. Synthesis of 5-Azido-5-methylhex-1-ene (57)

According to a known procedure 2-methylhex-5-en-2-ol (**56**) was synthesized as a colorless liquid with 96% yield, and was used without any further purification.[76]

A. L. Logothetis synthesized 5-azido-5-methylhex-1-ene (**57**) by reaction of 2-methylhex-5-en-2-ol (**56**) with HN_3 in the presence of H_2SO_4 and CH_3Cl as solvent at 0 °C to −5 °C, with 41–46% yield.[44a] The above method was modified to obtain 80% yield of (**57**).

To the stirred solution of 5M HN_3 (10 ml, 50 mmol) in $CHCl_3$ and 4-methylbenzenesulfonic acid (3.44 g, 20 mmol) was added 2-methylhex-5-en-2-ol (**56**) (3 g, 26.27 mmol) in $CHCl_3$ (10 ml) at 0 °C over several minutes. The reaction mixture was slowly warmed to room temperature and stirred for two hours. The mixture was diluted with ice water; the chloroform layer was separated, washed three times with water, and dried over $MgSO_4$. The solvent was removed at 20 °C to yield a crude product, which was purified by flash chromatography (95:5

hexane/ethyl acetate) to give 5-azido-5-methylhex-1-ene (**57**) as a light yellow oily liquid (2.92 g, 21.0 mmol, 80%).

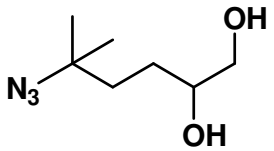


57

5-Azido-5-methylhex-1-ene (57): Light yellow oily liquid, 80% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.27 (s, 6H), 1.57 (m, 2H), 2.12 (m, 2H), 5.05 (m, 2H), 5.82 (m, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 25.98 (q, CH_3), 28.5 (t, CH_2), 40.5 (t, CH_2), 61.3 (s, C), 114.73 (t, CH_2), 138.0 (d, CH). – **IR** (CCl_4): $\tilde{\nu}$ = 2975 cm^{-1} (C–H), 2096 cm^{-1} (N_3), 1641 cm^{-1} (C=C).

4.4.2. Synthesis and Oxidation of 5-Azido-5-methylhexane-1,2-diol (58)

To the stirred solution of 5-azido-5-methylhex-1-ene (**57**) (2.0 g, 14.36 mmol) in MeOH (15 ml), was added $KMnO_4$ solution (4.74 g, 30 mmol), in water (200 ml) and $MgSO_4$ (4 g), drop wise by maintaining the temperature between 0 °C to 5 °C. After complete addition, the reaction mixture was stirred for further 2 hours at 0 °C to 5 °C. The reaction mixture was filtered and brown precipitates were removed. The filtrate was extracted with chloroform (5 × 15 ml), washed with NaCl solution, and dried over $MgSO_4$. The removal of solvent yielded 5-azido-5-methylhexane-1,2-diol (**58**) as a colorless liquid (2.36 g, 13.64 mmol, 95%), which was used for next step without any further purification.

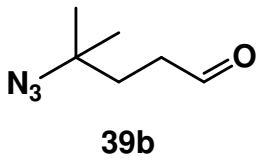


58

5-Azido-5-methylhexane-1,2-diol (58): Colorless liquid, 95% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.25 (s, 6H), 1.47 (m, 2H), 1.57 (m, 2H), 3.20 (br s, 2H), 3.43 (m, 1H), 3.63 (m, 2H). – **^{13}C NMR** ($CDCl_3$): δ = 26.0 (q, CH_3), 27.6 (t, CH_2), 37.3 (t, CH_2), 61.3 (s, C), 66.5 (t, CH_2), 72.1 (d, CH).

To a stirred solution of periodic acid (2.87 g, 15 mmol) in dry THF (10 ml) under nitrogen at 0 °C was added a solution of 5-azido-5-methylhexane-1,2-diol (**58**) (2.0 g, 11.54 mmol) in 15 ml of dry THF, slowly over a period of 1 hour. The reaction mixture was stirred for further one hour at room temperature. The solid was filtered off and extracted with cold THF. The solvent was removed under vacuum at room temperature to obtain a residue, which was dissolved in ethyl acetate (50 ml) and washed with saturated NaCl solution containing 15% sodium thiosulfate. The organic layer was dried over $MgSO_4$. Solvent was removed to obtain

crude 4-azido-4-methylpentanal (**39b**), followed by flash chromatography using $CHCl_3$ as eluant to afford **39b** as light yellow liquid (1.40 g, 9.91 mmol, 85%).

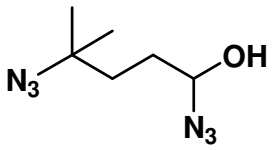


39b

4-Azido-4-methylpentanal (39b): Light yellow liquid, 85% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.29 (s, 6H), 1.81 (t, ^3J = 7.6 Hz, 2H), 2.54 (td, ^3J = 6.8 Hz, ^3J = 1.2 Hz, 2H), 9.79 (t, ^3J = 1.2 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 25.9 (q, CH_3), 33.2 (t, CH_2), 39.1 (t, CH_2), 61.2 (s, C), 201.3 (d, CHO). – **IR** (CCl_4): $\tilde{\nu}$ = 2719 cm^{-1} (C–H), 2102 cm^{-1} (N_3), 1729 cm^{-1} (C=O).

4.5. Synthesis of 1,4-Diazido-4-methylpentan-1-ol (54)

4-Azido-4-methylpentanal (**39b**) (114.17 mg, 1 mmol) was mixed with 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol). The mixture was stirred at room temperature to obtain an equilibrium mixture containing 1,4-diazido-4-methylpentan-1-ol (**54**). It was not possible to isolate pure 1,4-diazido-4-methylpentan-1-ol (**54**) from the equilibrium mixture.



54

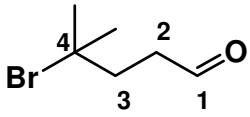
1,4-Diazido-4-methylpentan-1-ol (54): **^{1}H NMR** ($CDCl_3$): δ = 1.42 (s, 6H), 1.53 (m, 2H, diastereotopic protons), 1.66 (t, J = 6.0 Hz, 2H), 4.86 (t, J = 6.0 Hz, 1H). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 25.4 (q, CH_3), 30.9 (t, CH_2), 35.6 (t, CH_2), 61.2 (s, C), 85.9 (d, CH).

4.6 Synthesis of 4-Bromo-4-methylpentanal (37c)

5-Bromo-5-methylhex-1-ene (**59**) was prepared by following a known procedure with 85% yield, and was used for the next step without any further purification.[77]

The reaction was performed in a 500 ml round-bottomed, three-necked flask with magnetic stirrer, fitted with a gas inlet for ozonolysis, gas outlet, and a thermometer. The gas outlet was connected with a flask bearing a saturated solution of potassium iodide. 5-Bromo-5-methylhex-1-ene (**59**) (1 g, 5.65 mmol) was dissolved in 250 ml of dichloromethane. The flask was cooled to −78 °C and ozone was bubbled through the solution, approximately 1.5 hours at −78 °C, until a persistent brown color appears in the saturated solution of potassium iodide. Nitrogen gas was then bubbled through the solution for 30 min and dimethyl sulfide (3.75 ml, 50 mmol) was added. The reaction mixture was warmed slowly to

room temperature and stirred for 12 hours. The solvent and excess dimethyl sulfide was removed under vacuum at −20 °C to obtain a crude product. The crude mixture was purified by flash chromatography on silica gel, eluting with CH_2Cl_2 to yield 4-bromo-4-methylpentanal (**37c**) as a light yellow liquid (160 mg, 0.89 mmol, 16%) after the removal of solvent.

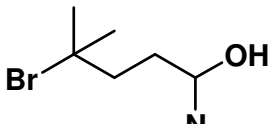


37c

4-Bromo-4-methylpentanal (37c): Light yellow liquid, 16% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.76 (s, 6H), 2.10 (t, ^3J = 7.2 Hz, 2H, H-3), 2.76 (td, ^3J = 7.6 Hz, ^3J = 1.2 Hz, 2H, H-2), 9.82 (t, ^3J = 1.2 Hz, 1H, H-1). – **^{13}C NMR** ($CDCl_3$): δ = 34.2 (q, CH_3), 38.8 (t, CH_2, C-3), 41.5 (t, CH_2, C-2), 66.2 (s, C-4), 201.0 (d, CHO, C-1). The assignment of the signals was made by ^{13}C, ^{1}H correlation (gHSQCAD spectrum). – **IR** (CCl_4): $\tilde{\nu}$ = 2719 cm^{-1} (C–H), 1729 cm^{-1} (C=O), 508 cm^{-1} (C–Br).

4.7. Synthesis of 1-Azido-4-bromo-4-methylpentan-1-ol (62)

4-Bromo-4-methylpentanal (**37c**) (40 mg, 0.22 mmol) was mixed with 2M HN_3 solution in $CDCl_3$ (1.0 mmol, 0.5 ml). The mixture was stirred at room temperature to obtain an equilibrium mixture containing 1-azido-4-bromo-4-methylpentan-1-ol (**62**). It was not possible to isolate pure 1-azido-4-bromo-4-methylpentan-1-ol (**62**) from the equilibrium mixture at room temperature.



62

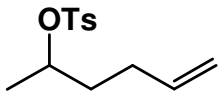
1-Azido-4-bromo-4-methylpentan-1-ol (62): **^{1}H NMR** ($CDCl_3$): δ = 1.72 (s, 6H), 1.84 (m, 2H, diastereotopic protons), 2.60 (t, ^3J = 7.2 Hz, 2H), 4.90 (t, ^3J = 6.0 Hz, 1H). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 33.7 (q, CH_3), 38.5 (t, CH_2), 41.1 (t, CH_2), 66.5 (s, C), 85.8 (d, CH).

4.8. Synthesis of 5-Azidohex-1-ene (167)

5-Azidohex-1-ene (**167**) was prepared by a three step reaction. Hex-5-en-2-ol (**165**)[78] was prepared by following a literature known method.

4.8.1. Synthesis of Hex-5-en-2-yl 4-methylbenzenesulfonate (166)

4-Methylbenzenesulfonyl chloride (6.2 g, 30 mmol) in 20 ml dry pyridine under argon was cooled with an ice bath and hex-5-en-2-ol (**165**) (2 g, 20 mmol) solution in dry pyridine (10 ml) was added slowly over a period of 30 minutes. The reaction mixture was warmed up slowly to room temperature and stirred for 18 hours. To the reaction mixture was added a 5% cold solution of HCl (100 ml). This mixture was stirred for further 20 minutes and then slowly warmed to room temperature. The above reaction mixture was extracted with toluene (4 × 15 ml) and washed with NaCl solution. The organic layer was dried over $MgSO_4$. Solvent was removed to obtain crude hex-5-en-2-yl 4-methylbenzenesulfonate (**166**), followed by flash chromatography using (hexane/ethyl acetate) as eluant to afford **166** as colorless oily liquid, (4.68 g, 18.4 mmol, 92%). The compound **166** was prepared by A. L. Logothetis in 1965 but NMR-data were not described.[44a]

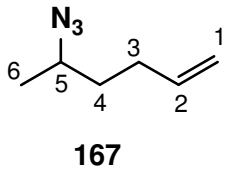


166

Hex-5-en-2-yl 4-Methylbenzenesulfonate (166): Colorless oily liquid, 92% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.20 (d, ^3J = 6.4 Hz, 3H), 1.55 (m, 1H), 1.64 (m, 1H), 1.92 (m, 2H), 2.37 (s, 3H), 4.56 (qt, ^3J = 6.4 Hz, ^3J = 6.2 Hz, 1H), 4.88 (m, 2H), 5.61 (m, 1H), 7.28 (m, 2H, Ar), 7.73 (m, 2H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 20.5 (q, CH_3), 21.3 (q, CH_3), 28.7 (t, CH_2), 35.3 (t, CH_2), 79.6 (d, CH), 115.1 (t, CH_2), 127.4 (d, CH, Ar), 129.5 (d, CH, Ar), 134.2 (s, C, Ar), 136.8 (d, CH), 144.3 (s, C, Ar).

4.8.2. Synthesis of 5-Azidohex-1-ene (167)

To the stirred solution of NaN_3 (1.5 g, 23 mmol) in MeOH (10 ml) at room temperature was added solution of hex-5-en-2-yl 4-methylbenzenesulfonate (**166**) (2 g, 7.86 mmol) in MeOH (25 ml), over several minutes. The reaction mixture was stirred at room temperature for 2 days. The mixture was filtered to remove solids and MeOH was removed under vacuum to get crude product, which was purified by flash chromatography on silica gel, eluting with CH_2Cl_2 to yield 5-azidohex-1-ene (**167**) as a colorless liquid (0.836 g, 6.68 mmol, 85%) after the removal of solvent. The compound **167** was prepared in 1965 by A. L. Logothetis but NMR-data were not given.[44a]



167

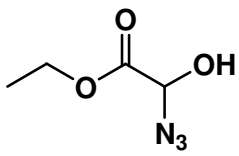
5-Azidohex-1-ene (167): Colorless liquid, 85% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.25 (d, ^3J = 6.4 Hz, 3H, H-6), 1.57 (m, 2H, H-4), 2.14 (m, 2H, H-3), 3.45 (m, 1H, H-5), 5.02 (m, 2H, H-1), 5.78 (m, 1H, H-2). – **^{13}C NMR** ($CDCl_3$): δ = 19.3 (q, CH_3, C-6), 30.1 (t, CH_2, C-3), 35.2 (t, CH_2, C-4), 57.2 (d, CH, C-5), 115.2 (t, CH_2, C-1), 137.3 (d, CH,C-2).

4.9. α-Azido Alcohol from Electron Poor Aliphatic Aldehydes

4.9.1. Synthesis of Ethyl 2-Azido-2-hydroxyacetate (65a)

50% Ethyl glyoxylate oligomer in toluene was distilled at atmospheric pressure at 130–185 °C (gradually increased over 30 min); until a small amount of residue remained. The distillate mixture was immediately redistilled ($Kp._{30\ Torr}$: 48–50 °C). After toluene was fractionated, pure ethyl glyoxylate was distilled at 48 °C at 30 Torr. Ethyl glyoxylate oligomerizes readily on standing at room temperature as well as in the freezer (–25 to –30 °C).

Ethyl glyoxylate (**64a**) (0.102 g, 1 mmol) and 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol) were mixed and stirred at room temperature for 10 minutes. The excess of solvent and HN_3 were distilled off at –40 °C under vacuum to obtain ethyl 2-azido-2-hydroxyacetate (**65a**) as colorless liquid. It was not possible to recondense **65a** and to remove the starting materials completely.



65a

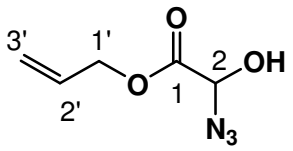
Ethyl 2-Azido-2-hydroxyacetate (65a): Colorless liquid, 92% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.35 (t, ^3J = 7.2 Hz, 3H), 3.89 (d, ^2J = 10.0 Hz, 1H, OH), 4.34 (q, ^3J = 7.2 Hz, 2H), 5.19 (d, ^2J = 10 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 13.7 (q, CH_3), 63.1 (t, CH_2), 80.4 (d, CH), 168.3 (s, C=O). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 3511 cm^{-1} (OH), 2115 cm^{-1} (N_3), 1747 cm^{-1} (C=O).

4.9.2. Synthesis of Allyl 2-Azido-2-hydroxyacetate (65b)

According to a known procedure allyl 2-oxoacetate **(64b)** was prepared as a yellow liquid with 69% yield, and was used without any further purification.[72b]

Allyl 2-oxoacetate (**64b**) (114.1 mg, 1.0 mmol) was mixed with 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol). The mixture was stirred at room temperature for 10 minutes. The excess of

solvent and HN_3 was distilled off at −40 °C under vacuum to obtain allyl 2-azido-2-hydroxyacetate (**65b**) as light yellow liquid. It was not possible to recondense **65b** and to remove starting materials completely.



65b

Allyl 2-Azido-2-hydroxyacetate (65b): Light yellow liquid, 90% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 4.70 (dd, ^3J = 6.0 Hz, ^4J = 2.4 Hz, 2H, H-1'), 5.19 (s, 1H, H-2), 5.33 (m, 2H, H-3'), 5.91 (m, 1H, H-2'). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 67.2 (t, CH_2, C-1'), 80.5 (d, CH, C-2), 119.7 (t, CH_2, C-3'), 130.3 (d, CH, C-2'), 168.0 (s, C=O). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 3521 cm^{-1} (OH), 2943 cm^{-1} (C–H), 2112 cm^{-1} (N_3), 1753 cm^{-1} (C=O), 1455 cm^{-1} (C=C).

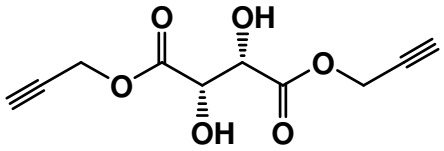
4.9.3. Reaction of Prop-2-ynyl 2-Oxoacetate (64c) with HN_3

4.9.3.1. Synthesis of Diprop-2-ynyl 2,3-Dihydroxysuccinate (69)

The known procedure for the preparation of allyl 2-oxoacetate (**64b**) was repeated with small changes to prepare prop-2-ynyl 2-oxoacetate (**65c**).[72b]

To a stirred solution of (2*R*,3*R*)-2,3-dihydroxysuccinic acid (**66**) (5 g, 33.3 mmol) in dry DMF (25 ml) under nitrogen at 0 °C, was added triethylamine (18.5 ml, 133 mmol). A solution of 3-bromoprop-1-yne (10.98 g, 92.29 mmol) in dry DMF (25 ml) was added slowly over a period of 3 hours, and reaction mixture was warmed to room temperature. The reaction mixture was stirred for 16 hours at room temperature.

The solvent was removed under vacuum at 20 °C. The residue was dissolved in 50 ml of ethyl acetate and washed with ice cold water, ice cold saturated $NaHCO_3$ solution, and saturated NaCl solution. The organic layer was dried over $MgSO_4$. The solvent was removed under vacuum to obtain (2*S*,3*S*)-diprop-2-ynyl 2,3-dihydroxysuccinate (**69**) as a colorless solid (5.87 g, 25.96 mmol, 78%), which was recrystallized from hexane and methanol (20:1) to furnish colorless crystals, with melting point (59–60° C).



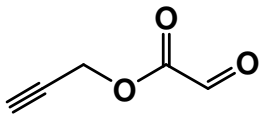
69

(2*S*,3*S*)-Diprop-2-ynyl 2,3-Dihydroxysuccinate (69): Colorless crystals, **Mp:** 59–60° C, 78% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 2.55 (t, ^4J = 2.4 Hz, 2H), 3.29 (d,

^3J = 8.0 Hz, 2H), 4.65 (d, ^3J = 7.6, 2H), 4.84 (m, 4H). – **^{13}C NMR** ($CDCl_3$): δ = 53.69 (t, CH_2), 71.9 (d, CH), 76.0 (d, CH), 76.4 (s, C≡C), 170.5 (s, C=O). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 3544 cm^{-1} (OH), 3307 cm^{-1} (C≡C–H), 2952 cm^{-1} (CH_2), 2134 cm^{-1} (C≡C), 1755 cm^{-1} (C=O), 1243 cm^{-1} (C–O). – **Anal. Calcd (%) for $C_{10}H_{10}O_6$** (226.18): C, 53.10; H, 4.46; O, 42.44. **Found:** C, 53.04; H, 4.49.

4.9.3.2. Synthesis of Prop-2-ynyl 2-Oxoacetate (64c)

To a stirred solution of periodic acid (5.00 g, 26.05 mmol) in dry THF (70 ml) under nitrogen at 0 °C was added a solution of diprop-2-ynyl 2,3-dihydroxysuccinate (**69**) (5.00 g, 22.11 mmol) in dry THF (20 ml), slowly over a period of 1 hour. The reaction mixture was stirred for further one hour at room temperature. The solid was filtered off and washed with cold THF. The solvent was removed under vacuum at room temperature to obtain a residue, which was dissolved in ethyl acetate (50 ml) and washed with saturated NaCl solution containing 15% sodium thiosulfate. The organic layer was dried over $MgSO_4$. Solvent was removed to obtain prop-2-ynyl 2-oxoacetate (**64c**) as a pale yellow oil, (2.32 g, 20.69 mmol, 94%), and was used without any further purification.



64c

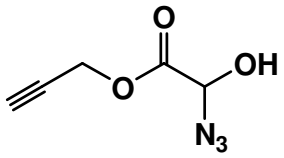
Prop-2-ynyl 2-Oxoacetate (64c): Pale yellow oil, 94% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 2.50 (t, ^4J = 2.4 Hz, 1H), 4.77 (d, ^4J = 2.4 Hz, 2H), 9.40 (s, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 53.52 (t, CH_2), 75.6 (d, CH), 76.0 (s, C≡C), 167.17 (s, C=O), 182.5 (d, CHO). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 3312 cm^{-1} (C≡C–H), 2978 cm^{-1} (C–H), 2134 cm^{-1} (C≡C), 1760 cm^{-1} (C=O), 1279 cm^{-1} (C–O).

Owing to unstability of compound **64c**, a correct HRMS or elemental analysis could not be obtained.

4.9.3.3. Synthesis of Prop-2-ynyl 2-Azido-2-hydroxyacetate (65c)

Prop-2-ynyl 2-oxoacetate (**64c**) (112.08 mg, 1.00 mmol) was mixed with 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol) at –20 °C. The mixture was slowly warmed to room temperature and stirred for 16 h. The excess of solvent and HN_3 was distilled off at –40 °C under vacuum to obtain prop-2-ynyl 2-azido-2-hydroxyacetate (**65c**) as light yellow liquid. It was not possible to recondense **65c** and to remove starting materials completely.

Prop-2-ynyl 2-Azido-2-hydroxyacetate (65c): Light yellow liquid, 92% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 2.59 (t, ^4J = 2.4 Hz, 1H), 4.80 (m, 2H), 5.24 (s, 1H). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 53.9 (t, CH_2), 75.7 (d, CH), 76.2 (s, C≡C), 80.4 (d, CH), 167.5 (s, C=O). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 3521 cm^{-1} (OH), 3312 cm^{-1} (H–C≡C), 2113 cm^{-1} (N_3), 1761 cm^{-1} (C=O), 1274 cm^{-1} (C–O).

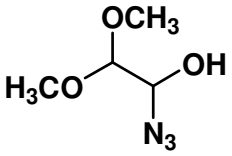


65c

4.9.4. Synthesis of 1-Azido-2,2-dimethoxyethanol (72):

2,2-Dimethoxyacetaldehyde (**71**) (104.1 mg, 1.0 mmol) and 5M HN_3 solution in $CDCl_3$ (2 ml, 10 mmol) were mixed and stirred at room temperature for 10 minutes at 0 °C, and was further stirred overnight at room temperature to obtain equilibrium mixture containing 1-azido-2,2-dimethoxyethanol (**72**). The excess of solvent and HN_3 was distilled off at −50 °C under vacuum to obtain 1-azido-2,2-dimethoxyethanol (**72**) as colorless liquid, which was carefully resolved cold $CDCl_3$ maintaining the temperature at −50 °C.

1-Azido-2,2-dimethoxyethanol (72): Colorless liquid, 90% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 3.46 (s, 3H, CH_3), 3.50 (s, 3H, CH_3), 3.9 (br s, 1H, OH), 4.21 (d, ^3J = 3.2 Hz, 1H, H-2), 4.86 (br m, 1H, H-1). – **^{13}C NMR** ($CDCl_3$): δ = 55.7 (q, CH_3), 56.1 (q, CH_3), 83.9 (d, CH, C-1), 104.0 (d, CH, C-2). The assignment of the signals is based on ^{13}C, ^{1}H correlation. – **IR** (CCl_4): $\tilde{\nu}$ = 3438 cm^{-1} (O–H), 2937 cm^{-1} (C–H), 2108 cm^{-1} (N_3), 1235 cm^{-1} (C–O).

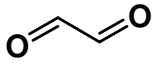


72

4.9.5. Synthesis of 1,2-Diazidoethane-1,2-diol (75)

By following a known procedure oxalaldehyde gas (**74**) was produced and a diluted solution in $CDCl_3$ was obtained which polymerizes on standing at room temperature.[52]

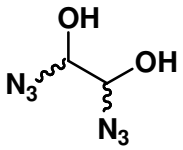
Oxalaldehyde (74): **^{1}H NMR** ($CDCl_3$): δ = 9.29 (s, 2H). – **^{13}C NMR** ($CDCl_3$): δ = 188.2 (d, CH).



74

Oxalaldehyde (**74**) was passed through 5M HN_3 solution in $CDCl_3$ (2 ml, 10 mmol) at −50 °C over a period of 15 minutes and stirred for further 10 minutes. The excess of solvent and HN_3 was distilled off at −50 °C under vacuum to obtain *meso*- and *racem*- 1,2-diazidoethane-1,2-

diol (**75**) as colorless liquid, which was carefully resolved in cold $CDCl_3$ keeping the temperature at −50 °C.



75
(*meso* + *rac*)

1,2-Diazidoethane-1,2-diol (*meso* and *rac*) (75): Colorless liquid, 97% NMR-yield. – **^{1}H NMR** ($CDCl_3$): δ = 3.21 (br d, 2H, OH), 4.98 (d, ^3J = 7.6 Hz, 2H). – **^{13}C NMR** ($CDCl_3$): δ = 84.5 (d, CH), 84.9 (d, CH). The assignment of signals for *meso*- and *racem*-**75** was not possible.

1,2-Diazidoethane-1,2-diol (*meso* and *racem*) (**75**) and acetone (2.9 g, 50 mmol) was stirred at −50 °C for further 20 minutes and then divided into two parts, one of which was stored in the refrigerator at −30 °C, and the 2nd was stirred at room temperature. Unfortunately, no reaction was observed at room temperature as well as at −30 °C after 15 days as well as after 30 days.

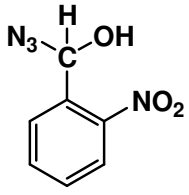
4.10. Reaction of Aromatic Aldehydes with HN_3

4.10.1. General Procedure for Synthesis

Aromatic aldehyde (**77**) (1.0 mmol) was mixed with 5M HN_3 solution in $CDCl_3$ (2 ml, 10 mmol). The mixture was stirred at room temperature for 30 minutes to obtain an equilibrium mixture containing α-azido Alcohols (**78**). It was not possible to isolate pure **78b** from the equilibrium mixture.

4.10.1.1. Synthesis of Azido(2-nitrophenyl)methanol (78b)

By utilizing the general procedure and starting with 2-nitrobenzaldehyde (**77b**) (151.12 mg, 1.0 mmol), equilibrium mixture containing azido(2-nitrophenyl)methanol (**78b**) was obtained.



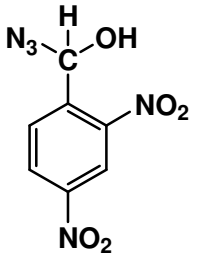
78b

Azido(2-nitrophenyl)methanol (78b): ^{1}H NMR ($CDCl_3$): δ = 6.52 (d, ^3J = 4.4 Hz, 1H), 7.48−7.91 (m, 4H, Ar), the OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 81.8 (d, CH), 124.7 (d, CH, Ar), 127.4 (d, CH, Ar), 129.8 (d, CH, Ar), 130.8 (d, CH, Ar), 133.5 (s, C, Ar), 149.0 (s, C, Ar).

4.10.1.2. Synthesis of Azido(2,4-dinitrophenyl)methanol (78c)

By utilizing the general procedure and starting with 2,4-dinitrobenzaldehyde (**77c**) (98.0 mg, 0.5 mmol), equilibrium mixture containing azido(2,4-dinitrophenyl)methanol (**78c**) was obtained.

Azido(2,4-dinitrophenyl)methanol (78c): ^{1}H NMR ($CDCl_3$): δ = 6.61 (s, 1H), 8.11 (d, ^{3}J = 8.8 Hz, 1H), 8.48 (dd, ^{3}J = 8.8 Hz, ^{3}J = 2.4 Hz, 1H), 8.77 (d, ^{3}J = 2.4 Hz, 1H), the OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 80.7 (d, CH), 120.2 (d, CH, Ar), 127.5 (d, CH, Ar), 129.2 (d, CH, Ar), 135.2 (s, C, Ar), 139.0 (s, C, Ar), 149.7 (s, C, Ar).

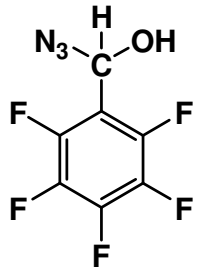


78c

4.10.1.3. Synthesis of Azido(perfluorophenyl)methanol (78d)

By utilizing the general procedure and starting with 2,3,4,5,6-pentafluorobenzaldehyde (**77d**) (98.0 mg, 0.5 mmol), equilibrium mixture containing azido(perfluorophenyl)methanol (**78d**) was obtained.

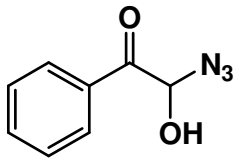
Azido(perfluorophenyl)methanol (78d): ^{1}H NMR ($CDCl_3$): δ = 6.09 (s, 1H), 6.22 (s, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 78.2 (d, CH), 110.5 (s, C, Ar).
It was not possible to assign the other values for **78d** due to complex couplings between C-F.



78d

4.11. Synthesis of 2-Azido-2-hydroxy-1-phenylethanone (83a)

2-Oxo-2-phenylacetaldehyde (**82a**) (1.0 g, 7.5 mmol) was mixed with 5M HN_3 solution in $CHCl_3$ (2 ml, 10 mmol). The mixture was stirred at room temperature for one day to obtain 2-azido-2-hydroxy-1-phenylethanone (**83a**) as light yellow crystalline solid with 98% yield after the removal of solvent, **83a** was recrystallized with *n*-pentane and $CHCl_3$.

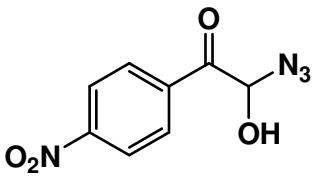


83a

2-Azido-2-hydroxy-1-phenylethanone (83a): 98% Isolated yield, light yellow crystalline solid, **Mp:** Decomposed to a fused mass at 39 °C. – **^{1}H NMR** ($CDCl_3$): δ = 4.99 (d, ^3J = 9.2 Hz, 1H, OH), 5.85 (d, ^3J = 8.8 Hz, 1H, CH), 7.56 (m, 2H, Ar), 7.67 (m, 1H, Ar), 8.05 (m, 2H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 80.4 (d, CH), 128.8 (d, CH, Ar), 129.2 (d, CH, Ar), 131.3 (s, C, Ar), 135.0 (d, CH, Ar), 192.2 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 3444 cm^{-1} (OH), 2110 cm^{-1} (N_3), 1696 cm^{-1} (C=O), 1599 cm^{-1} (Ar), 1451 cm^{-1} (Ar), 1282 cm^{-1} (C-O).

4.12. Synthesis of 2-Azido-1-(4-nitrophenyl)-2-hydroxyethanone (83b)

2-(4-Nitrophenyl)-2-oxoacetaldehyde (**82b**) was prepared according to the literature known method by L. Steinbach et al.[54] 2-(4-Nitroophenyl)-2-oxoacetaldehyde (**82b**) (1.0 g, 5.6 mmol) was mixed with 5M HN_3 solution in $CDCl_3$ (2 ml, 10 mmol). The mixture was stirred at room temperature for one day to obtain 2-azido-1-(4-nitrophenyl)-2-hydroxyethanone (**83b**) as yellow oily liquid with 93% yield after the removal of solvent.



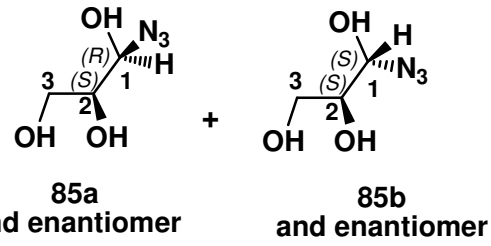
83b

2-Azido-1-(4-nitrophenyl)-2-hydroxyethanone (83b): Yellow oily liquid, 93% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 5.25 (br s, OH), 6.01 (s, 1H, CH), 8.25 (m, 2H, Ar), 8.39 (m, 2H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 81.4 (d, CH), 123.7 (d, CH, Ar), 130.3 (d, CH, Ar), 136.2 (s, C, Ar), 150.7 (s, C, Ar), 191.0 (s, C=O). – **^{1}H NMR** ($CDCl_3$, –50 °C): δ = 5.20 (br s, OH), 6.00 (s, 1H, CH), 8.25 (m, 2H, Ar), 8.40 (m, 2H, Ar). – **IR** (CCl_4): $\tilde{\nu}$ = 3468 cm^{-1} (OH), 2116 cm^{-1} (N_3), 1708 cm^{-1} (C=O), 1534 cm^{-1} (Ar), 1345 cm^{-1} (Ar), 1279 cm^{-1} (C-O).

4.13. Reaction of Sugars and Sugar Derivatives with HN_3

4.13.1. Synthesis of 1-Azidopropane-1,2,3-triol (85)

dl-Glyceraldehyde dimer (**84**) (90.0 mg, 0.5 mmol) and DMSO-d_6 (2 ml) were mixed with solution of 5M HN_3 in $CHCl_3$ (2 ml, 10 mmol), and stirred at room temperature for 2 days to obtain an equilibrium mixture containing α-azido alcohol. The excess of HN_3, and $CHCl_3$ was distilled off under vacuum at –30 °C to –20 °C to obtain (1*R*, 2*S*)-1-azidopropane-1,2,3-triol (**85a**) and (1*S*, 2*S*)-1-azidopropane-1,2,3-triol (**85b**) and corresponding enantiomers, solution in DMSO-d_6 in ratio of ca. 1:1.

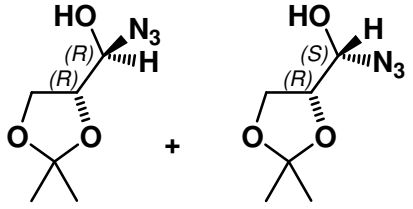


85a and enantiomer **85b and enantiomer**

(1*R*, 2*S*)-1-Azidopropane-1,2,3-triol (85a), (1*S*, 2*S*)-1-Azidopropane-1,2,3-triol (85b) and enantiomers: **^{1}H NMR** (DMSO-d_6): δ = 3.33–3.42 (m, 6H, diastereotopic proton), 4.63 (d, ^3J = 4.8 Hz, 1H, H-1), 4.71, ^3J = 3.6 Hz, 1H, H-1), 5.02 (d, ^3J = 3.2 Hz, 1H, OH), 5.17 (d, ^3J = 3.2 Hz, 1H, OH). The rest of OH-signals were covered by other signals. – **^{13}C NMR** (DMSO-d_6): δ = 62.0 (t, CH_2, C-3), 62.3 (t, CH_2, C-3), 74.1 (d, CH, C-2), 74.2 (d, CH, C-2), 84.8 (d, CH, C-1), 85.6 (d, CH, C-1). The assignment of signals was made by ^{13}C, ^{1}H correlation (gHSQCAD spectrum).

4.13.2. Synthesis of Azido(2,2-dimethyl-1,3-dioxolan-4-yl)methanol (89a)

(*R*)-2,2-Dimethyl-1,3-dioxolane-4-carbaldehyde (**88a**) (130.1 mg, 1.0 mmol) and DMSO-d_6 (2 ml) were mixed with solution of 5M HN_3 in $CDCl_3$ or CH_2Cl_2 (2 ml, 10 mmol), and stirred at room temperature for 20 minutes to obtain an equilibrium mixture (*R*)-azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (***like*-89a**) and (*S*)-azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (***unlike*-89a**) in the ratio of 1:1.5 but a clear assignment of the stereochemistry was not possible. The excess of HN_3, and $CDCl_3$ or CH_2Cl_2 was distilled off under vacuum at –50 °C, and the residue was carefully resolved in NMR-solvents e.g. $CDCl_3$, CD_2Cl_2, or DMSO-d_6.



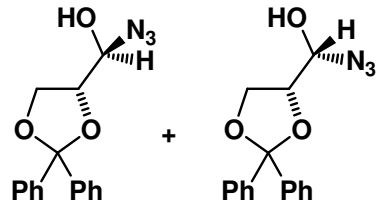
***like*-89a** ***unlike*-89a**

(*R*)-Azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (*like*-89a) and (*S*)-Azido((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (*unlike*-89a): Colorless liquid. – **^{1}H NMR** ($CDCl_3$): δ = 1.36 (s, 3H), 1.37 (s, 3H), 1.41 (s, 3H), 1.48 (s, 3H), 3.85–4.21 (m, 8H), 4.90 (br d, 2H, OH). – **^{13}C NMR** ($CDCl_3$): δ = 24.4 (q, CH_3), 24.5 (q, CH_3), 25.8 (q, CH_3), 25.9 (q, CH_3), 65.3 (t, CH_2), 65.4 (t, CH_2), 76.9 (d, CH), 77.0 (d, CH) 84.6 (d, CH), 84.9 (d, CH), 110.6 (s, $C(CH_3)_2$), 110.7 (s, $C(CH_3)_2$). – **^{1}H NMR** (CD_2Cl_2): δ = 1.33 (s, 3H), 1.34 (s, 3H), 1.44 (s, 3H), 1.45 (s, 3H), 3.51 (d, ^3J = 7.2 Hz, 1H, OH), 3.55 (d, ^3J = 8.8 Hz, 1H, OH), 3.81 (m, 2H, CH_2), 3.93 (dd, ^3J = 8.8 Hz, ^3J = 8.4 Hz, 2H, CH_2), 4.03–4.17 (m, 2H, 2CH), 4.84 (m, 1H, H-1), 4.89 (dd, ^3J = 8.4 Hz, ^3J = 8.0 Hz, 1H, H-1). – **^{13}C NMR** (CD_2Cl_2): δ = 24.8 (q, CH_3), 24.9 (q, CH_3), 26.2 (q, CH_3), 26.3 (q, CH_3), 65.6 (t, CH_2), 65.8 (t, CH_2), 77.32 (d, CH), 77.38 (d, CH), 84.7 (d, CH), 85.3 (d, CH), 110.5 (s, $C(CH_3)_2$), 110.7 (s,

$C(CH_3)_2$). – **^{1}H NMR** (CD_2Cl_2, –50 °C): δ = 1.29 (s, 3H), 1.30 (s, 3H), 1.41 (s, 3H), 1.43 (s, 3H), 3.80 (m, 2H, CH_2), 3.91 (m, 2H, CH_2), 4.01–4.14 (m, 2H, 2CH), 4.34 (d, ^3J = 8.4 Hz, 1H, OH), 4.72 (d, ^3J = 7.2 Hz, 1H, OH), 4.79 (m, 1H, H-1), 4.94 (dd, ^3J = 9.4 Hz, ^3J = 9.6 Hz, 1H, H-1). – **^{13}C NMR** (CD_2Cl_2, –50 °C): δ = 24.2 (q, CH_3), 24.3 (q, CH_3), 25.7 (q, CH_3), 25.8 (q, CH_3), 65.26 (t, CH_2), 65.33 (t, CH_2), 76.4 (d, CH), 76.7 (d, CH), 84.1 (d, CH), 84.6 (d, CH), 110.1 (s, $C(CH_3)_2$), 110.2 (s, $C(CH_3)_2$). The assignment of the signals was made by ^{13}C, ^{1}H correlation (gHSQCAD spectrum).

4.13.3. Synthesis of Azido(2,2-diphenyl-1,3-dioxolan-4-yl)methanol (89b)

2,2-Diphenyl-1,3-dioxolane-4-carbaldehyde (**88b**)[55] (254.0 mg, 1.0 mmol) was mixed with solution of 5M HN_3 in $CDCl_3$ or CD_2Cl_2 (2 ml, 10 mmol), and stirred at room temperature for 30 minutes to obtain an equilibrium mixture of (*R*)-azido((*R*)-2,2-diphenyl-1,3-dioxolan-4-yl)methanol (***like*-89b**) and (*S*)-azido((*R*)-2,2-diphenyl-1,3-dioxolan-4-yl)methanol (***unlike*-89b**)) in the ratio of 1:1.5 but assignment of the stereochemistry was not possible. The excess of HN_3, and $CDCl_3$ or CD_2Cl_2 was distilled off under vacuum at −50 °C and the residue was carefully resolved in NMR-solvents e.g. $CDCl_3$, CD_2Cl_2.



***like*-89b** ***unlike*-89b**

(*R*)-Azido((*R*)-2,2-diphenyl-1,3-dioxolan-4-yl)methanol (*like*-89b) and (*S*)-Azido((*R*)-2,2-diphenyl-1,3-dioxolan-4-yl)methanol (*unlike*-89b): Colorless liquid. – **^{1}H NMR** ($CDCl_3$): δ = 3.94-3.98 (m, 4H, $2CH_2$), 4.04 (d, ^3J = 8.0 Hz, 1H, OH), 4.05 (d, ^3J = 8.8 Hz, 1H, OH), 4.09-4.14 (m, 2H, 2CH), 4.85 (m, 2H), 7.28-7.32 (m, 10H, Ar), 7.42-7.46 (m, 10H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 65.7 (t, CH_2), 65.8 (t, CH_2), 77.1 (d, CH), 77.4 (d, CH), 84.6 (d, CH), 84.8 (d, CH), 110.6 (s, $C(Ph)_2$), 110.8 (s, $C(Ph)_2$), 125.6 (d, CH, Ar), 125.7 (d, CH, Ar), 125.82 (d, CH, Ar), 125.84 (d, CH, Ar), 128.0 (d, CH, Ar), 128.12 (d, CH, Ar), 128.15 (d, CH, Ar), 128.24 (d, CH, Ar), 128.28 (d, CH, Ar), 128.4 (d, CH, Ar), 140.64 (s, C, Ar), 140.64 (s, C, Ar). – **^{1}H NMR** (CD_2Cl_2, –50 °C): δ = 3.86-4.12 (m, 4H, $2CH_2$), 4.18 (d, ^3J = 8.0 Hz, 1H, OH), 4.21 (d, ^3J = 8.4 Hz, 1H, OH), 4.83 (m, 2H), 4.92 (m, 2H), 7.24-7.37 (m, 10H, Ar), 7.38-7.49 (m, 10H, Ar). – **^{13}C NMR** (CD_2Cl_2, –50 °C): δ = 65.4 (t, CH_2), 65.5 (t, CH_2), 76.5 (d, CH), 76.7 (d, CH), 83.9 (d, CH), 84.5 (d, CH), 109.9 (s, $C(Ph)_2$), 110.1 (s, $C(Ph)_2$), 125.0 (d, CH, Ar), 125.40 (d, CH, Ar), 125.45 (d, CH, Ar), 125.49 (d, CH, Ar), 127.7 (d, CH, Ar), 127.8 (d, CH, Ar), 127.9 (d, CH, Ar), 128.0 (d, CH, Ar), 128.09 (d, CH, Ar), 128.1 (d, CH,

Ar), 140.3 (s, C, Ar), 140.5 (s, C, Ar). The assignment of the signals was made by ^{13}C, ^{1}H correlation (gHSQCAD spectrum).

4.13.4. Reaction of α-D-Glucose (90) with HN_3

α-D-Glucose (**90**) (180 mg, 1 mmol) and DMSO-d_6 (2 ml) were mixed with a solution of 5M HN_3 in $CHCl_3$ (2 ml, 10 mmol) and stirred at room temperature for 6 h. The excess of HN_3 and $CHCl_3$ were distilled off under high vacuum at −30 °C to −20 °C to obtain a solution in DMSO-d_6. The DMSO-d_6 was distilled off under high vacuum at −30 °C to 20 °C to obtain a colorless oil which was dissolved in acetone-d_6 to compare with the ^{13}C NMR data for compound,[56] but the NMR data showed the presence of only compounds **90 + 92**.

4.14. α-Azido Alcohol from Ketones

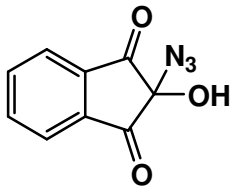
4.14.1. Reaction of Pentane-2,4-dione (93) with HN_3

Pentane-2,4-dione (**93**) (40 mg, 0.39 mmol) was mixed with 7M HN_3 solution in $CDCl_3$ (0.7 ml, 4.9 mmol). The mixture was stirred at room temperature to obtain 4-azido-4-hydroxypentan-2-one (**94**), but no reaction was observed at room temperature as well as at −25 to −30 °C after several weeks.

4.14.2. Synthesis of 2-Azido-2-hydroxyindane-1,3-dione (97a)

Indane-1,2,3-trione (**96**) was prepared from 2,2-dihydroxy-2H-indene-1,3-dione (**95**) by following a known method.[58]

Indane-1,2,3-trione (**96**) (50 mg, 0.31 mmol) was mixed with 5M HN_3 solution in $CDCl_3$ (0.7 ml, 3.5 mmol). The mixture was stirred at room temperature for one hour to obtain 2-azido-2-hydroxyindane-1,3-dione (**97a**) as orange crystalline solid with 92% yield after the removal of solvent, **97a** was recrystallized with *n*-pentane and $CHCl_3$ in the refrigerator at −25 to −30 °C. The above orange crystals are not stable at room temperature and decompose to give brown foam.



97a

2-Azido-2-hydroxyindane-1,3-dione (97a): Orange crystalline solid, 92% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 7.95 (m, 2H, Ar), 8.05 (m, 2H, Ar), the OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 81.1 (s, C), 124.8 (d, CH, Ar), 137.4 (d, CH, Ar), 138.9 (s, C, Ar), 192.0 (s, C=O). – **IR** ($CDCl_3$): 2139 cm^{-1} (N_3), 1776 cm^{-1} (C=O), 1735 cm^{-1} (C=O), 1469 cm^{-1} (Ar), 1361 cm^{-1} (Ar), 1047 cm^{-1} (C-O). – Solubility of 2-azido-2-hydroxyindane-1,3-dione (**97a**) in CCl_4 is very low that's why IR was measured in $CDCl_3$.

To the stirred solution of 2-azido-2-hydroxyindane-1,3-dione (**97a**) (101.5 mg, 0.5 mmol) in $CHCl_3$ (3 ml) at −30 °C was added cyclooctyne (108.18 mg, 1.0 mmol) and the reaction mixture was stirred at −30 °C for 1.5 hours. The solvent and excess of cyclooctyne was removed under vacuum at −30 °C to obtain 2-(4,5,6,7,8,9-hexahydrocycloocta[d][1,2,3]triazol-1-yl)-2-hydroxy-2H-indene-1,3-dione (**97b**) but product **97b** could not be achieved.

4.15. Reactions of α-Azido Alcohols

4.15.1. Photolysis of α-Azido Alcohols

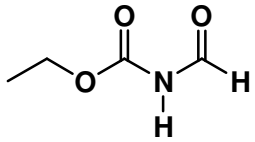
4.15.1.1. General Procedure for Photolysis of α-Azido Alcohols

Aldehyde **64** (1 mmol) and 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol) were mixed and stirred at room temperature for 16 h. The excess of solvent and HN_3 was distilled off at −50 °C under vacuum to obtain α-azido alcohols as colorless liquid, which was carefully resolved in precooled $CDCl_3$ keeping the temperature at −50 °C. The solution was photolysed at −50 °C for 8 hours to produce compound **100** and **102** in the ratio of ca. 1:1. The mixture was separated by column chromatography (hexane/ethyl acetate).

4.15.1.2. Photolysis of Ethyl 2-Azido-2-hydroxyacetate (65a)

By utilizing the general procedure and starting with ethyl glyoxylate (**64a**) (102.0 mg, 1.0 mmol), ethyl 2-amino-2-oxoacetate (**100a**) which is a commercially available compound, and ethyl formylcarbamate (**102a**)[59] were obtained. The mixture was separated by column chromatography (1:10 hexane/ethyl acetate) to give **100a** (35 mg, 42%) and **102a** (24 mg, 29%).

Ethyl Formylcarbamate (102a): Light brown oily liquid, 29% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.32 (t, ^3J = 6.8 Hz, 3H), 4.28 (q, ^3J = 6.8 Hz, 2H), 8.10 (br s, 1H), 8.97 (d, ^3J = 10.4 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 14.1 (q, CH_3), 62.9 (t, CH_2), 152.6 (s, C=O), 163.0 (d, CH). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 3403 cm^{-1} (N–H), 2986 cm^{-1} (C–H), 1764 cm^{-1} (C=O), 1228 cm^{-1} (C–O).

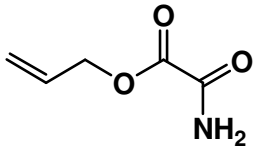


102a

4.15.1.3. Photolysis of Allyl 2-Azido-2-hydroxyacetate (64b)

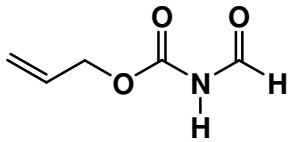
By utilizing the general procedure and starting with allyl 2-oxoacetate (**64b**)[51] (500.0 mg, 4.38 mmol), allyl 2-amino-2-oxoacetate (**100b**) and allyl formylcarbamate (**102b**), were obtained The crude mixture was purified by flash chromatography on silica gel, eluting with (1:1 hexane/ethyl acetate) to yield **102b** as a colorless liquid (178 mg, 1.4 mmol, 32%) and **100b** as a colorless crystalline solid (254 mg, 1.97 mmol, 45%), which was recrystallized from hexane and methanol (20:1) to furnish colorless crystals, with melting point (83 °C). Compound **100b** was reported by I. Kawamato et al. as starting material for the synthesis of penem antibiotic in 1987.[60]

Allyl 2-Amino-2-oxoacetate (100b): White crystalline solid. **Mp**: 83 °C, 45% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 4.77 (dd, ^3J = 6.0 Hz, ^4J = 2.4 Hz, 2H), 5.38 (m, 2H), 5.97 (m, 1H), 6.62 (br s, 1H, NH), 7.02 (br s, 1H, NH). – **^{13}C NMR** ($CDCl_3$): δ = 67.6 (t, CH_2), 120.4 (t, CH), 130.4 (d, CH), 158.4 (s, C=O), 159.4 (s, C=O). – **IR (CCl_4)**: $\tilde{\nu}$ = 3250 cm^{-1} (N–H), 1711cm^{-1} (C=O), 1464 cm^{-1} (C=C), 1210 cm^{-1} (C–O). – **Anal. Calcd (%) for $C_5H_7NO_3$** (129.11): C, 46.51; H, 5.46; N, 10.85. **Found:** C, 46.11; H, 5.34; N, 10.42.



100b

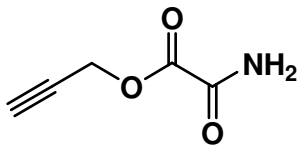
Allyl Formylcarbamate (102b): Colorless liquid, 32% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 4.71 (dd, ^3J = 6.0 Hz, ^4J = 2.4 Hz, 2H), 5.31 (m, 2H), 5.95 (m, 1H), 8.40 (br s, 1H, NH), 8.97 (d, ^3J = 10.0 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 67.2 (t, CH_2), 119.6 (t, CH_2), 130.8 (d, CH), 152.3 (s, C=O), 160.3 (d, CH). – **IR (CCl_4)**: 2836 cm^{-1} (C–H), 1771 (C=O), 1711 (C=O), 1464 (C=C), 1211 (C–N), 1176 (C–O). – **HR-MS ($C_5H_7NO_3$). Calculated:** for $[M+H]^+$ 130.0499. **Found:** 130.0540.



102b

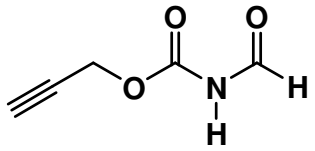
4.15.1.4. Photolysis of Prop-2-ynyl 2-Azido-2-hydroxyacetate (65c)

By utilizing the general procedure and starting with prop-2-ynyl 2-oxoacetate (**64c**) (500 mg, 4.46 mmol) prop-2-ynyl 2-amino-2-oxoacetate (**100c**) and prop-2-ynyl formylcarbamate (**102c**) were produced. The crude mixture was purified by flash chromatography on silica gel, eluting with (40:60 hexane/ethyl acetate) to yield **102c** as a light brown oily liquid (1.1 mmol, 141 mg, 25%) and **100c** as a colorless solid with melting point of 130 °C (209.5 mg, 1.65 mmol, 37%).



100c

Prop-2-ynyl 2-Amino-2-oxoacetate (100c): White crystalline solid. **Mp**: 130 °C, 37% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 2.56 (t, ^4J = 2.4 Hz, 1H), 4.87 (d, ^4J = 2.4 Hz, 2H), 5.91 (br s, 1H, NH), 6.93 (br s, 1H, NH). – **^{13}C NMR** ($CDCl_3$): δ = 54.3 (t, CH_2), 75.8 (s, C), 76.4 (d, CH), 157.1 (s, C=O), 159.1 (s, C=O). – **IR (CCl_4)**: $\tilde{\nu}$ = 3359 cm^{-1} (H–C≡C), 3250 (N–H), 1733 (C=O), 1216 (C–O). – **HR-MS ($C_5H_5NO_3$)**. **Calculated:** for $[M+Na]^+$ 150.0162. **Found:** 150.0139.



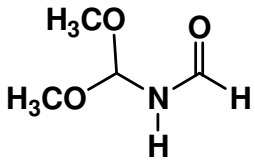
102c

Prop-2-ynyl Formylcarbamate (102c): Light brown liquid, 25% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 2.57 (t, ^4J = 2.4 Hz, 1H), 4.82 (d, ^4J = 2.4 Hz, 2H), 7.96 (br s, 1H, NH), 8.96 (d, ^3J = 10.4 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 54.0 (t, CH_2), 76.2 (d, CH), 76.3 (s, C), 151.7 (s, C=O), 162.4 (d, HC=O). – **IR (CCl_4)**: $\tilde{\nu}$ = 3382 cm^{-1} (H–C≡C), 2897 cm^{-1} (H–C=O), 1771 cm^{-1} (C=O), 1711 cm^{-1} (C=O), 1211 cm^{-1} (C–O). – **HR-MS ($C_5H_5NO_3$)**. **Calculated:** for $[M+Na]^+$ 150.0162. **Found:** 150.0167.

4.15.1.5. Photolysis of 1-Azido-2,2-dimethoxyethanol (72)

By utilizing the general procedure and starting with 2,2-Dimethoxyacetaldehyde (**71**) (500 mg, 480 mmol), a mixture of 2,2-dimethoxyacetamide (**100d**) and *N*-(dimethoxymethyl)formamide (**102d**) was obtained. The mixture was separated by column chromatography using (hexane/ethyl acetate 5:95) to give **100d** as a colorless solid (190 mg, 1.59 mmol, 33%) and **102d** light yellow oily liquid (180 mg, 1.51 mmol, 31%) after removal of the solvent. Compound **102d** is unstable and decomposed on standing at room temperature. The compound **100d** is a commercially available compound.

***N*-(Dimethoxymethyl)formamide (102d):** Light yellow oily liquid, 31% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 3.40 (s, 6H, CH_3), 4.69 (s, 1H), 8.02 (s, 1H), 8.15 (d, ^3J = 10.4 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 54.8 (q, CH_3), 103.1 (d, CH), 161.4 (d, CH). – **IR** (CCl_4): $\tilde{\nu}$ = 2836 cm^{-1} (C–H), 1720 cm^{-1} (C=O), 1160 cm^{-1} (C–O). – **HR–MS** **($C_4H_9NO_3$)**. c**alculated:** for $[M+H]^+$ 119.05824. **Found:** 119.0769. Compound **102d** is unstable and a correct **HR–MS** could not be obtained.

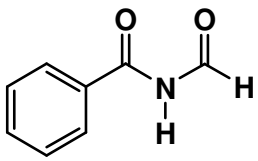


102d

4.15.1.6. Photolysis of 2-Azido-2-hydroxy-1-phenylethanone (83a)

2-Azido-2-hydroxy-1-phenylethanone (**83a**) was prepared by the general method. Compound **83a** (1.00 g, 5.64 mmol) in 5 ml of $CHCl_3$ was photolysed at –50 °C for 8 hours to produce *N*-formylbenzamide (**123**) and benzoic acid (**129**). The crude mixture was purified by flash chromatography on silica gel, eluting with (hexane/ethyl acetate 40:60) to yield *N*-formylbenzamide (**123**) as a colorless solid (252.3 mg, 1.69 mmol, 30%) and benzoic acid (**129**) as a colorless crystalline solid (185 mg, 1.52 mmol, 27%) after the removal of solvent, **129** is a commercially available compound. Compound **123** was prepared by another method in 1951 by Q. N. Thompson et al.[79]

***N*-Formylbenzamide (123):** Colorless crystalline solid, **Mp:** 80 °C, 30% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 7.56 (m, 2H, Ar), 7.65 (m, 1H, Ar), 7.97 (m, 2H, Ar) 9.39 (d, ^3J = 9.6 Hz, 1H), 9.85 (br s, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 127.9 (d, CH, Ar), 129.0 (d, CH, Ar), 131.0 (s, C, Ar), 133.9 (d, CH, Ar), 164.4 (d, CH), 166.5 (s, C=O).



123

4.15.2. Oxidation of α-Azido Alcohols

4.15.2.1. General Procedure for Oxidation of α-Azido Alcohols

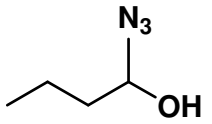
Aldehyde **1** (1 mmol) was mixed with 2M HN_3 solution in $CDCl_3$ (5 ml, 10 mmol). The mixture was stirred at room temperature to obtain an equilibrium mixture containing α-azido alcohol **3**. To this mixture was added solid pyridinium chlorochromate (PCC, 1 g, 4.63 mmol) at –50 °C (for aliphatic aldehydes) or at –20 °C (for aromatic aldehydes) over several minutes

under argon, and the reaction mixture was stirred for further 5 h and then filtered through a short plug of silica gel at −50 °C to −20 °C yielding acyl azide **124** in $CDCl_3$.

4.15.2.2. Oxidation of 1-Azidobutan-1-ol (3c)

1-Azidobutan-1-ol (**3c**) was obtained by utilizing the general procedure for the synthesis of α-azido alcohols

1-Azidobutan-1-ol (3c): ^{1}H NMR ($CDCl_3$): δ = 0.89 (t, ^3J = 7.6 Hz, 3H), 1.37 (m, 2H, diastereotopic protons), 1.60 (m, 2H, diastereotopic protons), 3.93 (br s, OH), 4.84 (t, ^3J = 6.4 Hz, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 13.2 (q, CH_3), 15.3 (t, CH_2), 38.0 (t, CH_2), 86.0 (d, CH).

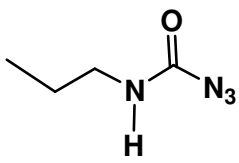


3c

By utilizing the general procedure and starting with 1-azidobutan-1-ol (**3c**), butyryl azide (**124c**) was prepared in $CDCl_3$ (97%).[64] Butyryl azide (**124c**) solution was completely transformed into **125c** on standing at room temperature after 4 hours. 1-Isocyanatopropane **125c** reacted with HN_3 to produce propylcarbamoyl azide (**126c**),[65] at room temperature after 16 hours.

The treatment of butyric acid (**127**) with PCC in the presence HN_3 at –50 °C to –30 °C did not lead to butyryl azide (**124c**), this control experiment was performed to investigate the mechanism of reaction.

Propylcarbamoyl Azide (126c): Colorless liquid, 100% NMR-yield. – **^{1}H NMR** ($CDCl_3$): δ = 0.92 (t, ^3J = 7.2 Hz, 3H), 1.54 (tq, ^3J = 7.6 Hz, ^3J = 6.8 Hz, 2H), 3.18 (q, ^3J = 6.8 Hz, 2H), 5.23 (br s, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 11.1 (q, CH_3), 22.8 (t, CH_2), 42.7 (t, CH_2), 156.7 (s, C=O). – **IR** ($CDCl_3$): $\tilde{\nu}$ = 3445 cm^{-1} (N–H), 2147 cm^{-1} (N_3), 1710 cm^{-1} (C=O), 1228 cm^{-1} (C–N).

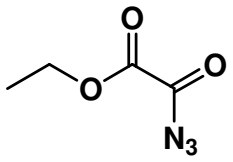


126c

4.15.2.3. Synthesis of Ethyl 2-Azido-2-oxoacetate (124d)

By utilizing the general procedure and starting with ethyl glyoxylate (**64a**) (102.0 mg, 1.0 mmol), ethyl 2-azido-2-oxoacetate (**124d**) was obtained as a colorless liquid (122.00 mg, 0.85

mmol, 86%) after the removal of solvent. The compound **124d** was prepared by another method by T. Curtius, and K. Hochschwender in 1915.[68]

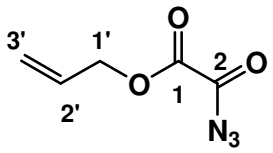


124d

Ethyl 2-Azido-2-oxoacetate (124d): Colorless liquid, 86% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.37 (t, ^3J = 7.6 Hz, 3H), 4.35 (q, ^3J = 7.2 Hz, 2H). – **^{13}C NMR** ($CDCl_3$): δ = 13.7 (q, CH_3), 63.8 (t, CH_2), 157.0 (s, C=O), 164.2 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2985 cm^{-1} (C–H), 2146 cm^{-1} (N_3), 1761 cm^{-1} (C=O), 1722 cm^{-1} (C=O), 1183 cm^{-1} (C–O).

4.15.2.4. Synthesis of Allyl 2-Azido-2-oxoacetate (124e)

By utilizing the general procedure and starting with allyl 2-oxoacetate (**64b**) (114.1 mg, 1.0 mmol), allyl 2-azido-2-oxoacetate (**124e**) was obtained as a light yellow liquid (134 mg, 0.87 mmol, 87%) after removal of the solvent.

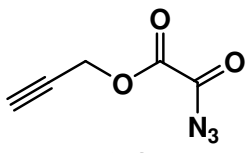


124e

Allyl 2-Azido-2-oxoacetate (124e): Light yellow liquid, 87% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 4.79 (dd, ^3J = 6.0 Hz, ^4J = 2.4 Hz, 2H, H-1'), 5.41 (m, 2H, H-3'), 5.94 (m, 1H, H-2'). – **^{13}C NMR** ($CDCl_3$): δ = 68.0 (t, CH_2, C-1'), 120.7 (t, CH_2, C-3'), 130.0 (d, CH, C-2'), 156.8 (s, C=O), 164.0 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2146 cm^{-1} (N_3), 1759 cm^{-1} (C=O), 1719 cm^{-1} (C=O), 1582 cm^{-1} (C=C), 1181 cm^{-1} (C–O).

4.15.2.5. Synthesis of Prop-2-ynyl 2-Azido-2-oxoacetate (124f)

By utilizing the general procedure and starting with prop-2-ynyl 2-oxoacetate (**64c**) (112.08 mg, 1.0 mmol), prop-2-ynyl 2-azido-2-oxoacetate (**124f**) was obtained as a light yellow liquid (131.5 mg, 0.85 mmol, 86%) after removal of the solvent.



124f

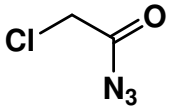
Prop-2-ynyl 2-Azido-2-oxoacetate (124f): Light yellow liquid, 86% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 2.58 (t, ^4J = 2.4 Hz, 1H), 4.87 (d, ^4J = 2.8 Hz, 2H). – **^{13}C NMR** ($CDCl_3$): δ = 54.7 (t, CH_2), 75.3 (d, CH), 76.8 (s, C≡C), 156.3 (s, C=O), 163.4 (s, C=O). – **^{1}H NMR** (CD_2Cl_2): δ = 2.60 (t, ^4J = 2.4 Hz, 1H), 4.86 (d, ^4J = 2.8 Hz, 2H). – **^{13}C NMR** (CD_2Cl_2): δ = 54.9 (t, CH_2), 75.8 (d, CH), 76.8 (s, C≡C), 156.5 (s, C=O), 163.7 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ =

3311 cm^{-1} (H–C≡C), 2953 cm^{-1} (H–C), 2111 cm^{-1} (N_3), 1768 cm^{-1} (C=O), 1722 cm^{-1} (C=O), 1280 cm^{-1} (C–O).

4.15.2.6. Synthesis of 2-Chloroacetyl Azide (124g)

By utilizing the general procedure and starting with 2-chloroacetaldehyde (**30a**) (78.5 mg, 1 mmol), 2-chloroacetyl azide (**124g**) was obtained as a colorless liquid (101.5 mg, 0.85 mmol, 85%) after removal of the solvent. The compound (**124g**) was prepared by another method by P. Frøyen in 1993.[67]

2-Chloroacetyl Azide (124g): Colorless liquid, 85% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 4.06 (s). – **^{13}C NMR** ($CDCl_3$): δ = 42.5 (t, CH_2), 174.0 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2949 cm^{-1} (C–H), 2145 cm^{-1} (N_3), 1717 cm^{-1} (C=O).

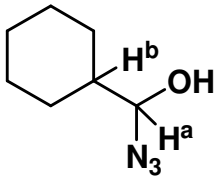


124g

4.15.2.7. Oxidation of Azido(cyclohexyl)methanol (3d)

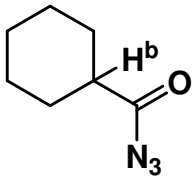
By utilizing the general procedure and starting with cyclohexanecarbaldehyde (**1d**) (112.17 mg, 1.00 mmol), cyclohexanecarbonyl azide (**124h**) was obtained as a colorless liquid (136.3 mg, 0.89 mmol, 89%) after removal of the solvent.

Azido(cyclohexyl)methanol (3d): ^{1}H NMR ($CDCl_3$): δ = 0.96–1.37 (m, 11H), 4.62 (d, ^3J = 6.0 Hz, 1H, HC–O). The OH-signal was covered by other signals. – **^{13}C NMR** ($CDCl_3$): δ = 24.6 (t, CH_2), 25.2 (t, CH_2), 27.4 (t, CH_2), 43.4 (d, CH, H*C*–COH), 90.0 (d, CH, HC–O).



3d

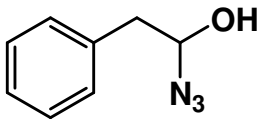
Cyclohexanecarbonyl Azide (124h): Colorless liquid, 89% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.15–1.90 (m, 10H), 2.26 (tt, ^3J = 10.8 Hz, ^3J = 3.6 Hz, 1H, HC–C=O). – **^{13}C NMR** ($CDCl_3$): δ = 25.2 (t, CH_2), 25.5 (t, CH_2), 28.7 (t, CH_2), 45.4 (d, CH), 183.3 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2936 cm^{-1} (C–H), 2134 cm^{-1} (N_3), 1717 cm^{-1} (C=O).



124h

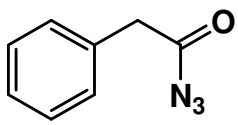
4.15.2.8. Oxidation of 1-Azido-2-phenylethanol (3f)

By utilizing the general procedure and starting with 2-phenylacetaldehyde (**1f**) (120.15 mg, 1.00 mmol), 2-phenylacetyl azide (**124i**) was obtained as a colorless liquid (143.4 mg, 0.89 mmol, 89%) after removal of the solvent. This product was completely transformed into **125i** on standing at room temperature after 8 h.[64]



3f

1-Azido-2-phenylethanol (3f): ^{1}H NMR ($CDCl_3$): δ = 2.87 (dd, ^2J = 13.6 Hz, ^3J = 5.2, 1H, diastereotopic proton), 2.91 (dd, ^2J = 13.6 Hz, ^3J = 5.6 Hz, 1H, diastereotopic proton), 3.52 (br s, OH), 5.14 (t, ^3J = 5.2 Hz, 1H), 7.14–7.25 (m, 5H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 42.2 (t, CH_2), 86.0 (d, CH), 127.7 (d, CH, Ar), 128.7 (d, CH, Ar), 129.5 (d, CH, Ar), 134.8 (s, C, Ar)

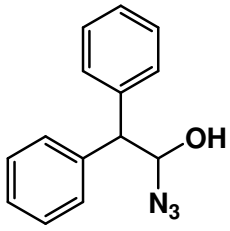


124i

2-Phenylacetyl Azide (124i): Colorless liquid, 89% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 3.54 (s, 2H), 7.17–7.27 (m, 5H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 43.5 (t, CH_2), 127.5 (d, CH, Ar), 128.7 (d, CH, Ar), 129.3 (d, CH, Ar), 132.8 (s, C, Ar), 178.3 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 3033 cm^{-1} (C–H), 2137 cm^{-1} (N_3), 1718 cm^{-1} (C=O), 1496 cm^{-1} (Ar), 1455 cm^{-1} (Ar).

4.15.2.9. Oxidation of 1-Azido-2,2-diphenylethanol (3e)

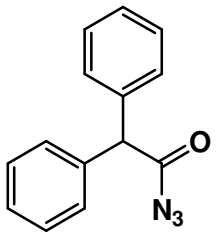
By utilizing the general procedure and starting with 2,2-diphenylacetaldehyde (**1e**) (196.24 mg, 1.00 mmol), 2,2-diphenylacetyl azide (**124j**) was obtained as a colorless liquid (208.3 mg, 0.87 mmol, 88%) after removal of the solvent. This product was completely transformed into (**125j**) on standing at room temperature after 8 h. The compound **124j** was prepared by another method by C. O. Kangani et al. in 2007 but the compound **125j** was taken for **124j**.[69]



3e

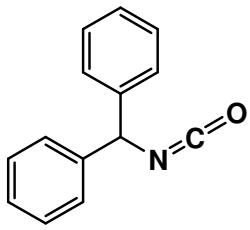
1-Azido-2,2-diphenylethanol (3e): ^{1}H NMR ($CDCl_3$): δ = 3.45 (d, ^3J = 6.8 Hz, OH), 4.12 (d, ^3J = 6.8 Hz, 1H), 5.59 (t, ^3J = 7.2 Hz, 1H), 7.17–7.31 (m, 10H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 56.8 (d, CH), 87.1 (d, CH), 128.5 (d, CH, Ar), 128.8 (d, CH, Ar), 128.9 (d, CH, Ar), 138.8 (s, C, Ar).

2,2-Diphenylacetyl Azide (124j): Colorless liquid, 88% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 4.96 (s, 1H), 7.29–7.37 (m, 10H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 58.6 (d, CH), 127.6 (d, CH, Ar), 128.2 (d, CH, Ar), 128.4 (d, CH, Ar), 137.3 (s, C, Ar), 179.4 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 3103 cm^{-1} (C–H), 2113 cm^{-1} (N_3), 1719 cm^{-1} (C=O), 1495 cm^{-1} (Ar), 1452 cm^{-1} (Ar).



124j

(Isocyanatomethylene)dibenzene (125j): Colorless liquid, 90% NMR-yield. – **^{1}H NMR** ($CDCl_3$): δ = 5.85 (s, 1H), 7.31–7.37 (m, 10H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 62.0 (d, CH), 126.4 (d, CH, Ar), 127.2 (d, CH, Ar), 128.7 (d, CH, Ar), 132.3 (s, C, Ar). The signal for N=C=O group was not observed. – **IR** (CCl_4): $\tilde{\nu}$ = 3103 cm^{-1} (C–H), 2253 cm^{-1} (N=C=O), 1493 cm^{-1} (Ar), 1450 cm^{-1} (Ar).

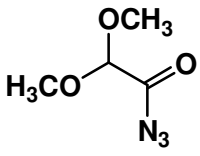


125j

4.15.2.10. Synthesis of 2,2-Dimethoxyacetyl Azide (124k)

By utilizing the general procedure and starting with 2,2-dimethoxyacetaldehyde (**71**) (104.1 mg, 1 mmol), 2,2-dimethoxyacetyl azide (**124k**) was obtained as a colorless liquid (127.3 mg, 0.87 mmol, 88%) after removal of the solvent.

2,2-Dimethoxyacetyl Azide (124k): Colorless liquid, 88% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 3.44 (s, 6H, 2×CH_3), 4.74 (s, 1H, CH). – **^{13}C NMR** ($CDCl_3$): δ = 54.2 (q, CH_3), 99.6 (d, CH), 174.4 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2836 cm^{-1} (C–H), 2141 cm^{-1} (N_3), 1733 cm^{-1} (C=O), 1177 cm^{-1} (C–O).

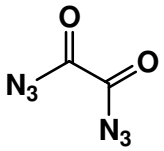


124k

4.15.2.11. Synthesis of Oxalyl Azide (124l)

By following the general procedure and starting with 1,2-diazidoethane-1,2-diol (**75**) (10 mmol), oxalyl azide (**124l**) was obtained as colorless solid (1.14 g, 8.2 mmol, 82%) after removal of solvent. The compound **124l** was prepared by another method in 1964 by H. Roesky et al.[70]

Oxalyl Azide (124l): Colorless solid, 82% isolated yield. – **^{13}C NMR** ($CDCl_3$): δ = 163.7 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2159 cm^{-1} (N_3), 2107 cm^{-1} (N_3), 1731 cm^{-1} (C=O), 1715 cm^{-1} (C=O).



124l

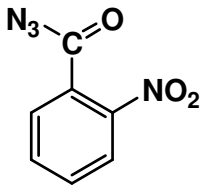
4.15.2.12. Synthesis of Benzoyl Azide (128a)

According to the general procedure, benzaldehyde (**77a**) (106.1 mg, 1.0 mmol) at −20 °C to RT was reacted to get benzoyl azide (**128a**) as colorless oil (117.6 mg, 0.8 mmol, 80%) after the removal of solvent. Compound **128a** is a commercially available compound. The reaction of benzoic acid (**129**) with PCC and HN_3 did not lead to benzoyl azide (**128a**). Treatment of benzaldehyde (**77a**) with PCC in $CHCl_3$ at –20 °C did not give benzoic acid (**129**).

4.15.2.13. Synthesis of 2-Nitrobenzoyl Azide (128b)

According to the general procedure, 2-nitrobenzaldehyde (**77b**) (151.1 mg, 1.0 mmol) at −20 °C to RT was reacted to get 2-nitrobenzoyl azide (**128b**) as light yellow solid (161.3 mg, 0.84 mmol, 84%) after removal of solvent. The compound **128b** was prepared by another method with melting point of 39 °C in 1983 by G. Weber et al.[80]

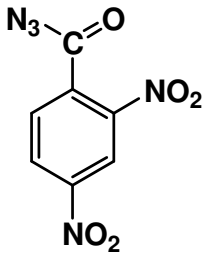
2-Nitrobenzoyl Azide (128b): Light yellow solid, 84% isolated yield, **Mp:** Decomposes at 72 °C. – **^{1}H NMR** ($CDCl_3$): δ = 7.69 (m, 2H, Ar), 7.78 (m, 1H, Ar), 7.87 (m, 1H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 124.0 (d, CH, Ar), 129.8 (d, CH, Ar), 132.7 (d, CH, Ar), 132.9 (d, CH, Ar), 134.0 (s, C, Ar), 148.4 (s, C, Ar), 171.2 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2133 cm^{-1} (N_3), 1712 cm^{-1} (C=O), 1482 cm^{-1} (Ar), 1445 cm^{-1} (Ar), 1348 cm^{-1} (NO_2).



128b

4.15.2.14. Synthesis of 2,4-Dinitrobenzoyl Azide (128c)

According to the general procedure, 2,4-dinitrobenzaldehyde (**77c**) (196.1 mg, 1.0 mmol), at −20 °C to RT was reacted to get 2,4-dinitrobenzoyl azide (**128c**) as light yellow solid (203 mg, 0.86 mmol, 86%). The compound **128c** was prepared by another method with melting point of 68 °C in 1938 by C. Naegeli et al.[81]



128c

2,4-Dinitrobenzoyl Azide (128c): Light yellow solid, 86% isolated yield, **Mp:** Begin to decomposes at 68 °C. – **^{1}H NMR** ($CDCl_3$): δ = 7.69 (m, 1H, Ar), 7.75 (m, 1H, Ar), 7.88 (m, 1H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 119.7 (d, CH, Ar), 124.1 (d, CH, Ar), 129.8 (d, CH, Ar), 132.7 (s, C, Ar), 132.8 (s, C, Ar), 134.0 (s, C, Ar), 171.2 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2133 cm^{-1} (N_3), 1712 cm^{-1} (C=O), 1537 cm^{-1} (Ar), 1445 cm^{-1} (Ar), 1348 cm^{-1} (NO_2).

4.15.2.15. Attempted Generation of Formyl Azide (130)

(a). Oxidation of Azidomethanol (13) by PCC

Azidomethanol (**13**) was obtained by using the general method of preparation as colorless solid at −50 ˚C, which was carefully resolved in cold $CDCl_3$ keeping the temperature at −50 ˚C. By utilizing the general procedure of oxidation, formyl azide (**130**) could not be obtained, rather, NMR-data showed that it was formic acid (**131**) which was further reacted with cyclooctyne, but no 4,5,6,7,8,9-hexahydrocycloocta[d][1,2,3]triazole-1-carbaldehyde (**132**) was detected.

(b). Swern Oxidation of Azidomethanol (13)

Oxalyl chloride (41.2 µl, 0.48 mmol) and CD_2Cl_2 (0.5 ml) were cooled down to −78 °C under argon and then a solution of dry DMSO (68.4 µl, 0.96 mmol) in CD_2Cl_2 (0.5 ml) was added drop wise and the mixture was stirred for 10 min at −78 °C. Thereafter, a solution of azidomethanol (**13**) (ca. 29.2 mg, 0.4 mmol) in CD_2Cl_2 (0.5 mL) was added drop wise and the solution was stirred for another 30 min at −78 °C before NEt_3 (282.8 µl, 2.0 mmol) was added and then the reaction mixture was warmed up to −50 °C and ^{1}H NMR, ^{13}C NMR (coupled and decoupled) was measured and compared with formic acid (**131**), which showed that the product formed was formic acid. This was further confirmed by adding a small amount of formic acid solution to the NMR-solution of the reaction mixture.

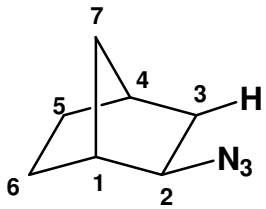
(c). Reaction of 1,2-Diazidoethane-1,2-diol (75) with Periodic Acid or with *N*- Iodosuccinimide

By following the general procedure, 1,2-diazidoethane-1,2-diol (**75**) (1 mmol) in $CDCl_3$ (1 ml) and periodic acid (2.19 mmol, 0.5 g) or *N*-iodosuccinimide (3 mmol, 0.67 g) at −50 °C were reacted to get formyl azide (**130**), but NMR-data showed that no product **130** was formed.

4.15.3. Reaction of Norbornene and its Derivatives with HN_3

4.15.3.1. Reaction of Norbornene (134) with HN_3

Norbornene (**134**) (1.00 g, 10.62 mmol) was added to solution of HN_3 in $CHCl_3$ (25 ml, 2M, 50 mmol). The reaction mixture was stirred at room temperature for one day. The excess amount of hydrazoic acid and $CHCl_3$ was distilled off at 0 ˚C under fume hood and reaction mixture was concentrated. The crude product was purified by flash column chromatography using $CHCl_3$ to give *exo*-2-azidobicyclo[2.2.1]heptane (**108**) as a colorless oil (0.949 g, 6.92 mmol, 66 %). This compound was prepared by a different method in 1992.[72]

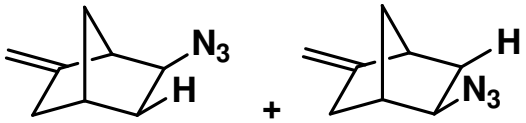


108

***exo*-2-Azidobicyclo[2.2.1]heptane (108):** Colorless oil, 66% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.07 (dd, ^3J = 9.4 Hz, ^3J = 2.0 Hz, 2H, H-5 or H-6, diastereotopic protons), 1.12 (dd, ^3J = 8.0 Hz, ^3J = 2.4 Hz, 2H, H-5 or H-6, diastereotopic protons), 1.17 (pseudo dm, ^3J = 11.2 Hz, 1H, H-7), 1.41-1.52 (m, 3H, H-7′, H-5′, H-3), 1.55 (m, 1H, H-5′ or H-6′), 1.62 (ddd, ^3J = 10.8 Hz, ^3J = 7.6 Hz, ^3J = 2.4 Hz, 1H, H-3′), 2.30 (m, 2H, H-1, H-4), 3.47 (br d, ^3J = 7.0 Hz, 1H, H-2). – **^{13}C NMR** ($CDCl_3$): δ = 25.9 (t, C-5 or C-6), 28.3 (t, C-5 or C-6), 35.2 (t, C-7), 35.5 (d, C-1 or C-4), 38.1 (t, C-3), 41.7 (d, C-1 or C-4), 64.3 (d, C-2). The assignment of carbon signals in compound **108** was made with the help of 2D-spectra, gHSQCAD and gHMBCAD. – **IR** ($CDCl_3$): $\tilde{\nu}$ = 2843 cm^{-1} (C-H), 2096 cm^{-1} (N_3).

4.15.3.2. Reaction of 5-Methylene-2-norbornene (142) with HN_3

5-Methylene-2-norbornene (**142**) (100 mg, 1 mmol) was mixed with 2M HN_3 solution in $CHCl_3$ (5 ml, 10 mmol) and stirred at room temperature for one day. The excess of hydrazoic acid and $CHCl_3$ was distilled off at −20 °C and the reaction mixture was concentrated. The crude product was purified by flash column chromatography on silica gel using $CHCl_3$ to give a mixture of *exo*-2-azido-6-methylenebicyclo[2.2.1]heptane (**144a**) and *exo*-2-azido-5-methylenebicyclo[2.2.1]heptane (**144b**) in the ratio of 1:1.8 as a colorless oily liquid (89.0 mg, 0.6 mmol, 60%) after the removal of solvent. It was not possible to separate and make clear assignment to **144a** and **144b**.

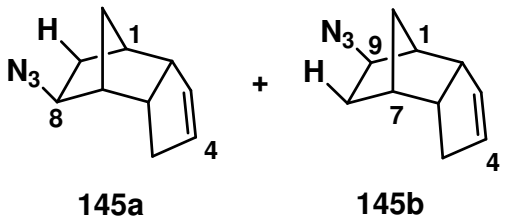


144a **144b**

***exo*-2-Azido-6-methylenebicyclo[2.2.1]heptane (144a) and *exo*-2-Azido-5-methylenebicyclo[2.2.1]heptane (144b):** Colorless oily liquid, 60% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.38 (dm, *J* = 8.0 Hz, 2H, diastereotopic protons), 1.48-1.62 (m, 4H, diastereotopic protons), 1.67-1.77 (m, 2H, diastereotopic protons), 1.78-1.87 (m, 2H, diastereotopic protons), 2.22-2.24 (m, 2H), 2.44 (pseudo d, *J* = 4.11 Hz, 1H), 2.71 (d, *J* = 4.0 Hz, 1H), 2.78 (m, 1H), 3.36-3.56 (m, 2H), 3.58 (dm, *J* = 7.6 Hz, 1H), 4.48 (m, 1H), 4.60 (m, 1H), 4.76 (m, 1H), 5.01 (m, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 34.5 (t, CH_2), 35.6 (t, CH_2), 36.0 (t, CH_2), 36.4 (d, CH), 37.2 (t, CH_2), 37.4 (t, CH_2), 38.1 (t, CH_2), 42.5 (d, CH), 44.8 (d, CH), 51.0 (d, CH), 63.5 (d, CH), 63.7 (d, CH), 103.1 (t, CH_2), 106.2 (t, CH_2), 149.9 (s, C), 152.4 (s, C). – **IR** (CCl_4): $\tilde{\nu}$ = 2967 cm^{-1} (C-H), 2843 cm^{-1} (C-H), 2090 cm^{-1} (N_3), 1666 cm^{-1} (C=C).

4.15.3.3. Reaction of 1,3-Cyclopentadiene Dimer (143) with HN_3

1,3-Cyclopentadiene dimer (tricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene) (**143**), (132.0 mg, 1.0 mmol) was mixed with 2M HN_3 solution in $CHCl_3$ (5 ml, 10 mmol) and stirred at room temperature for one day. The excess of hydrazoic acid and $CHCl_3$ was distilled off at −20 °C and the reaction mixture was concentrated. The crude product was purified by flash column chromatography on silica gel using $CHCl_3$ to give a mixture of *exo*-8-azidotricyclo[5.2.1.$0^{2,6}$]dec-3-ene (**145a**) and *exo*-9-azidotricyclo[5.2.1.$0^{2,6}$]dec-3-ene (**145b**) in the ratio of 1:1.4 as a colorless oily liquid (99 mg, 0.57 mmol, 57%) after the removal of solvent. It was not possible to separate and make clear assignment to **145a** and **145b**.

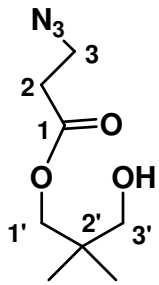


145a **145b**

***exo*-8-Azidotricyclo[5.2.1.0^{2,6}]dec-3-ene (145a) and *exo*-9-Azidotricyclo[5.2.1.0^{2,6}]dec-3-ene (145b):** Colorless oily liquid, 57% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.22 (dm, *J* = 12.0 Hz, 1H), 1.28 (dm, *J* = 13.6 Hz, 1H), 1.40-1.45 (m, 2H), 1.58-1.62 (m, 1H), 1.65-1.72 (m, 2H), 1.78-1.84 (m, 1H), 2.06 (m, 1H), 2.10 (m, 1H), 2.21-2.32 (m, 4H), 2.37-2.40 (m, 2H), 2.48-2.55 (m, 1H), 2.56-2.63 (m, 1H), 2.99-3.04 (m, 1H), 3.07-3.13 (m, 1H), 3.44 (ddd, *J* = 7.6 Hz, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H), 3.50 (pseudo d, *J* = 7.2 Hz, 1H), 5.50 (m, 1H), 5.56 (m, 1H), 5.64 (m, 2H). – **^{13}C NMR** ($CDCl_3$): δ = 30.6 (t, CH_2), 31.5 (t, CH_2), 32.4 (t, CH_2), 34.0 (d, CH), 37.9 (t, CH_2), 38.4 (t, CH_2), 39.4 (d, CH), 40.2 (d, CH), 40.9 (d, CH), 41.0 (d, CH), 44.8 (d, CH), 46.6 (d, CH), 51.55 (d, CH), 51.57 (d, CH), 58.8 (d, CH), 61.2 (d, CH), 130.4 (d, CH),131.1 (d, CH), 131.5 (d, CH), 132.3 (d, CH). – **IR** (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1} (C-H), 2855 cm^{-1} (C-H), 2098 cm^{-1} (N_3), 1453 cm^{-1} (C=C).

4.15.3.4. Reaction of 6,6-Dimethyl-4,8-dioxaspiro[2.5]oct-1-ene (148) with HN_3

6,6-Dimethyl-4,8-dioxaspiro[2.5]oct-1-ene (**148**) (140.0 mg, 1.0 mmol) was mixed with 2M HN_3 solution in $CHCl_3$ (5 ml, 10 mmol) and stirred at room temperature for one day. The excess amount of hydrazoic acid and $CHCl_3$ was distilled off at −20 °C to yield 3-hydroxy-2,2-dimethylpropyl 3-azidopropanoate (**149**) as light yellow liquid (142 mg, 0.81 mmol, 82%).



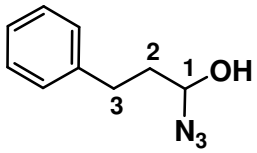
149

3-Hydroxy-2,2-dimethylpropyl 3-Azidopropanoate (149): Light yellow liquid, 82% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 0.92 (s, 6H, CH_3), 2.16 (br s, 1H, OH), 2.60 (t, ^3J = 6.4 Hz, 2H, H-2), 3.32 (s, 2H, H-3′), 3.58 (t, ^3J = 6.4 Hz, 2H, H-3), 3.98 (s, 2H, H-1′). – **^{13}C NMR** ($CDCl_3$): δ = 21.4 (q, CH_3), 33.8 (t, CH_2, C-2), 36.3 (s, $C(Me)_2$), 46.7 (t, CH_2, C-3), 68.1 (t, CH_2, C-3′), 69.8 (t, CH_2, C-1′), 171.4 (s, C=O). For the assignments of carbon signals in compound **149**, 2D-spectra, gHSQCAD and gHMBCAD were used. – **IR** (CCl_4): $\tilde{\nu}$ = 3542 cm^{-1}(OH), 2106 cm^{-1} (N_3), 1740 cm^{-1} (C=O).

4.15.4. Reaction of α-Azido Alcohol with HN_3 in the Presence of *p*-Toulenesulfonic Acid

4.15.4.1. Reaction of 3-Phenylpropanal (154) with HN_3

3-Phenylpropanal (**154**) (100.0 mg, 0.746 mmol) was mixed with 5M HN_3 solution in $CDCl_3$ (2 ml, 10 mmol). The mixture was stirred at room temperature for 10 minutes to obtain an equilibrium mixture containing 1-azido-3-phenylpropan-1-ol (**155**). It was not possible to isolate pure 1-azido-3-phenylpropan-1-ol (**155**) from the equilibrium mixture.

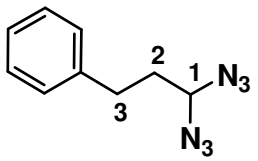


155

1-Azido-3-phenylpropan-1-ol (155): ^{1}H NMR ($CDCl_3$): δ = 1.96 (m, 2H, H-2 diastereotopic protons), 2.73 (t, ^3J = 7.8 Hz, 2H, H-3), 3.94 (br s, 1H, OH), 4.88 (t, ^3J = 6.2 Hz, 1H, H-1), 7.20–7.31 (m, 5H, Ph). – **^{13}C NMR** ($CDCl_3$): δ = 30.4 (t, CH_2), 37.3 (t, CH_2), 85.3 (d, CH), 125.9 (d, CH, Ph), 128.1 (d, CH, Ph), 128.3 (d, CH, Ph), 140.4 (s, Ph).

4.15.4.2. Synthesis of 1,1-Diazido-3-phenylpropane (156)

To the stirred solution of 3-phenylpropanal (**154**) (100.0 mg, 0.746 mmol) and 5M HN_3 solution (2 ml, 10 mmol) was added slowly *p*-toluenesulfonic acid (0.12 g, 0.746 mmol) solution in $CDCl_3$. The mixture was stirred at room temperature for 6 hours to obtain 1,1-diazido-3-phenylpropane (**156**) as colorless oil (108 mg, 0.53 mmol, 72%).



156

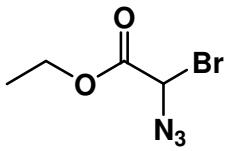
1,1-Diazido-3-phenylpropane (156): Colorless oil, 72% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.99 (td, ^3J = 7.6 Hz, t, ^3J = 6.4 Hz, 2H, H-2), 2.73 (t, ^3J = 7.6 Hz, 2H, H-3), 4.57 (t, ^3J = 6.8 Hz, 1H, H-1), 7.17–7.33 (m, 5H, Ph). – **^{13}C NMR** ($CDCl_3$): δ = 30.8 (t, CH_2), 35.3 (t, CH_2), 77.1 (d, CH), 126.3, d, CH, Ph), 128.2 (d, CH, Ph), 128.5 (d, CH, Ph), 139.6 (s, Ph). – **^{1}H NMR** (CD_2Cl_2): δ = 1.99 (td, ^3J = 7.6 Hz, t, ^3J = 6.4 Hz, 2H, H-2), 2.73 (t, ^3J = 7.6 Hz, 2H, H-3), 4.62 (t, ^3J = 6.8 Hz, 1H, H-1), 7.17–7.34 (m, 5H, Ph). – **^{13}C NMR** (CD_2Cl_2): δ = 31.2 (t, CH_2), 35.8 (t, CH_2), 77.6 (d, CH), 126.6, d, CH, Ph), 128.6 (d, CH, Ph), 128.8 (d, CH, Ph), 140.2 (s, Ph).

4.15.5. Reaction of α-Azido Alcohol with PBr_3

4.15.5.1. Reaction of Ethyl 2-Azido-2-hydroxyacetate (65a) with PBr_3

By utilizing the general procedure and starting with ethyl glyoxylate (**64a**) (102.0 mg, 1.00 mmol), ethyl 2-azido-2-hydroxyacetate (**65a**) was obtained as colorless liquid, which was carefully resolved in cold $CHCl_3$ (5 ml) keeping the temperature at −50 °C. To the above solution containing **65a** was added PBr_3 (0.406 g, 1.5 mmol) at −50 °C to −30 °C over several minutes under argon, and the reaction mixture was stirred for further 5 hours at −30 °C to give ethyl 2-azido-2-bromoacetate (**159**) in a clean reaction. After removal of the solvent, the crude product was purified by flash chromatography on silica gel, eluting with $CHCl_3$ to yield ethyl 2-azido-2-bromoacetate (**159**) as a light yellow liquid (201 mg, 0.97 mmol, 97%) after the removal of solvent. The compound **159** was prepared in 1994 by another method by Y. Takeuchi et al. but no ^{13}C NMR data were given.[74]

Ethyl 2-Azido-2-bromoacetate (159): Light yellow liquid, 97% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.31 (t, ^3J = 7.2 Hz, 3H), 4.28 (q, ^3J = 7.6 Hz, 2H), 5.34 (s, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 13.7 (q, CH_3), 57.5 (d, CH), 63.1 (t, CH_2), 165.4 (s, C=O).

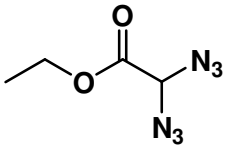


159

4.15.5.2. Synthesis of Ethyl 2,2-Diazidoacetate (160)

To a stirred solution of TMGA (N,N,N',N'-tetramethylguanidinium azide) (316.4 mg, 2.0 mmol) in dry $CHCl_3$ (5 ml) was added slowly ethyl 2-azido-2-bromoacetate (**159**)[74] (208 mg, 1 mmol) in dry $CHCl_3$ (5 ml) at −60 °C over several minutes. The reaction mixture was slowly warmed up to room temperature over a time interval of 2 hours. After removal of the solvent crude product was purified by flash chromatography on silica gel, eluting with (hexane/ethyl acetate 60:40) to yield ethyl 2,2-diazidoacetate (**160**) as a colorless liquid (156.5 mg, 0.92 mmol, 92%) after the removal of solvent. Y. Takeuchi et al. prepared compound **160** in 1994 by another method.[74]

Ethyl 2,2-Diazidoacetate (160): Colorless liquid, 92% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 1.35 (t, ^3J = 7.2 Hz, 3H), 4.32 (q, ^3J = 7.6 Hz, 2H), 4.85 (s, 1H). – **^{13}C NMR** ($CDCl_3$): δ = 14.0 (q, CH_3), 63.1 (t, CH_2),



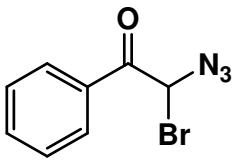
160

73.3 (d, CH), 165.0 (s, C=O).

4.15.5.3. Synthesis of 2-Azido-2-bromo-1-phenylethanone (163a)

By following the general procedure, 2-azido-2-hydroxy-1-phenylethanone (**83a**) was prepared. To **83a** (500 mg, 2.8 mmol) in $CDCl_3$ (5 ml) was added PBr_3 (1.0 g, 3.6 mmol) at −50 °C to −30 °C over several minutes under argon, and the reaction mixture was stirred for further 5 hours at −30 °C to give 2-azido-2-bromo-1-phenylethanone (**163a**) in a clean reaction. The reaction mixture was diluted with ether/hexane (1:1, 25 ml), washed twice with water, and twice with brine, dried over $MgSO_4$, and the solvent was distilled off under vacuum to yield 2-azido-2-bromo-1-phenylethanone (**163a**). The crude product was purified by flash chromatography on silica gel, eluting with $CHCl_3$ to yield 2-azido-2-bromo-1-phenylethanone (**163a**) as a light yellow liquid (647.80 mg, 2.71 mmol, 96%) after the removal of solvent.

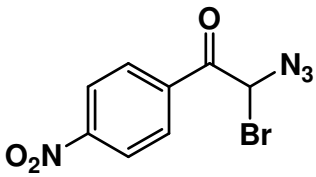
2-Azido-2-bromo-1-phenylethanone (163a): Light yellow liquid, 96% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 6.24 (s, 1H, CH), 7.45-7.63 (m, 5H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 60.8 (d, CH), 128.9 (d, CH, Ar), 129.1 (d, CH, Ar), 131.2 (s, C, Ar), 134.9 (d, CH, Ar), 187.6 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2109 cm^{-1} (N_3), 1698 cm^{-1} (C=O), 1599 cm^{-1} (Ar), 1450 cm^{-1} (Ar), 697 cm^{-1} (C-Br).



163a

4.15.5.4. Synthesis of 2-Azido-2-bromo-1-(4-nitrophenyl)ethanone (163b)

By following the general procedure, 2-azido-2-hydroxy-1-(4-nitrophenyl)ethanone (**83b**) was prepared. To **83b** (500 mg, 2.25 mmol) in $CDCl_3$ (5 ml) was added PBr_3 (0.67 g, 2.50 mmol) at −50 °C to −30 °C over several minutes under argon, and the reaction mixture was stirred for further 5 hours at −30 °C to give 2-azido-2-bromo-1-(4-nitrophenyl)ethanone (**163b**) in a clean reaction. After workup as described for **163a**, the crude product was purified by flash chromatography on silica gel, eluting with $CHCl_3$ to yield 2-azido-2-bromo-1-(4-nitrophenyl)ethanone (**163b**) as a light yellow sticky solid (619 mg, 2.17 mmol, 97%) after the removal of solvent.



163b

2-Azido-2-bromo-1-(4-nitrophenyl)ethanone (163b): Light yellow sticky solid, 97% isolated yield. – **^{1}H NMR** ($CDCl_3$): δ = 6.29 (s, 1H, CH), 8.17 (m, 2H, Ar), 8.36 (m, 2H, Ar). – **^{13}C NMR** ($CDCl_3$): δ = 61.2 (d, CH), 124.0 (d, CH, Ar), 130.1 (d, CH, Ar), 136.1 (s, C, Ar), 150.9 (s, C, Ar), 186.1 (s, C=O). – **IR** (CCl_4): $\tilde{\nu}$ = 2114 cm^{-1} (N_3), 1707 cm^{-1} (C=O), 1534 cm^{-1} (Ar), 1345 cm^{-1} (Ar), 908 cm^{-1} (C-Br).

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Selbständigkeitserklärung

Hiermit erkläre ich, daß ich die vorliegende Arbeit selbständig und nur unter Verwendung der angegebenen Literatur und Hilfsmittel angefertigt habe.

Chemnitz, den 07.10.2011

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Publications, Presentations and Poster Exhibitions

Publications

- Reactions of Unsaturated Azides, Part 26. Viability of 4,5-Dihydro-1,2,3,4-oxatriazoles Reinvestigated.
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Poster Exhibitions and Workshops

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