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# MECHANISM OF PHENYL AZIDE-1,2-CYCLONONADIENE ADDUCT FORMATION AND ISOMERIZATION OF THIS ADDUCT

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A Thesis
Presented to
the Faculty of the Graduate School
University of the Pacific

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In Partial Fulfillment
of the Requirement for the Degree
Masters of Science

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by
Isom Harrison, Jr.
July 1978

# ACKNOWLEDGMENTS

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DEDICATED

to Edith, Lorice, Treva and Viola (Mom)

# Table of Contents

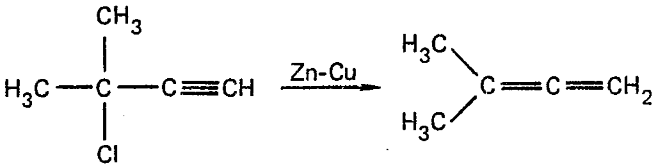
## Historical Background

Allene and some of its homologs were prepared and characterized as early as 1860.[1] They are compounds with two cumulated double bonds and are the simplest of the cumulenes. Despite the fact that compounds containing cumulated double bonds (allenes and cumulenes) have been known for several decades, until relatively recently, comparatively little was known about their chemical behavior. This can be explained by the fact that until about 15 years ago no convenient general method for their preparation was available.[2]

In the late 50's and early 60's the best route for preparing allenes was the one reported by Bailey and Pfeifer.[3] This general method involved the dehydro-halogenation of a 1,2,3,-tribromo derivative, followed by removal of bromine from the dibromo olefin with zinc.

One method involves thermal rearrangement of acetylenes to allenes. This method proved to be unfavorable because of the poor yields of allene obtained.
For example, Favorskii[4] obtained a low yield of 1,1-dimethylallene (1) by heating isopropylacetylene.

More recently, Ginzberg[5] obtained 1,1-dimethylallene (1) in 63% yield by reducing 3-chloro-3-methyl-1-butyne (2) with a zinc-copper couple. Purification and recovery was unsuccessful because of the low yield of allene produced and the difficulty of removing small amounts of isomeric acetylene.



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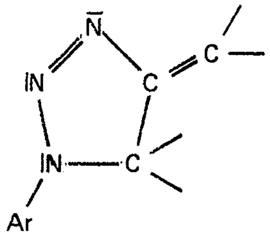
In 1958, La Flamme and Von Doering[6] reported that 1,1-dibromocyclopropanes, which are prepared by the method of Von Doering and Hoffman[7] react with magnesium or highly dispersed sodium to give allenes in reasonable yields. The products were usually contaminated with acetylenes and cyclopropanes. Skattebol[2] investigated the reaction of 1,1-dibromocyclopropanes with alkyl lithium compounds. The 1,1-dibromocyclopropane derivatives were treated in ethereal solutions of either methyl or butyllithium usually at $-30^{\circ}$ to $-40^{\circ}$. The reaction products were analyzed by gas chromatography and infrared spectroscopy. In most cases, allenes were practically the sole products, but occasionally small amounts of acetylenic compounds were detected, particularly when n-butyllithium was used. Generally methyllithium proved to be the most convenient lithium reagent since difficulties were occasionally encountered in separating completely the butyl bromide product from the allenes when butyllithium was used. Also, the greater tendency to form acetylenic side products with butyllithium as indicated above made methyllithium the better choice.

Favorskii[8] was the first to report the synthesis of a cyclic allene. He reported that 1,2-cycloheptadiene was the product obtained when 1-chloro-2-bromocycloheptene in ether solution was treated with sodium metal. However, Ball and Sandor[9] later showed that the work of Favorskii on the preparation of 1,2-cycloheptadiene was in error. They found that the only volatile product obtained when sodium reacted with 1-chloro-2-bromocycloheptene was cycloheptene.

In 1952, Blomquist and Co-workers[10] were able to successfully prepare 1,2-cyclodecadiene but then only as a mixture with the analogous cyclic acetylenes. However, more recently, pure 1,2-cycloalkadienes have been prepared by treating the appropriate gem-dibromocyclopropane with an alkyl lithium reagent.[11]

A number of 1,3-additions reactions have been recently studied.[12] The 1,3-addition of a reagent such as an aryl azide to an allenic double bond can potentially occur to give two types of isomeric products, 3 and 4. Shecter[12] reacted a number of different azides with tetramethylallene (5). He reported that an adduct having the type 3 structure results when the highly electronegative picryl azide reacts with tetramethylallene (5). He



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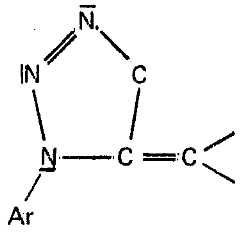

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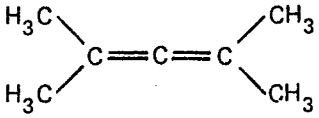

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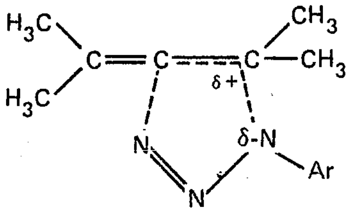
proposed that the transition state resembles 6. This



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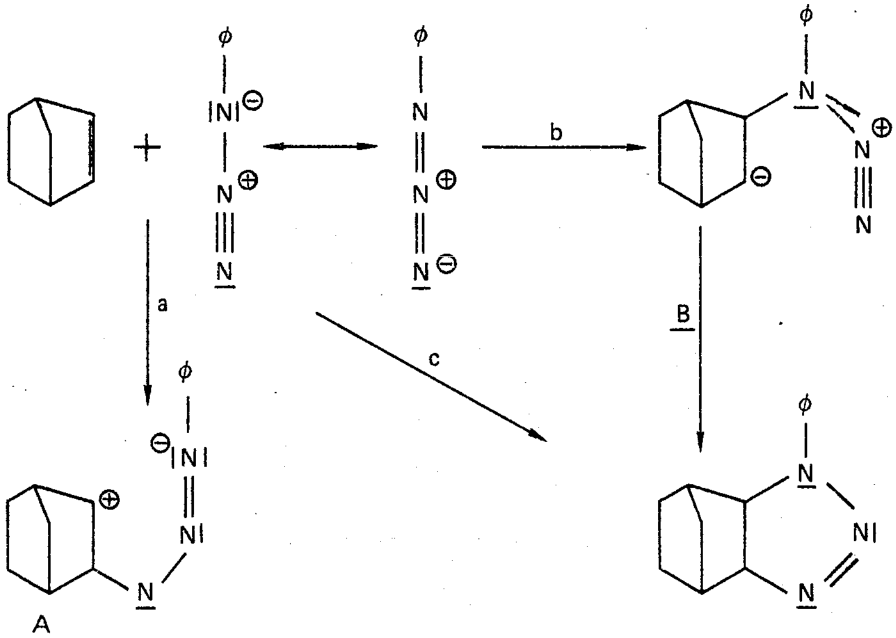
proposal is consistant with the fact that picryl azide reacts with tetramethylallene indicating stabilization of the transition state by the electron withdrawing groups on the aromatic ring; and is also consistent with the work of Huisgen and others[13] that supports a concerted process in the addition of aryl azides to simple alkenes with the type of charge separation indicated in 6. In studying the mechanism of the addition of phenyl azide to alkenes, Huisgen proposed that in the addition of phenyl azide to a double bond, three mechanisms are conceivable: (a) the terminal azide nitrogen might accept the pair of π-electrons fron the carbon-carbon double bond forming intermediate A followed by its ring closure (b) the nitrogen adjacent to the aromatic ring might donate a pair of electrons to the carbon-carbon double bond to form B which subsequently closes; (c) both ends of the 1,3-dipole may add at the same time. Doubts concerning mechanisms (a) and (b) were immediately raised because the sluggish reacting organic azide displays neither strong electrophilic nor strong nucleophilic character. The concerted process (c) is immune to such objections because in (c) a synchronous shift of electrons results in the formation of two new C-N bonds and allows all atoms to achieve stable octets without having to bear a formal charge.



Kinetic solvent effects offer a means of distinguishing the synchronous from the two-step mechanism. The rate determining first steps of paths (a) and (b) form zwitterions A and B the charges of which are isolated by a tetrahedral carbon atom. Good solvents for ions should facilitate such processes. On the other hand, mechanism (c) is attended by some loss of dipolar character and should be slightly retarded by increasing solvent polarity. Huisgen[13] measured the rate of addition of phenyl azide to a strained double bond in several solvents. The results showed no dramatic change with increasing polarity of the solvent. The rate constants differed by less than a factor of two. The modest trend is even slightly opposed to the dielectric constants of the solvents. This is consistent with the polycenter mechanism (c) which calls for some decrease in polarity in the activation process.

In 1964, a kinetic investigation on the addition of aryl azides to norbornene by Scheiner and Co-workers[26] showed the reaction is insensitive to solvent polarity and is characterized by a large negative entropy of activation ($\Delta S\#=-34.9$). The relatively large negative values indicate a highly ordered transition state, as expected for a simultaneous multicenter process. They also assumed that the magnitude and sign of the $\Delta s$ values did not reflect large solvation changes. However, the authors could not explain a sizable substituent effect ($\rho = +\,0.84$ at $25^{\circ}$) which was inconsistent with a multicenter process. The relative indifference to solvent polarity found by Scheiner and Co-workers parrallels a similar insensitivity reported for the addition of diphenyldiazomethane to 2,3-dicarbethoxy-2,3-diazobicyclo[2.2.1]hept-5-ene.[21] This result is consistent with Huisgen's view of 1,3-dipolar addition as a multicenter process in which both new bond are formed simultaneously.[13] More recently, Wedegaertner[14] has found that the reaction of phenyl azide with 1,2-cyclononadiene gave 10-phenyl-10,11,12-triaza-$\Delta^{11}$-bicyclo[7.3.0]duodec-1-ene.

## Statement of Problem

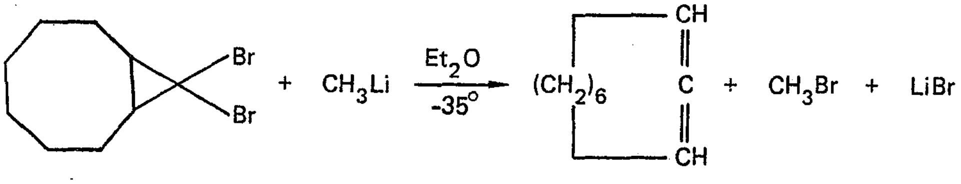
A major purpose of this research was to investigate the mechanism of aryl azide addition to allenes. Much evidence has accumulated in support of a concerted mechanism for aryl azide additions to simple alkenes.[13] Consistent with these findings, this addition is a symmetry allowed process[24]. The analagous aryl azide additions to allenes have received little mechanistic study. The approach taken in this work was to probe the mechanism by using optically active 1,2-cyclonanadiene, observing the stereochemistry of the adduct formed upon addition of phenyl azide.

Another goal was to investigate the isomerization of the phenyl azide-1,2-cylononadiene adduct, 10-phenyl-10,11,12-triaza-$\Delta^{11}$-bicyclo [7.3.0]duodec-1-ene (7) to the previously unknown aromatic isomer 4,5-heptamethylene-1-phenyl-1,2,3-triazole (14).

## Results and Discussion

### I. Preparation of 1,2-cyclononadiene

1,2-cyclononadiene (1,2-CND) was prepared from 9,9-dibromobicyclo [6.1.0] nonane[17] by the method of Skattebol and Solomon[17] in which 9,9-dibromobicyclo 6.1.0 nonane in anhydrous ether at -35° to -40° was treated dropwise over 2 hr with a solution of methyllithium. A faster addition of methyllithium than that reported by the above authors was sometimes used because solid methyllithium and lithium halide separated out and plugged the tip of the dropping funnel. After 2 hr, the reaction mixture was washed with water until neutral. The mixture was dried over anhydrous magnesium sulfate. Filtration and distillation of the residue using a 40 cm column, gave a 75-80% yield of pure 1,2-CND. Since 1,2-CND dimerizes at high temperature,[17] it was distilled in vacuo and stored in a refrigerator. Its tendency to dimerize makes it desirable to use freshly prepared 1,2-CND immediately. However, if kept at 10-15°, it can be stored for 1 to 2 weeks before much dimerization occurs.



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## II. Partial Resolution of 1,2-Cyclononadiene

1,2-cyclononadiene (1,2-CND) was partially resolved by the selective destruction of one enantiomer using the chiral hydroborating agent sym-tetraisopinocamphyldiborane (9). Initial work utilized the procedure described by Byrd and Caserio[19]. Since the optical purity of 1,2-CND obtained in this manner appeared to be rather low and this author was not able to duplicate even these optical purities, experiments were initiated that sought to develop a procedure for obtaining 1,2-CND in higher optical purity. Two tactics suggested themselves as potentially useful to increase selectivity in the asymmetric hydroboration of 1,2-CND: 1) inverse addition (adding 9 to an excess of 1,2-CND) and 2) lower reaction temperature. Since 9 precipitates from solution as a paste, it is difficult to transfer in small amounts and inverse addition procedures were not attempted. A series of reactions were carried out at different temperatures (Table I). The best specific rotation for 1,2-CND reported by Byrd and

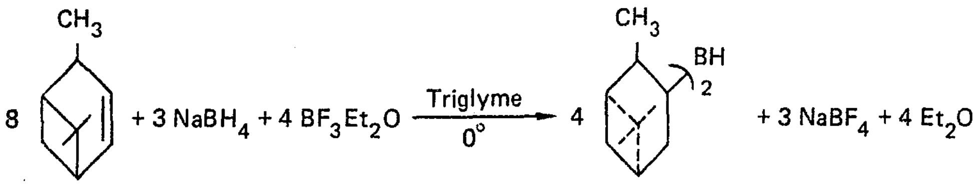
Caserio[19] $[\alpha]_D^{24}$ + $26.5^{\circ}$ (neat); reaction: 2.5 hr. at $-12^{\circ}$; Moore *et al*[22] $[\alpha]_D^{22}$ + $27.4^{\circ}$ (neat), $[\alpha]_D^{22}$ reaction: 30 min at $0^{\circ}$ , and this author $[\alpha]_D^{24}$ - $29.0^{\circ}$ (C. .005, pentane), reaction: 1.0 hr at $0^{\circ}$, were not substantially different. A brief description of procedures attempted follows.

Asymmetric hydroboration of 1,2-cyclononadiene (run number 1) was carried out by the method of Brown and co-workers[18] with a few modificatons in the procedure as reported by Byrd and Caserio[19]. Boron trifluoride etherate in triglyme was added slowly to a stirred solution of (-)-α-pinene (83% optical purity) $[\alpha]_D^{20}$ $-42.5^{\circ} \pm 0.1$ (neat), and sodium borohydride in triglyme at $0^{\circ}$. After stirring for 20 hr at $0^{\circ}$, the suspension of sym (+)-tetraisopinocamphenyldiborane (9) was cooled to $-12^{\circ}$,. This product precipitated as a thick white paste as the reaction proceeded. After the temperature is lowered to $-12^{\circ}$, the racemic allene was added in a single batch. The mixture was stirred for an additional 2.5 hours and distilled under reduced pressure between $50\text{-}70^{\circ}$ at 4 mm. The distillate was washed with distilled water to remove triglyme. The recovered unreacted allene was fractionally distilled giving (+)-1,2-cyclononadiene $[\alpha]_D^{24}$ + $9.5^{\circ} \pm 0.1$ (neat, uncorrected for α-pinene). G. C. Analysis showed 87% (+)-1,2-CND with 13% α-piene impurity, thus for this 1,2-CND sample $[\alpha]_D^{24}$ + $17.2^{\circ} \pm 0.1$ (neat, when corrected for α-pinene).

In run number 2, α-pinene $[\alpha]_D^{20}$ + $46.09^{\circ} \pm$ I0.01 (neat, 90.2% optical purity) was used. It was allowed to react with diborane for 20 hr at $0^{\circ}$ to form 9. The mixture was then cooled to $-12^{\circ}$. The unreacted allene (1,2-CND) was recovered by distillation ($50\text{-}70^{\circ}$, 4 mm) followed by extraction with water to remove triglyme. The combined organic phases were dried over $MgSO_4$ and fractionally distilled. Distillation afforded 1,2-CND $[\alpha]_D^{27}$ $-15.3^\circ \pm 0.1$ (neat). Gas chromatographic analysis was not performed on this product.

A series of other resolutions were carried out using (+)-α-Pinene $[\alpha]_D^{24}$ $+ 46.09^\circ \pm 0.01$ (neat, 90.2% optical purity). The procedures followed for these reactions were similar to the ones previously used by Moore and co-workers.[22] Smaller amounts of reagents were used in these experiments than in the above reactions. Moore found that 9 was formed from the diborane and (+)-α-Pinene within 4 hr at 0° and shorter reaction times for this reagent were thus used. They also found that at 0° the reaction of 9 with 1,2-CND was complete within 5 min. They were able to obtain an optical rotation for 1,2-CND of $[\alpha]_D^{24}$ $+ 27.4^\circ$ for a G.C. collected sample. Based on Moore's et al[22] procedure, reaction conditions were varied by this author in order to try to increase the optical rotation (optical purity) of 1,2-CND. It was found that the greatest optical rotation for 1,2-CND was achieved by reaction of 9 with racemic 1,2-CND at 0° for 1 hr, $[\alpha]_D^{24}$ $-29.00^\circ$ $\pm 0.01$ (C. 0.005, pentane). In run number 3 given below, the details are discussed.

In run number 3, (+)-α-Pinene, $[\alpha]_D^{20}$ $+ 46.09^\circ \pm 0.01$ (neat, 90.2% optical purity) was allowed to react with diborane for 4 hr at 0° to form 9. The ice bath was removed



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and it was replaced by a dry-ice-acetone bath ($-72^{\circ}$). A precooled solution of 1,2-CND ($0^{\circ}$) was added to the reaction mixture. The dry-ice-acetone bath was then replaced with a dry-ice-$CCL_4$ bath ($-20^{\circ}$). The reaction mixture was stirred at $-20^{\circ}$ for an additional 2 hr. The reaction was quenched with water and pentane was added. The organic phase was washed with water, dried($MgSO_4$) and concentrated by rotatory evaporation. Distillation followed by preparative glc gave optically active 1,2-CND, $[\alpha]_D^{24}$ $-13.51^{\circ}$ ± 0.01 (C. 0.0079 g/ml, pentane), free of α-pinene.

In run number 4, (+)-α-Pinene $[\alpha]_D^{24}$ + 46.09 ± 0.01 (90.2% optical purity) was allowed to react with the diborane for 4 hr at $0^{\circ}$ to form 9. The ice bath was removed and it was replaced by a dry-ice-acetone bath ($-72^{\circ}$). A precooled solution of 1,2-CND ($0^{\circ}$) in lmL of ether was added all at once. The dry-ice-acetone bath was then replaced by a dry-ice-$ccl_4$ bath ($20^{\circ}$) and the reaction mixture was stirred for one hour. The dry-ice-$CCL_4$ bath was replaced by an ice bath and the reaction mixture was stirred for another hour. The reaction mixture was quenched with water and pentane was added. The organic phase was washed with water, dried ($MgSO_4$), and concentrated. Distillation followed by preparative glc gave optically active 1,2-CND $[\alpha]_D^{24}$ $-9.01^{\circ}$ ± 0.01 (C. 0.055, pentane) free of α-pinene per G.C. analysis.

In run number 5, (+)-α-Pinene $[\alpha]_D^{24}$ + 46.09 ± 0.01 (90.2% optical purity) was allowed to react with the diborane for 4 hr at $0^{\circ}$ to form 9. A precooled solution of 1,2-CND ($0^{\circ}$) was added to 9 and the mixture was stirred for an additional hour at $0^{\circ}$. The reaction was then quenched with water and pentane was added. The organic phase was washed with water, dried ($MgSO_4$) and concentrated by rotatory

TABLE I. 1,2-Cyclononadiene Resolution Experiments

| Run Number | $[\alpha]_D^{24}$ 1,2-CND Conc. g/ml | $[\alpha]_D^{24}$ α-pinene | Moles 1,2-CND | Temp for Rx of 9 with 1,2-CND | Time hr** | % Yield 1,2-CND |
|---|---|---|---|---|---|---|
| 1 | +17.2°* (neat) | −42.5° | 0.246 | −12° | 2.5 | 68% |
| 2 | −15.3° (neat) | +46.09° | 0.246 | −12° | 2.5 | 67% |
| 3 | −13.51° (C. 0.0079) | +46.09° | 0.0033+ | −20° | 1.0 | --- |
|  |  |  |  | 0° | 1.0 | --- |
| 4 | −9.00° (C. 0.055) | +46.09° | 0.0018+ | −20° | 2.0 | --- |
| 5 | −29.00° (C. 0.005) | +46.09° | 0.0033+ | 0° | 1.0 | --- |
| 6 | −12.72° (C. 0.030) | +46.09° | 0.127 | 0° | 0.5 | --- |

*Corrected for α-pinene

**Reaction time after 1,2-CND added to 9

+Reactions run on micro scale

evaporation. Distillation followed by preparative glc gave optically active 1,2-CND $[\alpha]_D^{24}$ -29.00° ± 0.01 (C. 0.005, pentane) free of α-pinene. The three reactions mentioned above (runs 3, 4, 5) were carried out using very small quantities of reagent (4.4 mmol or less).

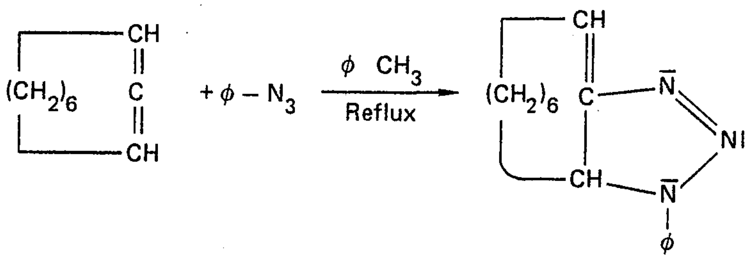
One other resolution was carried out at 0° on a larger scale using (+)-α-Pinene, $[\alpha]_D^{24}$ + 46.09° ± 0.01 (neat, 90.2% optical purity). In run number 6, α-pinene was allowed to react with the diborance for 4 hours at 0° to form 9. then a precooled solution of 1,2-CND (0°) was added and the reaction mixture was stirred for an additional 30 minutes. The flask was arranged for distillation. The unreacted 1,2-CND was recovered by distillation at 1 mm. The distillate was washed with water and dried. Distillation at room temperature followed by preparation glc gave optically active 1,2-CND, $[\alpha]_D^{24}$ - 12.72° ± 0.01 (C. 0.003 pentane). The infrared spectrum of this optically active 1,2-CND (IR-2) was essentially identical to an authentic sample of racemic 1,2-CND (IR-1).

Although a fair variation in specific rotation of 1,2-CND was observed, the results do not suggest any advantage is to be gained by carrying out the reaction out at lower temperatures. In fact, the highest specific rotation was obtained from a 0° run.

## III Reaction of Optically Active 1,2-Cyclononadiene with Phenyl Azide:

It had previously been shown[14] that 1,2-CND and phenyl azide, when refluxed overnight in toluene under nitrogen, gave a 1:1 adduct (7). It was obtained as a viscous yellow oil upon removal of the solvent. The oil was kept at room termperature for 3 to 4 days for crystallization to occur. Recrystallization from pet. ether (60-110°)

gave pure 10-phenyl-10,11,12-triaza-Δ"-bicyclo[7.3.0]duodec-1-ene (7), MP 90-96°.[14]



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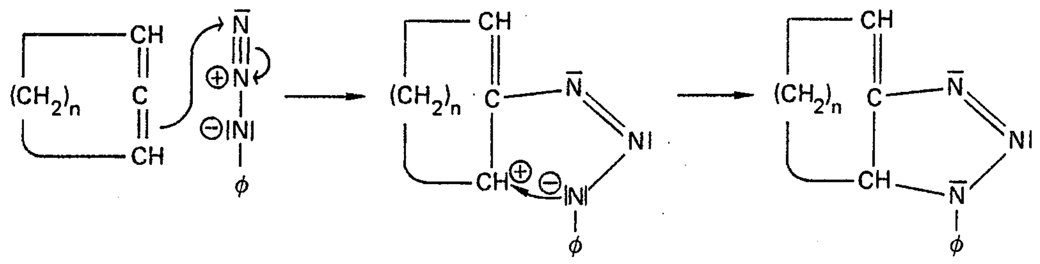
Since 1,2-CND had previously been partially resolved[19], optically active 1,2-CND was used to probe the mechanism of phenyl azide-allene addition. There are two types of possible mechanistic pathways: a pathway in which a stepwise process takes place or a concerted process in which all bond making and breaking steps occur simultaneously. In the case of a stepwise process involving formation of a symmetrical intermediate, if optically active 1,2-CND were used, there would be a loss of optical activity in the product. An example of such a possible stepwise process is shown in Scheme I.

Scheme I:



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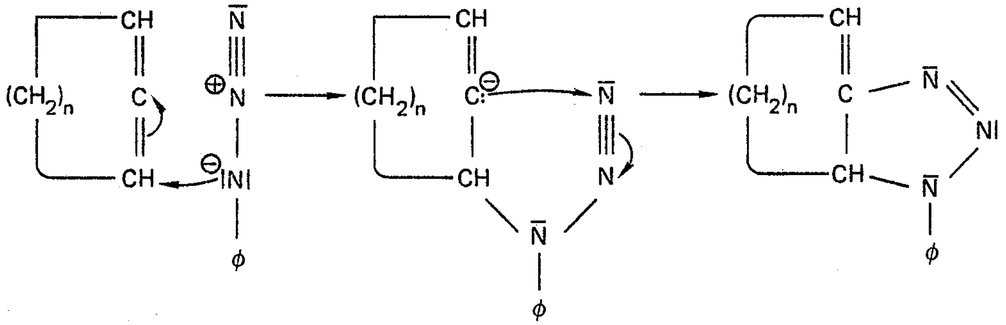
The above stepwise process involving a positive charge on carbon in the intermediate is one of several that can be written for the reaction. In addition to the carbonium ion mechanism in Scheme I, a carbanion mechanism and a diradical mechanism can be proposed.

A type of intermediate formed by an initial addition to the terminal allenic carbon is shown in Scheme II.

Scheme II:



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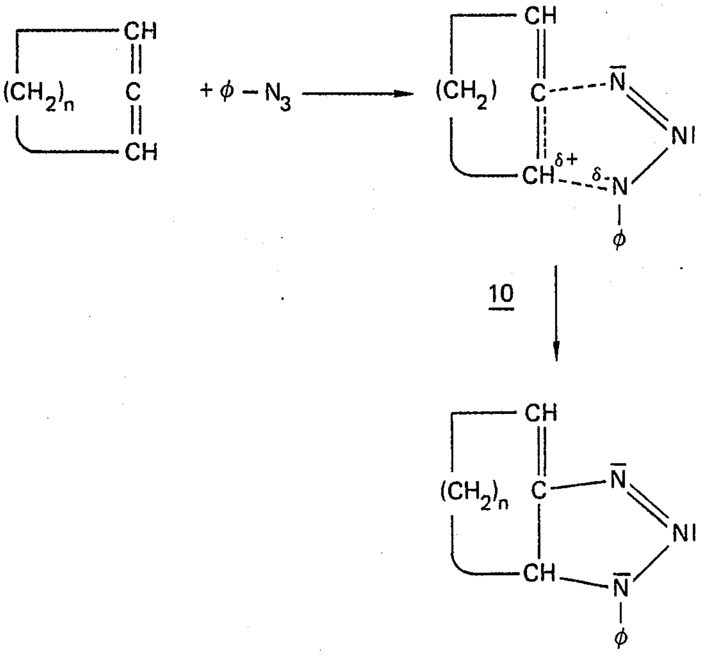
Partial retention of optical activity would be consistent with this stepwise process because initial attachment would create a chiral carbon and would be expected to be stereoselective leading to at least partial retention of optical activity.

In the concerted process (Scheme III) the reaction of optically active 1,2-CND would be expected to be stereoselective and lead to at least some retention of activity since addition to one side of the double bond would be sterically preferred and all bond making and breaking occurs simultaneously. The transition state might resemble (10) with stabilization of the partial negative charge on nitrogen by the phenyl group.[13]

Scheme III:



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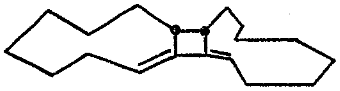
The reaction of phenyl azide with optically active 1,2-cyclononadiene was carried out. The 1,2-CND used contained 13% α-pinene impurity (gc. analysis): $[\alpha]_D^{24}$ + 9.5° ± 0.1, (neat, uncorrected for α-pinene). After gently refluxing for 10 hours under nitrogen, the solvent (toluene) was removed and the viscous yellow oil was kept several days at room temperature to crystallize. The yellow needle-like crystalline crude adduct was dissolved in chloroform and the rotation of the mixture was taken using a 2 dm micro polarimeter tube. Due to impurities, light could not penetrate the mixture. Therefore, the adduct was recrystallized from pet. ether (b.p. 60-110°). The recrystallized adduct was dissolved in chloroform and the rotation was measured. The recrystallized 7 had a specific rotation, $[\alpha]_D^{24}$ + 9.7° ± 0.1 (c. 0.1, $CHCl_3$), M.P. 90-94°. TLC analysis showed that no 1,2-CND dimer was present in the adduct 1.0% dimer could be detected.

In a control run, excess racemic 1,2-CND (0.016 mole) was mixed with optically active (+)-α-Pinene (0.007 mole) $[\alpha]_D^{24}$ - 42.5° ± 0.1 (neat, 83% optical purity) and allowed to react with phenyl azide (0.010 mole). After refluxing under nitrogen in toluene, the solvent was removed by rotatory evaporation. The crude yellow mixture was allowed to stand several days at room temperature to crystallize. The product was recrystallized from pet. ether and the rotation was measured. It was found that the product did not rotate polarized light, $[\alpha]_D^{24}$ 0.000° ± 0.000, and was therefore racemic. It can thus be concluded that the α-pinene impurity in the 1,2-CND plays no role (no asymmetric induction) in the production of the optically active adduct, 7.

In order to make certain that the rotation of optically active 7 was real, the possibility that the rotation of adduct 7 was due partly to impurities was considered.

α-pinene impurity could lead to a significant error in measuring the rotation of 7. Since α-pinene has the opposite sign of rotation compared to the adduct (7), the rotation of 7 couldn't solely be due to unreacted α-pinene. Unreacted α-pinene could, however, partially cancel the adduct (7) rotation. GC. analysis of the optically active 1,2-CND used showed that the allene contained 13% α-pinene impurity. However, recrystallization of the adduct 7 would be expected to remove small amounts of α-pinene present in the adduct.

1,2-CND dimer, if present in adduct 7, could cause a significant error in the rotation of 7 because when the dimer forms from optically active 1,2-CND, it is also optically active.[17] The exact rotation of the 1,2-CND dimer is not known but it has been predicted to be about the same as that of the allene.[17] Dimerization of optically active 1,2-CND (125°, 70 min) has been reported to give an essentially quantitative yield of a mixture of three isomers, 11, 12, and 13.



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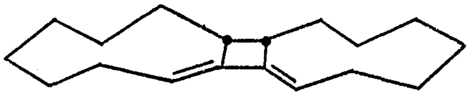

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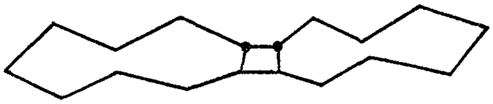
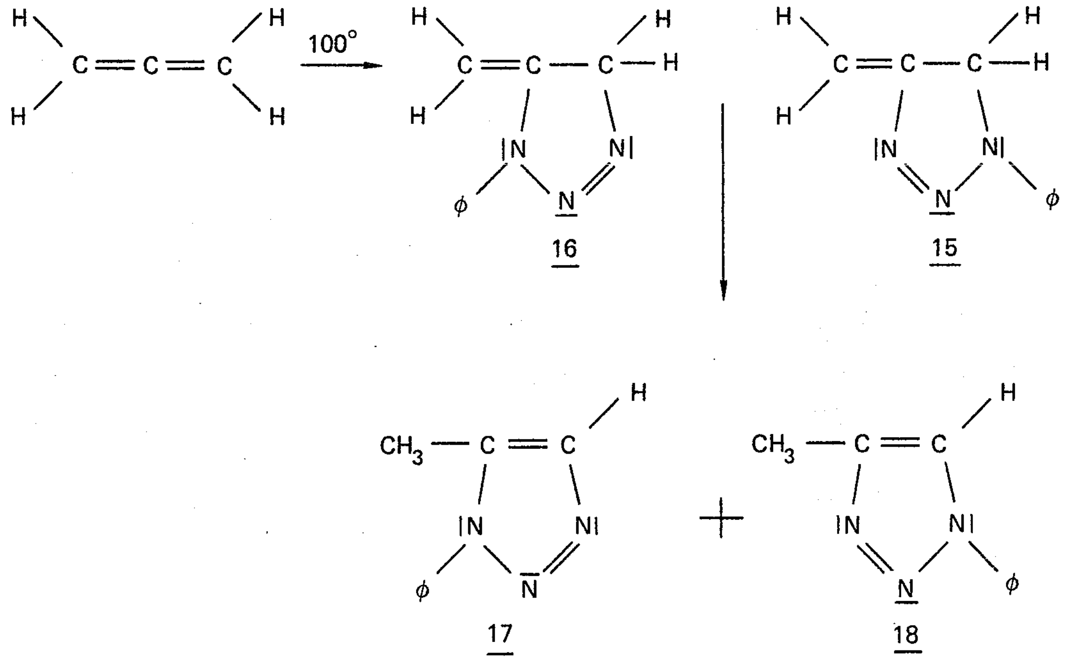
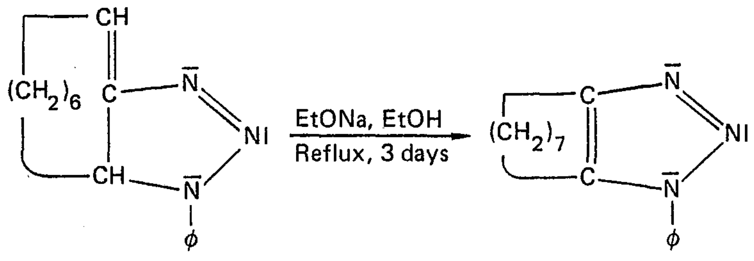


13

Dimerization stemming from the combination of d-allene with d-allene (or ℓ-with ℓ) gives 11 while combination of d-allene with ℓ-allene gives 12 and 13. However, optically active 1,2-CND azide with allene (1,2-propadiene) at 50-100$^{\circ}$ has been shown to yield only5-methyl-1-phenyl-1,2,3-triazole (18) and 4-methyl-1-phenyl-1,2,3-triazole (17).[25] No evidence for the precursor triozolines, 4-methylene-1-phenyl-1,2,3-triazoline (15) and 5-methylene-1-phenyl-1,2,3-triazoline (16) in the reaction mixture could be obtained even when the reaction was carried out at 50$^{\circ}$.[25] The isomerization of 7 to the expected more stable aromatic triazole 14 was, therefore, examined.



Preliminery experiments were carried out in order to establish the conditions necessary to facilitate the isomerization of 10-phenyl-10,11,12-triaza-$\Delta^{11}$-bicyclo[7.3.0]duodec-1-ene (7) into its aromatic isomer (14).

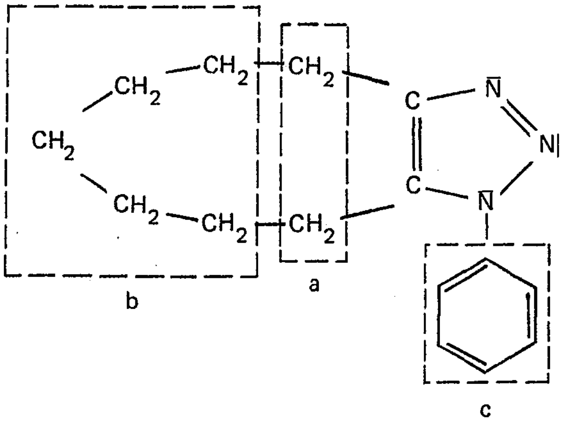


7 14

In the initial experiment, optically active 1:1 adduct 7 was dissolved in ethyl alcohol and the rotation was measured. The adduct had a specific rotation, $[\alpha]_D^{25} - 2.4^{\circ} \pm 0.01$ (c. .006 g/ml, EtOH). Then 1 M sodium ethoxide was added to 7 and the rotation was again measured. The specific rotation did not change. Since 14 is achiral, isomerization to it was followed by observing the decrease in the solutions ability to rotate polarized light. After one hour at room temperature, the rotation was measured and no change had occured in the specific rotation. The mixture was then refluxed overnight under nitrogen. The mixture was filtered to remove a slight turbidity and the rotation was again measured. The specific rotation of the mixture had decreased to $[\alpha]_D^{25} - 1.00^{\circ} \pm 0.01$ (EtOH). The mixture was refluxed an additional 3 days under nitrogen. The mixture was filtered and the rotation was measured. This mixture did not rotate polarized light, $[\alpha]_D^{25} = 0.00 \pm 0.01$. The solvent was removed by rotatory evaporation. The crude mixture was analyzed by infrared (IR) spectrophotometry and Nuclear Magnetic Resonance (NMR). Both spectra indicated that the starting material had been destroyed and that this crude material was impure. The remaining material was left sitting to see if crystallization would occur.

Based on the above experiment, a scaled up reaction of 7 with sodium ethoxide was carried out. After refluxing for three days under nitrogen, the solvent was removed by rotatory evaporation. The product was extracted with ether and the organic phase was washed with water until neutral and dried over anhydrous magnesium sulfate. The solvent was removed by rotatory evaporation and an IR spectrum was taken of the sample. The spectrum showed some - OH absorption and some C-0 absorption. This was attributed to the presence of a small amount of ethyl alcohol. Pet. ether was added to the sample and removed by rotatory evaporation. This procedure was repeated three times to remove the ethanol. Then, the mixture was left sitting to crystallize. Crystallization occured within three or four hours. The brown crystalline solid was recrystallized from a pet. ether-benzene mixture (3:1) and afforded a white crystalline solid (71.5%), which had the correct analysis for 14 ($C_{15}H_{19}N_3$): M.P. 77-78°; MS, M/e 241 (P, 3.44%), 77 (100%) and 213 (35%); UV ($CH_3OH$), λ max 211 mm (ε 12,400) which is in reasonable agreement with values for 5-methyl-1-phenyl-1,2,3-triozole and 4-methyl-1-phenyl-1,2,3-triazole[25] of λmax 207 and λmax 207 respectively. This is in contrast to the UV spectrum (95% ETOH) of the non-aromatic isomer ~~11~~ 7 λmax 352 nm (ε 1.2 x $10^4$).[14] The NMR spectrum was consistent with structure 14 (Scheme IV). It showed a singlet at δ 1.4 (rel. area 10.08) corresponding to 10 aliphatic methylene protons (b). The broad

Scheme IV



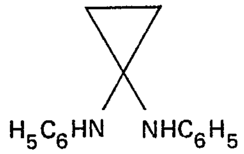
14

response at δ 2.6-3.0 (rel. area 3.88) is consistent with four methylene protons (a) adjacent to the triazole ring. Absorption at δ 7.5-7.8 (rel. area 5.08) corresponds to five aromatic protons (c) in the benzene ring.[27] This is in contrast to the NMR spectrum of the non-aromatic isomer 7 which showed δ 0.9-2.7 (12H,M), 4.3-4.7 (1H,M), 6.02-6.43 (1H,M), and 6.85-7.7 (5H, $-C_6H_5$, M).[14] The IR spectrum showed major peaks at 1600 $cm^{-1}$ which corresponds to C-C absorption of the aromatic system and 750 $cm^{-1}$ which corresponds to absorption of C-H deformations of a mono substituted benzene ring.[28] TLC $R_f$ values for 14 and the starting material 7 were 0.64 for 7 and 0.83 for 14. No spot for the starting material 7 was evident in the product 14. It was established that 0.97% or less starting material could have been detected.

## V. Isomerization of 7 in N-methylaniline:

Compounds 17 and 18 resulted when phenyl azide reacted with allene in an autoclave at 50-100° for 3 days to 3 weeks.[25] 1,1-Dianilinocyclopropane

(19) also formed in this reaction. This basic compound is the most likely catalyst for the isomerization of the initial adducts 15 and 16 to 17 and 18 respectively. In view of the relatively slow isomerization of 7 to 14 by refluxing sodium ethoxide-ethonol, it was deemed appropriate to examine the



19

kinetic stability of 7 under conditions comparable to those employed in the reaction of phenyl azide with allene.

Optically active 7 $[\alpha]_D^{24}$ - 1.13° ± 0.01 ($CHCL_3$) was heated to 108° ± 4° for eight days in an N-methylaniline solution under nitrogen. Due to the dark color of the solution at the end of this time, the rotation could not be measured to see if optical activity had been destroyed or remained unchanged. However, TLC analysis (after workup, see experimental) showed that 7 had been isomerized to 14 with 7 present in very small quantity. Also, a very faint spot was detected for an unidentified product.

The expected isomerization of 7 to its aromatic isomer 14 occurs in good yield with sodium ethoxide catalysis. Treatment of 7 in an N-methylaniline solution for 8 days at 108° gives mainly 14. However, both starting material (7) and an unidentified side product were identified by TLC. It is thus reasonable that in the reported reaction of phenyl azide with allene[25] at 100° for 3 days to 3 weeks, that initially formed adducts 15 and 16 could isomerize to the observed products, aromatic isomers 17 and 18 respectively, by the base catalysis afforded by 1,1-dianilinocyclopropane (19) which also formed as a product in this reaction. However, in the phenyl azide-allene reaction, even at 50°, no 15 or 16 could be detected. When one considers that the base catalyst 1,1-dianilinocyclopropane is at much lower concentration in this reaction than is the comparable base catalyst N-methylaniline in the isomerization of 7 to 14, it appears that the isomerizations of 15 and 16 to 17 and 18, respectively, are more rapid since a small amount of starting material was detected in the isomerization of 7 to 14 in N-methylaniline for 8 days at 108°.

## SUMMARY

Optically active 1,2-cyclononadiene and phenyl azide react to give an optically active adduct, 10-phenyl-10,11,12-triazo-$\Delta^{11}$-bicyclo [7.3.0]duodec-1-ene (7). Retention of optical activity is inconsistent with formation of an achiral intermediate. It is most reasonably interperted in terms of a symmetry allowed concerted process. Compound 7 is isomerized to 1-phenyl-4,5-heptamethylene-1,2,3-triozole (14) by heating with sodium ethoxide in ethonol or N-methylaniline.

Various experimental conditions were used for increasing the optical purity of 1,2-cyclononodiene. Lower temperature and smaller amount of reagents were used. The best value for the optical rotation of 1,2-cyclononodiene achieved by this author was $[\alpha]_D^{24}$ - 29.00° ± 0.01.

# EXPERIMENTAL

## I. Introduction

The chemicals used in this investigation were pentane, bromoform, anhydrous ether, cyclooctene, triglyme, α-pinene, boron triflouride etherate, methyllithium, toluene and pet. ether. Details are given below:

Pentane (reagent grade from petroleum, 99% pure, purified by oleum) was obtained for Eastman Kodak Company and was used without additional treatment.

Bromoform was obtained (practical grade) from Matheson, Coleman and Bell and was used after redistillation under vacuum.

Cyclooctene obtained from Matheson, Coleman and Bell was redistilled from calcium hydride under reduced pressure.

Triglyme (99% pure) was obtained from Aldrich Chemical Company and was used without further treatment.

α-pinene[19] $[\alpha]_D^{25}$ - 42.5°, (83% optical purity) and α-pinene $[\alpha]_D^{25}$ + 46.09° (90.2% optical purity) was obtained from Aldrich Chemical Company and was used without additional treatment.

Boron trifluoride etherate was obtained form J. T. Baker Company. Ether (10 ml) was added to 500 ml of boron trifluoride etherate[23] and distilled from 2 g of calcium hydride in an all glass apparatus at 46°/10 mm. The hydride is reported to remove volatile acid and reduce bumping.

Methyllithium (1.5 M in ether) was obtained from Foote Mineral Company and was used without additional treatment.

Toluene was obtained from J. T. Baker Chemical Company and was used without additional treatment

Petroleum ether (b.p. 60-110°) was redistilled from calcium hydride.

The solids used during this investigation were sodium borohydride and potassium t-butoxide.

Sodium borohydride, obtained from Matheson, Coleman and Bell, was used without additional treatment.

Dry potassium-t-butoxide (98% pure) was obtained from K&K Laboratories, Inc., and was used without additional treatment.

The instruments used during this investigation are as follows:

A Perkin-Elmer 137 Infrared spectrophotometer, polarimeters (Rudolph model 956 and Perkin-Elmer 241), aerograph gas chromatograph (model A-350-B), a Varian Anaspect EM600 spectrometer , Perkin-Elmer Model UV spectrophotometer, a JEOL MH-100 Nuclear Magnetic Resonance spectrophotometer and an AEI-MSI2 mass
Spectrometer.

## II. Preparation of 9,9-dibronobicyclo[6.1.0]nonane

The method used for preparing 9,9-dibronobicyclo[6.1.0]nonane was the one described by Von Doering and Hoffman.[7] To a stirred slurry of 248 g (1.85 mole) of potassium-t-butoxide in 700 ml of dry pentane and 118 g (1.07 mole) of cyclooctene at 0° was added 313 g (1.20 mole) of bromoform in 100 ml of pentane over a period of 9 hr. The mixture was stirred for an additional 12 hr at 0°. The reaction mixture was then washed with 500 ml of water and the aqueous layer was removed. This aqueous mixture was then extracted with 500 ml of pentane. The combined organic phases were washed with 200 ml portions of water and dried over anhydrous magnesium sulfate. The magnesium sulfate was removed by filtration and the pentane was removed by rotatory evaporation. The crude product (346 g) was distilled at 1 mm. The low boiling forerun was rejected (b.p. 40-100°) but the other fractions (b.p. 101-112°) were combined and fractionally distilled. A yield of 210 g of 9,9-dibromobicyclo[6.1.0]nonane, b.p. 77-79° at 0.15 mm, $h_D^{25}$ = 1.5510 (lit: b.p. = 80-82° at 1 mm, $\eta_D^{25}$ - 1.5520) was obtained. The infrared spectrum (IR-4) showed no absorption in 1650 $cm^{-1}$ region. This spectrum was essentially identical to that of an authentic sample of 9,9-dibromobicyclo[6.1.0]nonane.[1]

## IIa. Preparation of 1,2-Cyclononadiene (8)

Into a 2-L three-mecked flask fitted with a pressure equalized dropping funnel, stirrer and nitrogen inlet tube was added 100 ml of anhydrous ether under nitrogen and 106 g (0.374 mole) of 9,9-dibromobicyclo[6.1.0]nonone. The flask was cooled with a dry ice-acetone bath to -30 to -40°. Methyllithium (450 ml, 1.5 M in ether) was added dropwise for 2 hr. The reaction mixture was stirred an additional 30 min and 100 ml of water was added dropwise to decompose excess methyllithium. An additional 400 ml of water was added and the ether layer was separated. The aqueous layer was extracted with four 30 ml portions of ether. The combined ether extracts were washed with 30 ml portions of water until neutral (using phenopthalein as indicator) and dried over anhydrous magnesium sulfate. The solution was filtered and distilled. The

1,2-cyclononadiene distilled at 70-72° (30.7 g, 45% yield) under reduced pressure using a water pump. The infrared absorption spectrum (IR-1) showed an absorption at 1950 $cm^{-1}$ but no absorption in the 2300-2000 $cm^{-1}$ region. This spectrum was essentially identical to that of an authentic sample of 1,2-cyclononadiene.[1]

## III. Preparation of Phenyl Azide[20]

In a one liter three-mecked flask fitted with a stirrer, thermometer and dropping funnel, was placed 300 ml of water and 55.5 ml of concentrated hydrochloric acid. The flask was surrounded by an ice-salt bath, the stirrer was started, and 35.5 g (0.31 mole) of phenylhydrazine was added dropwise (5-10 min). Phenylhydrazine hydrochloride separated out as fine white plates. Stirring was continued and after the temperature had fallen to 0°, 100 ml of ether was added. A solution of 25 g of technical grade sodium nitrite in 30 ml of water was added from the dropping tunnel at such a rate that the termperature never rose above 5° (20-30 min). The reaction mixture was subjected to steam distillation until about 300 ml of distillate was obtained. The ether solution was separated from the distillate and the aqueous layer was extracted once with 25 ml of ether. The combined ether extracts were dried over anhydrous calcium chloride. The dried solution was filtered and placed in a flask arranged for vacuum distillation. The flask must be surrounded by a cylindrical wire screen and a laboratory safety glass shield must be interposed between the operator and the apparatus. The flask was immersed in a water bath at 25-30° and the ether was removed under reduced pressure. The temperature of the bath was raised to 50-65°

and the product was distilled under reduced pressure. A yield of 18.1 g (75%, b.p. 25-26° at 1 mm) of the pale yellow phenyl azide was obtained (IR-2).

## VI. Partial Resolution of 1,2-cyclononadiene (8):

A. Run 1: The asymmetric hydroboration of 1,2-cyclononadiene was carried out by the method of Brown and coworkers[18] as modified by Caserio.[19] Borontriflouride etherate (17.5g, 0.123 mole) was added to a stirred solution of (-)-α-pinene (33.5g, 0.246 mole, $[\alpha]_D^{27}$ $-42.5^\circ \pm 0.1$, 83% optical purity) and sodium borohydride (5.1g, 0.135 mole) in 70 ml of triglyme at 0° for 20 hours. The resultant suspension of sym-(+)-tetraisopino-camphenyldiborane (9) was then cooled to -12° with an ice-salt bath. (±)-1,2-cyclononadiene (30g, 0.246 mole) was added all at once. After stirring the mixture for an additional 2.5 hours at -12°, unreacted 1,2-cyclonoadiene was recovered by distillation (50-70°, 4 mm) followed by extraction with water to remove triglyne from the distillate. The aqueous layer was extracted with ether. The combined organic phases were dried ($MgSO_4$) and fractionally distilled (68-70°, 16 mm) and afforded 11.5 g (77% yield assuming only half of 1,2-CND was consumed) of 1,2-cyclononadiene, $[\alpha]_D^{27}$ $+9.5^\circ \pm 0.1$ (neat); $[\alpha]_D^{27}$ $+17.2^\circ \pm 0.1$ (neat, corrected for α-pinene). Gas chromatographic analysis (5 ft x 0.25 in aluminum column packed with 20% SF-96 on 60/80 mesh firebrick, helium flow 60 ml/min, injector = 229°, detector = 249°, column = 148°) showed two peaks with retention times of 6.9 min and 3.4 min which correspond to 87% 1,2-cyclononadiene and 13% α-pinene, respectively. When a mixture of weighed samples of 1,2-cyclononadiene and α-pinene were examined under these gas chromatographic conditions, it was established that peak and weight ratios were identical within experimental error. Peak identities were established by co-injection of known 1,2-cyclononadiene and α-pinene. This 87% pure 1,2-cyclononadiene showed infrared absorption in the 1950 $cm^{-1}$ region. The spectrum (IR-1A) was essentially identical to a previous spectrum of racemic 1,2-cyclononadiene with a few impurity peaks occuring at 790 $cm^{-1}$ (fairly intense) and at about 1345 $cm^{-1}$ amd 1360 $cm^{-1}$ which are attributable to α-pinene.

Run 2: Using the above procedure for asymmetric hydroboration of 1,2-cyclononadiene, α-pinene, $[\alpha]_D^{24}$ + 46.90° ± 0.01 (neat, 90.2% optical purity) was used. Boron trifluoride etherale (17.5g, 0.123 mole) was added to a stirred solution of (+)-α-pinene (33.5g, 0.246 mole), $[\alpha]_D^{24}$ + 46.09° ± 0.01 (neat) 90.2% optical purity and sodium borohydride (5.1 g, 0.135 mole) in 70 ml of triglyme at 0°. The mixture was stirred and maintained at 0° for 20 hr. The resulting suspension of sym-(-)-tetraisocamphenyldiborane (9) was cooled to -12° with an ice-salt bath. (±)-1,2-Cyclononadiene (30g, 0.246 mole) was added all at once. After stirring the mixture for an additional 2.5 hr at -12°, unreacted 1,2-cyclononadiene was recovered by distillation (50-70°, 4 mm) followed by extraction with water to remove triglyme from the distillate. The aqueous layer was removed and extracted with ether. The combined organic phases were dried ($MgSO_4$) and fractionally distilled (b.p. 70-71°, 16 mm) and afforded 11.1 g of 1,2-cyclononadiene, $[\alpha]_D^{27}$ - 15.3° ± 0.1 (neat). Gas chromatographic analysis was not performed on this mixture.

## IVB. Partial Resolution of 1,2-Cyclononadiene (8) on Micro Scale[22]

Run 3: Boron trifluoride etherate (0.316g, 2.22 mmol) in 2 ml of triglyne was added slowly to a stirred slurry of (+)-α-pinene, $[\alpha]_D^{24}$ + 46.09° ± 0.01 (neat), 90.2% optical purity; 0.604g, 4.44 mmol and sodium borohydride (0.070g, 1.85 mmol) in 2 ml of triglyne at 0°. After reacting 4 hr to form 9, the reaction was cooled (-72°) using a dry-ice-acetone bath. Then a precooled solution (0°) of 1,2-cyclononadiene (0.366 g, 3.33 mmol) was added all at once. The dry-ice-acetone bath was removed and was replaced by a dry-ice-$CCl_4$ bath. The reaction mixture was stirred for 1 hr at -20°. The dry-ice-$CCl_4$ bath was replaced by an ice bath (0°) and the reaction mixture was stirred for an additional hr. The reaction mixture was quenched with water and pentane was added. The pentane layer was separated, washed with water, dried ($MgSO_4$) and concentrated (rotatory evaporation). Distillation at room temperature (1 mm) followed by preparative glc gave optically active 1,2-cyclononadiene, $[\alpha]_D^{24}$ - 13.51° ± 0.01 (c. 0.0079 g/ml, pentane).

Run 4: Boron trifluoride etherate (0.316 g, 2.22 mmol) in 2 ml of triglyme was added slowly to a stirred slurry of (+)-α-pinene, $[\alpha]_D^{24}$ + 46.09° ± 0.01 (neat, 90.2% optical purity); 0.604 g, 4.44 mmol and sodium borohydride (0.070g, 1.85 mmol) in 2 ml of triglyme at 0°. Within one hr, a thick white precipitate formed. After 4 hr at 0°, the reaction mixture was cooled (-72°) in a dry-ice-acetone bath and a precooled solution (0°) of 1,2-CND (8) (0.366 g, 3.33 mmol) in 1 ml of ether was added all at once. The dry-ice-acetone bath was removed and replaced with a dry-ice-$CCl_4$ bath. The mixture was stirred for an additional 2 hr at -20°. The mixture was allowed to warm to 0° (~7 min) and the reaction mixture was quenched with water and pentane was added. The pentane layer was separated, washed with water, dried ($MgSO_4$) and concentrated (rotatory evaporation). Distillation at room temperature (1 mm) followed by preparative glc gave optically active 1,2-cyclononadiene, $[\alpha]_D^{24}$ - 9.00° ± 0.01 (C. 0.55, pentane).

Run 5: The same amounts of reagents were used as in the previous run. α-pinene, $[\alpha]_D^{24}$ + 46.09° ± 0.01 (neat, 90.2% optical purity) was allowed to react with the diborane for 4 hr to form 9 at 0°. A precooled solution (0°) of 1,2-cyclononadiene was added all at once. The mixture was stirred for 1 hr at 0°. The reaction was quenched with water and pentane was added. The pentane layer was separated, washed with water, dried ($MgSO_4$) and concentrated (rotatory evaporation). Distillation followed by preparative glc gave optically active 1,2-cyclononadiene, $[\alpha]_D^{24}$ - 29.00° ± 0.01 (C. 0.005, pentane).

Run 6: The above reaction was run on a larger scale at 0°. Boron trifluoride etherate (9.1 g, 0.064 mole) in 15 ml of triglyme was added slowly to a stirred slurry of (+)-α-pinene, $[\alpha]_D^{24}$ + 46.09° ± 0.01 (neat, 90.2% optical purity; 17.3g, 0.127 mole) and sodium borohydride (3.4 g, 0.087 moles) in 85 ml of triglyme at 0°. Within one hr, a thick white precipitate formed. After α-pinene had reacted with the diborane for 4 hr to form 9, a precooled solution (0°) of 1,2-cyclononadiene (15.5 g, 0.127 mole) in 75 ml of ether was added all at once to the stirred diborane reagent. After 30 min, the unreacted 1,2-cyclononadiene was recovered by distillation (40-70°, 1 mm) followed by extraction with water to remove triglyme from the (11.5 g) distillate. The distillate was dried over anhydrous $MgSO_4$. Distillation afforded 74% yield of 1,2-cyclononadiene. Preparative glc gave optically active 1,2-cyclononadiene, $[\alpha]_D^{24}$ - 12.72° ± 0.01 (c. 0.03, pentane).

## V. Reaction of (+)-1,2-Cyclononadiene (8) with Phenyl Azide[14]

1.22 g (0.01 mole) of (+)-1,2-cyclononadiene and 1.19 g (0.01 mole) of phenyl azide in 15 ml of toluene under nitrogen were heated in an oil bath to gentle reflux. After 10 hr, the toluene was evaporated under reduced pressure rotatory evaporation. The residual viscous yellow oil was kept at room temperature several days for crystallization to occur. Recrystallization from pet. ether (60-110°) gave 0.51 g (21% yield) of 1:1 adduct 7, M.P. 90-94°. Mass spectral data (MS-2): M/e 241 (P, 7.875), Base peak 77 (100%), M/e 213 (36.50%). NMR (NMR-2); 0.9-2.7 (12H,m), 4.3-4.7 (lH,m), 6.02-6.43 (lH,m). 6.85-7.7 (5H, $C_6H_5$,m).

## VI. Reaction of (+)-1,2-Cyclononadiene (8) With Phenyl Azide

1.22 g (0.0087 mole) of optically active 1,2-CND (8) $[\alpha]_D^{27}$ + 9.5° ± 0.1 ($[\alpha]_D^{27}$ + 17.2° ± 0.1 corrected for 13% α-pinene impurity) and 1.0 g (0.0080 mole) of phenyl azide in 15 ml of toluene under nitrogen were heated in an oil bath to gentle reflux. After 10 hr, the toluene was removed by rotatory evaporation leaving a viscous yellow oil. The oil was kept 2 to 3 days at room temperature in order for crystallization to occur. The adduct 7 was then recrystallized from pet. ether (60-110°) to give 0.5202 g (23.6% yield) of 1:1 adduct, 10-phenyl-10,11,12-triaza-$\Delta^{11}$-bicyclo[7.3.0]duodec-1-ene (7). The adduct (7) had a specific rotation, $[\alpha]_D^{27}$ + 9.7° ± 0.1 (c. 0.1 g/ml, $CHCl_3$), M.P. 90-94°. TLC analysis showed no traces of 1,2-CND dimer (1.0% could be detected).

In two similar runs with 1,2-cyclononadiene, $[\alpha]_D^{27}$ + 9.5° ± 0.1 (neat, uncorrected); $[\alpha]_D^{27}$ + 17.2° ± 0.1 (neat, corrected for α-pinene) the adduct obtained had specific rotations, $[\alpha]_D^{27}$ + 9.4° ± 0.1 (0.5113 g, 23% yield) and $[\alpha]_D^{27}$ + 9.5° ± 0.1 (0.5011 g, 22.5% yield).

In another reaction, a G.C. collected sample of (-)-1,2-cyclononadiene with a specific rotation, $[\alpha]_D^{24}$ - 12.72 ± 0.01 (c. 0.03 g/ml, pentane) produced a 1:1 adduct (7) with a specific rotation, $[\alpha]_D^{24}$ - 4.01° ± 0.01 (c. 0.01 g/ml, pentane) (0.6054 g, 27% yield).

## VII. Thin Layer chromatography of 1:1 Adduct (7) to test for 1,2-CND dimer

To test for the presence of dimer in the adduct (7), 1.4 mg ($4.22 \times 10^{-6}$ mole) of 1,2-cyclononadiene dimer was dissolved in 10 ml of chloroform. One ml of the resulting solution was added to 10.4 mg ($4.31 \times 10^{-5}$ mole) of 7 for TLC analysis. The mixture was spotted on a plate coated with silica gel G.F. with a capillary tube. Benzene was used as solvent for the mobile phase. The spots were developed in iodine vapor. The distances traveled were 8.4 cm for solvent, 7.9 cm for dimer, and 2.5 cm for adduct (7). This corresponds to $R_f$ values of 0.94 for dimer and 0.29 for 7.

The same spotting technique used for TLC of 7 was used to detect 7 in 14. 1.2 mg ($4.23 \times 10^{-6}$ mole) of 7 was dissolved in 10 ml of chloroform. One ml of the resulting solution was added to 10.2 mg of 14 ($4.23 \times 10^{-5}$ mole). The corresponding $R_f$ values were 0.83 for 14 and 0.63 for 7. In the case of dimer in 7, 0.97 mole % (or 1.0 weight%) could be detected and 1.0 mole % of 7 in 14 could be detected.

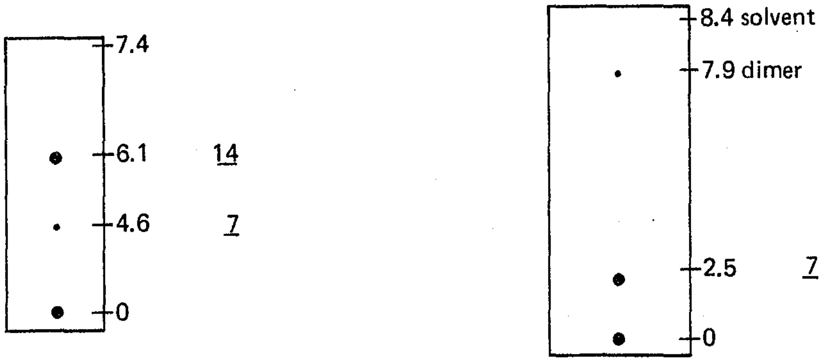


Diagram A

## VIII. Reaction of 1,2-CND (8) and Phenyl Azide With Added (-)-α-Pinene

2.0 g (0.016 mole) of ($\pm$)-1,2-cyclononadiene was added to 1.0 g (0.007 mole) of α-pinene, $[\alpha]_D^{27}$ - 42.5° ± 0.1 (neat, 83% optical purity) and was allowed to react with Phenyl Azide (1.19 g, 0.010 mole). After refluxing for 10 hr in 15 ml of toluene under nitrogen, the solvent was removed by rotatory evaporation. The crude yellow mixture was kept several days at room temperature for crystallization to occur. The adduct was recrystallized from pet. ether (bp 80-110°). The adduct, (0.5902 g, m.p. 90-95°; 36.8% yield) showed no optical rotation, $[\alpha]_D^{27}$ 0.00 ± 0.01.

## IX. Isomerization of 7:

The following preliminary experiment was carried out in order to establish the conditions necessary to facilitate the isomerization of 10-phenyl-10,11,12-triaza-$\Delta^{11}$-bicyclo[7.3.0]duodec-1-ene (7) into its aromatic isomer 14.

0.066g ($2.7 \times 10^{-4}$ mole) of optically active 7 was dissolved in 10 ml of ethyl alcohol and the rotation was measured. The mixture had a specific rotation $[\alpha]_D^{25}$ - 2.40° ± 0.01 (c. 0.006 g/ml, EtOH). Then 10 ml of 1M sodium ethoxide was added to 7 and the rotation was measured. The specific rotation did not change. After one hr, the rotation was measured again and no change had occured. The mixture was then refluxed overnight under nitrogen. The mixture was then filtered (to remove turbidity) and the rotation was measured. The mixture had a specific rotation of $[\alpha]_D^{25}$ - 1.00° ± 0.01 (EtOH). The mixture was then refluxed for an additional 3 days under nitrogen. The mixture was filtered, extracted with ether, washed with water, dried ($MgSO_4$) and the rotation was measured. This mixture did not rotate polarized light, $[\alpha]_D^{25}$ 0.000 ± 0.001. The solvent was then removed by rotatory evaporation and the crude mixture was analyzed by IR and NMR. Both spectra indicated that the starting material had been destroyed and that the material was impure. The crude mixture gave a small amount of crystalls upon standing for several days.

Based on the above experiment, the scaled up isomerization reaction of 7 with sodium ethoxide was carried out.

1.0 g (0.004 mole) of 7 in 10 ml of ethanol and 30 ml of 1M sodium ethoxide was refluxed for three days under nitrogen. The solvent was then removed by rotatory evaporation. The product was extracted with ether and the organic phase was washed with water until neutral and dried over anhydrous magnesium sulfate. The solvent was removed by rotatory evaporation giving a 0.814g residue. The IR spectrum of this crude product showed some -OH absorption and some C-O absorption. Pet. ether was added to the product and rotatory evaporated to remove any ethanol present. This procedure was repeated three times. The product was left sitting to crystallize. The brown crystalline solid was recrystallized in pet. ether-benzene (3:1). Recrystallization afforded a white crystalline solid (0.701 g, 70.1% yield), M.P. 77-78°. Anal. calcd. for $C_{15}H_{19}N_3$ (14): C, 74.69; H, 7.93; N, 17.42. Found: C, 74.56; H, 7.83; N, 17.33. UV (UV-1): λmax 211 mm (ε 12,400); Mass spectrum (MS-1); M/e 241 (P, 3.44%), 213 (32.16%), base peak M/e 77 ($C_6H_5$, 100%); NMR (NMR-1) $CDCl_3$; δ 1.42 (S, 10H; rel. area 10.08), δ 2.6-3.0 (4H; rel. area 3.88), δ 7.5-7.8 (5H; rel. area 5.04).

## X. Isomerization of 7 in N-methylaniline:

0.0761 g of optically active 1:1 adduct (7) in 10 ml N-methylaniline was heated (108°) for 8 days under nitrogen. The rotation of the product could not be taken because of the dark color of the solution. TLC analysis of the crude material could not be performed because of interferene from N-methyalaniline. The mixture was then extracted with pentane and the organic layer separated. The organic phase was washed with dilute HCl to remove N-methylaniline. Then the organic phase was washed with water several times to remove HCl from the mixture. The mixture was dried over ($MgSO_4$), filtered, and the solvent was evaporated. Evaporation left a viscous brown material. The residue was dissolved in 1 ml of chloroform and TLC analysis was performed. TLC analysis showed that 3 components were present with $R_f$ values of 0.32 (7), 0.89 and 0.83 . The starting material was spotted on the same plate with the unknown. It was shown that the component with $R_f$ value 0.32 was starting material and was present in very small quantity (compared to 14). The chloroform was then evaporated and the brown material was left to crystallize.

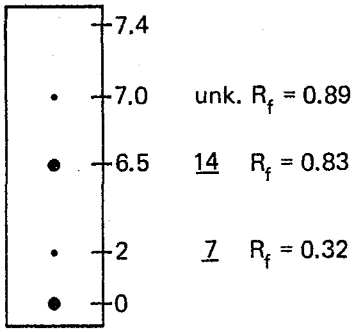


Diagram B

## Sample Calculations

### Estimated Optical Purity 1:1 Adduct (7)

$$\frac{17.2}{175^{\circ}} = \frac{9.5^{\circ}}{Z}$$

$$Z = 96.6^{\circ *}$$

$Z$ = estimated specific rotation, $[\alpha]_D$ of optically pure adduct 7.

$17.2^{\circ}$ = specific rotation of 1,2-CND (<u>8</u>)

$175^{\circ}$ = estimated specific rotation of optically pure 1,2-CND[17].

$9.5^{\circ}$ = specific rotation of 1:1 adduct.

*This value is based on the assumption that the reaction prodeeds with complete retention of optical activity.

### Specific Rotation of 1,2-CND corrected for α-Pinene:

$$[\alpha]_{exp} = X\,[\alpha]_{\alpha\text{-pinene}} + (1-X)\,[\alpha]_{CND}$$

$$9.5^{\circ} = 0.13\,(-42.5^{\circ}) + (1-0.13)\,[\alpha]_{CND}$$

$$9.5^{0} = 5.5 + 0.87\,[\alpha]_{CND}$$

$$17.2^{\circ} = [\alpha]_{CND}$$

$X$ = Wt. fraction of α-pinene = 0.13

$1-X$ = Wt. fraction of 1,2-CND = 0.87

$9.5^{\circ}$ = rotation measured for 1,2-CND before correction for α-pinene $= [\alpha]_{exp}$

# Bibliography

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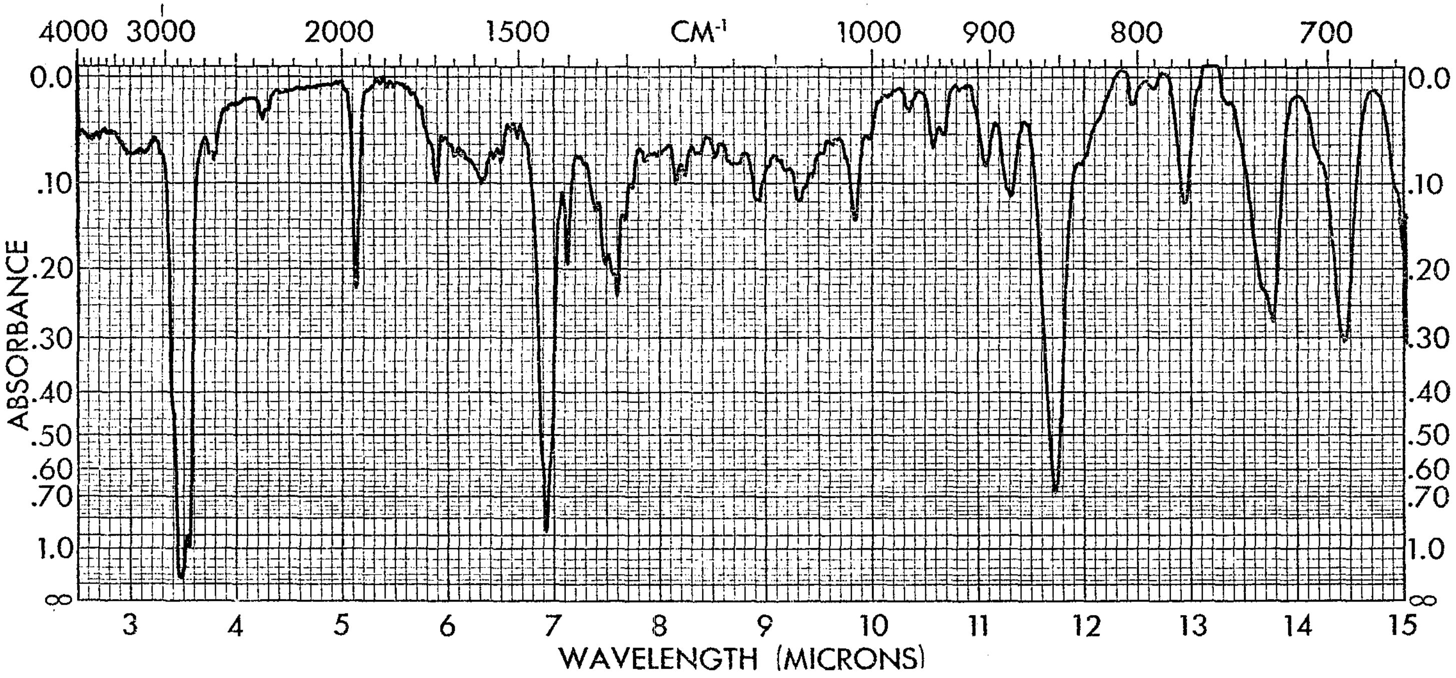
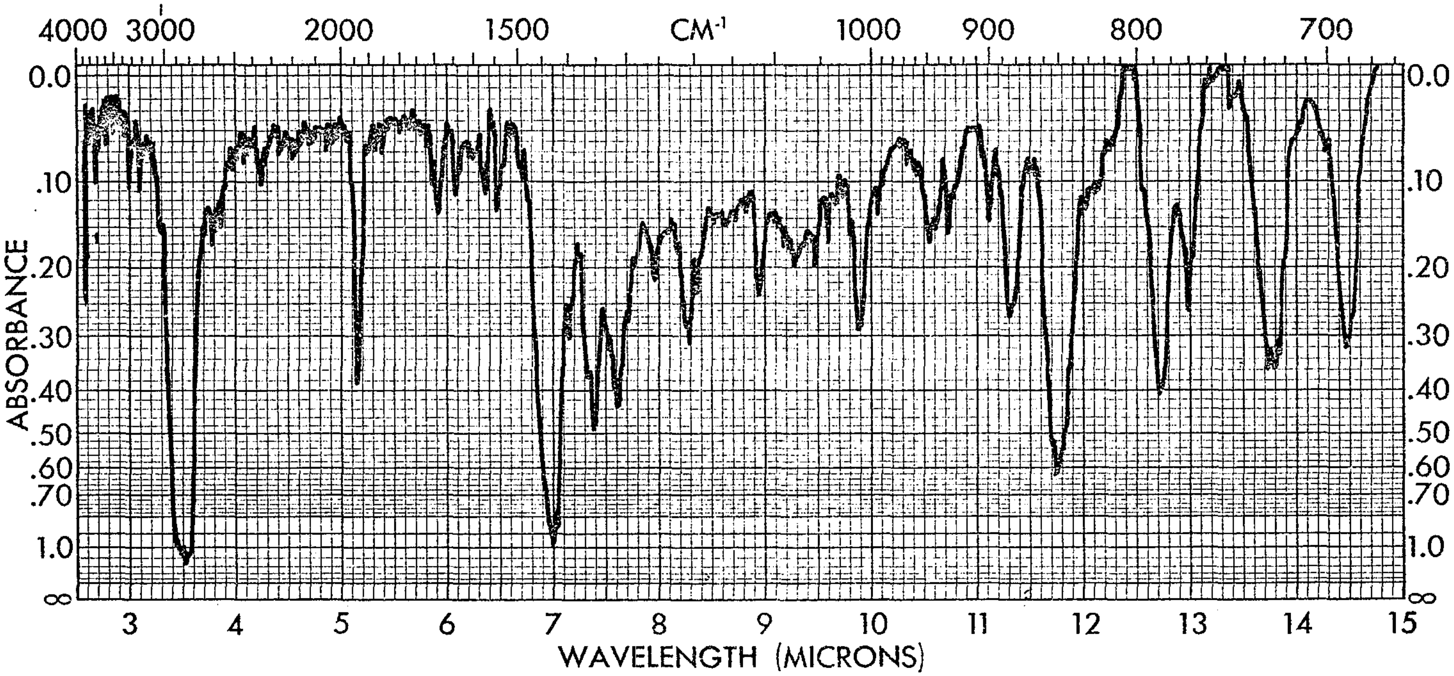


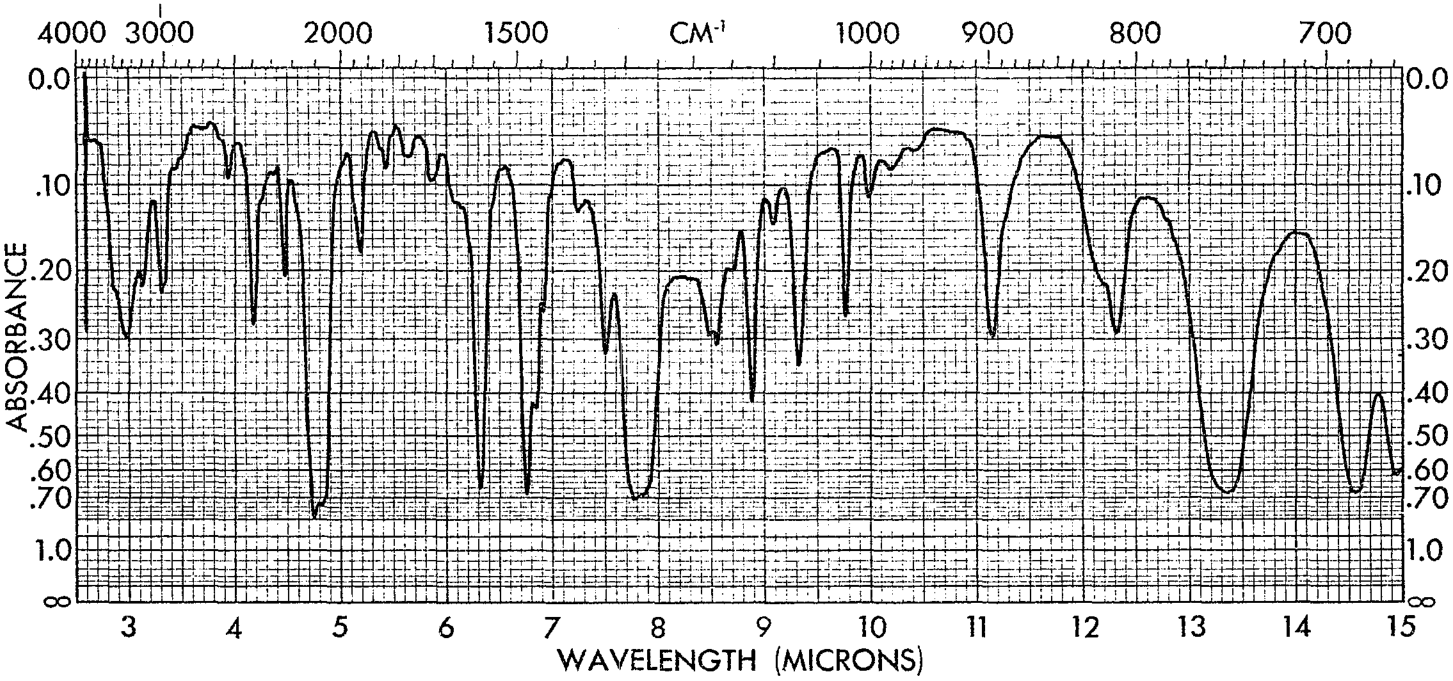
1. IR-1

1,2-Cyclononadiene (neat).



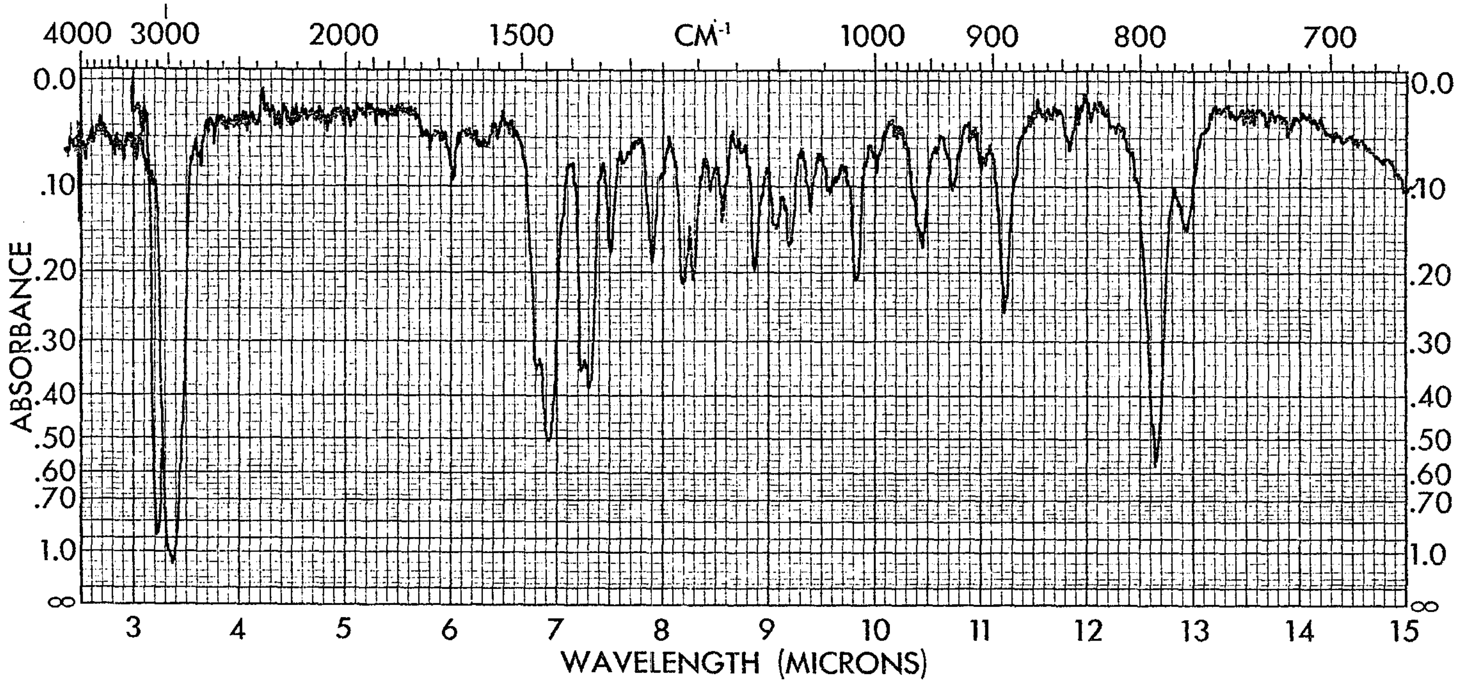
2. IR-1A

Optically Active 1,2-Cyclononadiene (neat).



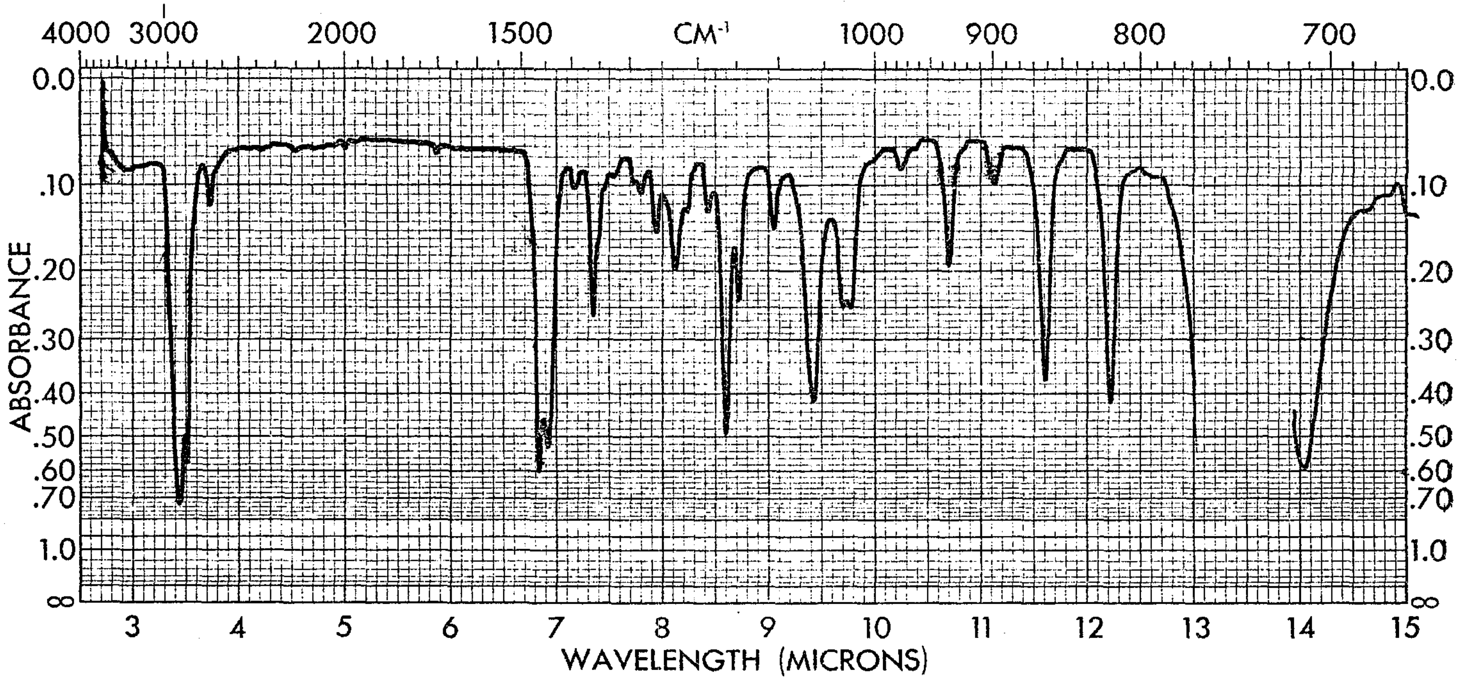
3. IR-2

Phenyl Azide (neat).



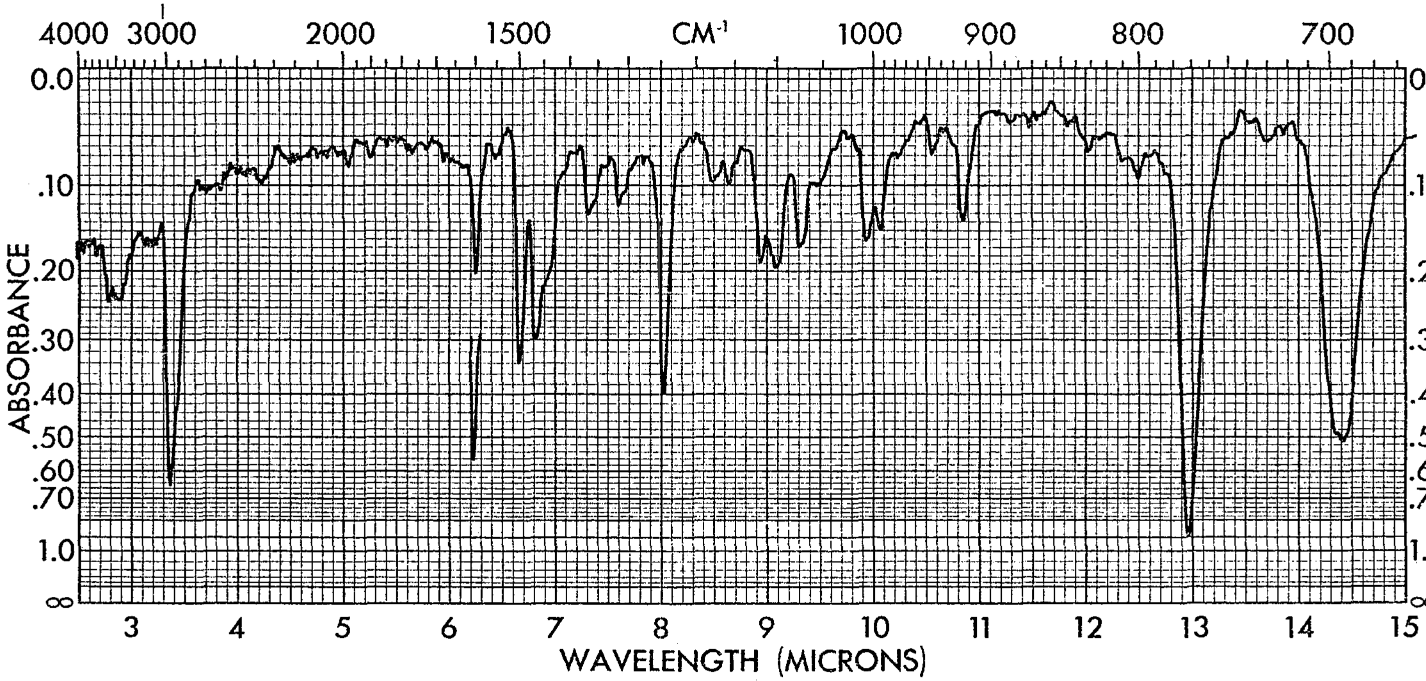
4. IR-3

(+)-α-pinene.



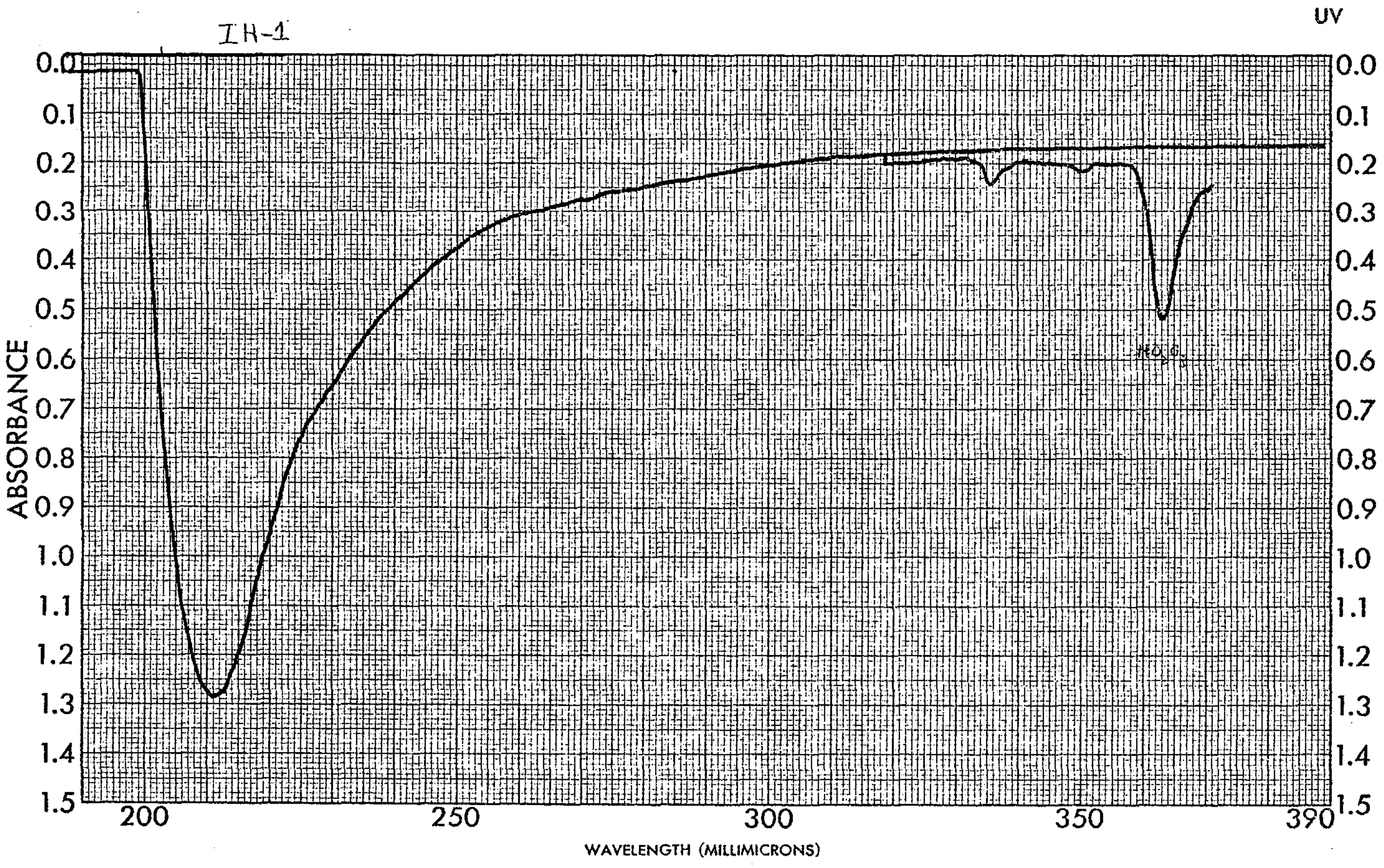
5. IR-4

9,9-dibromobicyclo[6.1.0]nonane.



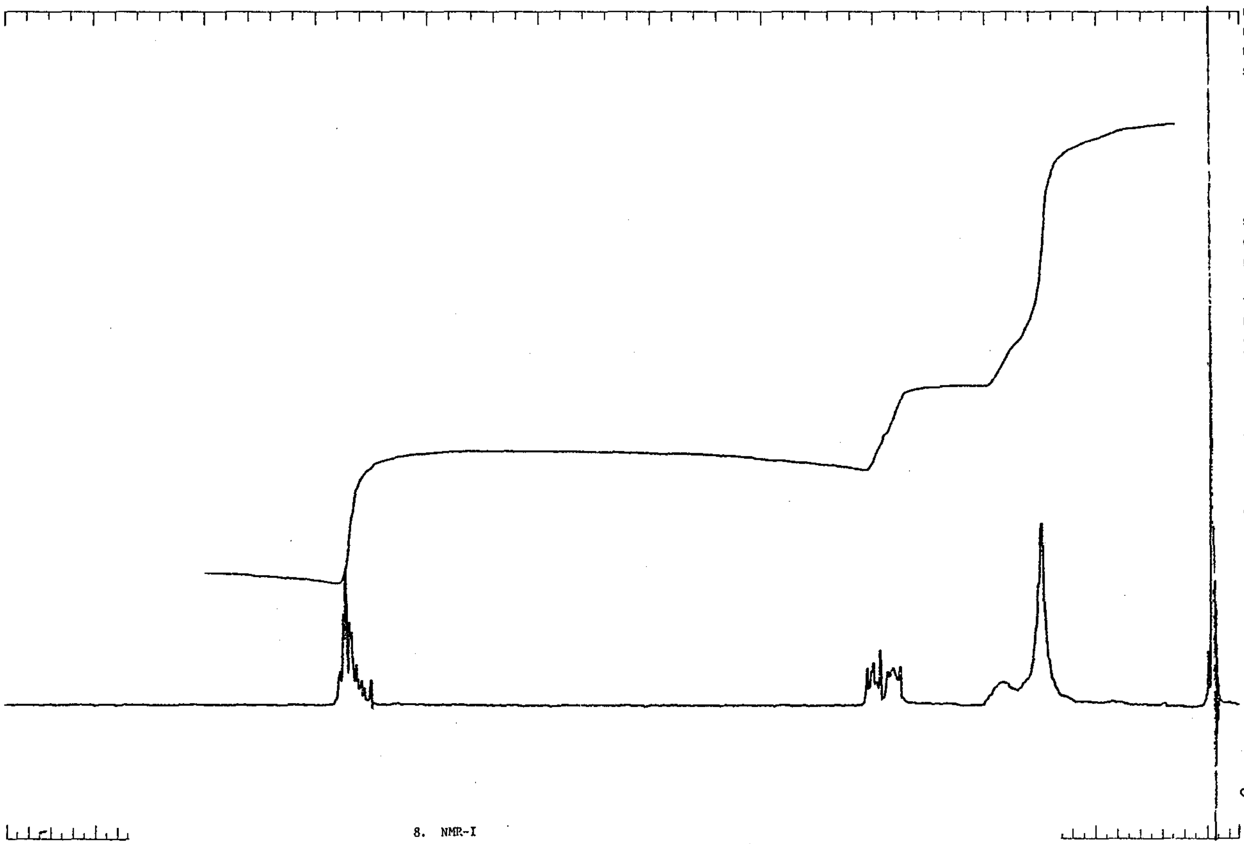
6. IR-5

1-phenyl-4,5-heptomethylene-1,2,3-triazole (<u>14</u>).



7. UV-1

1-phenyl-4,5-heptamethylene-1,2,3-triazole (<u>14</u>)
(c. 1.04 × $10^{-4}$, MeOH).



SPECTRUM NO. 1
DATE 11-18-77
FREQ. 100
NUCLEUS ¹H
SAMPLE

SOLVENT
CONC.
REFERENCE TMS
LOCK EXT
TEMP. RT °C
R.F. LEVEL 0.3
A.F. LEVEL ANALYTICAL MOD 7
LOCK –
SD –
AMPLITUDE 2.5×10
ANALYTICAL –
LOCK –
INTEGRATOR 3(2.5×10)
FILTER 10
OFFSET 0 Hz PPM
_FREQ._FIELD/FREQ._FIELD
OPERATOR WPG
REMARKS

SWEEP TIME (SEC.)
25 50 100 [✓ 250] 500
1000 2500 5000 10000

SWEEP WIDTH (Hz)(X0.01PPM)
27 54 108 270 540
[✓ 1080] 2700 5400 10800

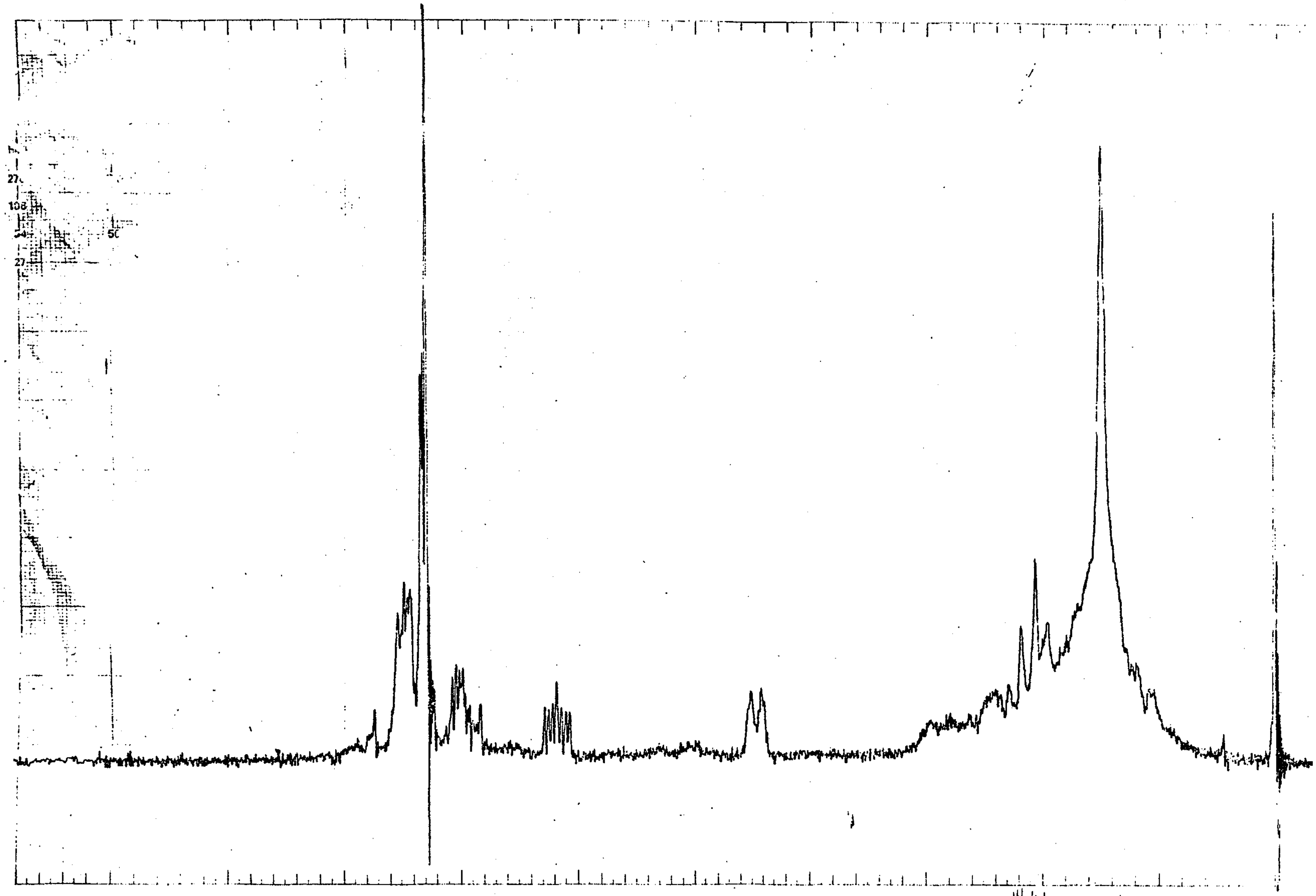
WIDE SWEEP (GAUSS)
10.8 27 54 108 540

8. NMR-I

1-phenyl-4,5-heptamethylene-1,2,3-triazole (14).

9. NMR-2

10-phenyl-10, 11, 12-triaza-$\Delta^{11}$-bicyclo [7.3.0] doudec-1-ene (7).



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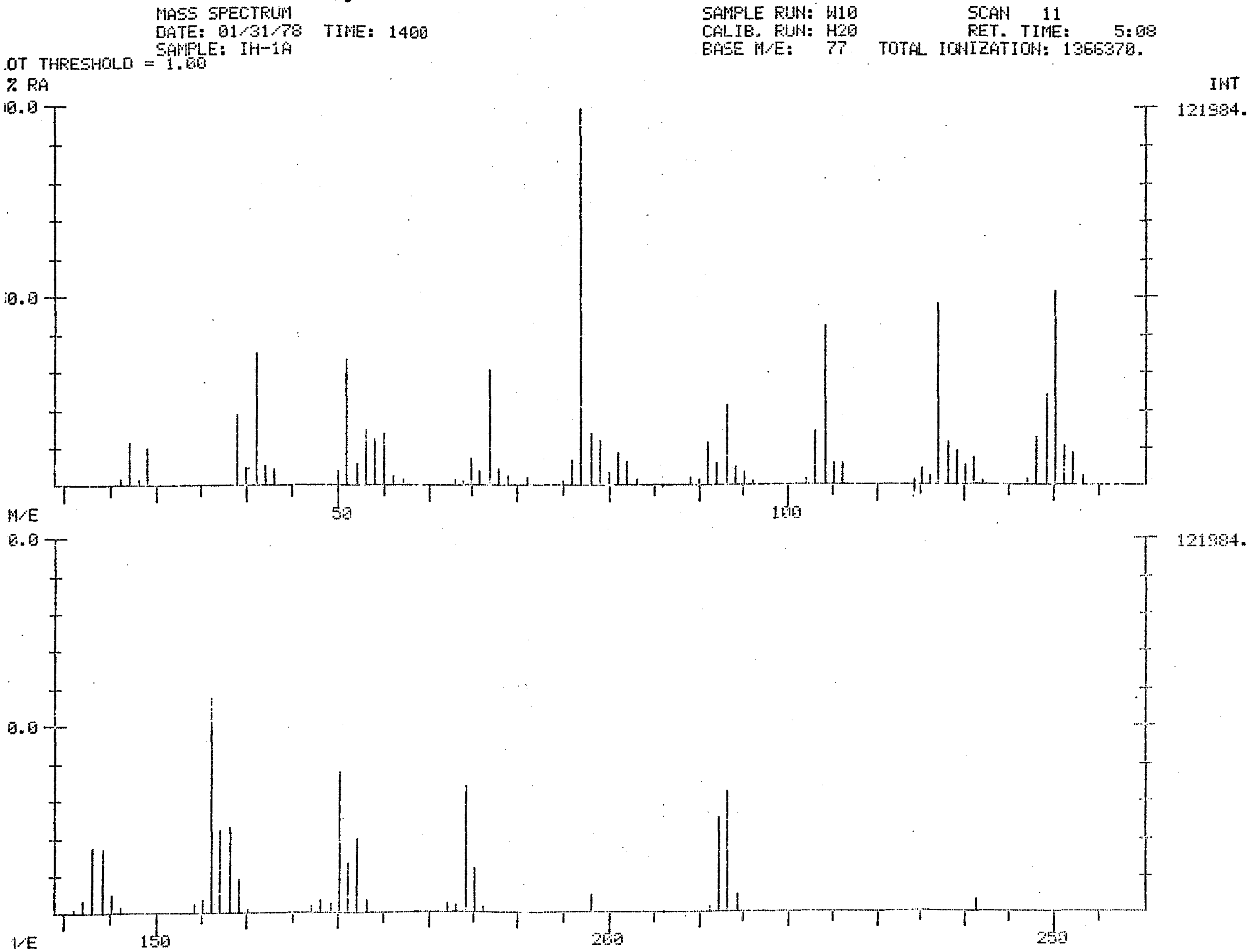


10. MS-1

1-Phenyl-4,5-heptamethylene-1,2,3-triazole (14).

```
DATE. 0[illegible]/31/78  TIME: 1100  CAL ID  RUN: H20             RET. TIME:     5.08
SAMPLE: IH-1A                      BASE M/E:    77    TOTAL IONIZATION: 1366370.
LIST THRESHOLD =  1.00 % RELATIVE ABUNDANCE

PEAK     NOMINAL        %        %
 NO.      MASS          RA       TI        INT

 22        39         18.89     1.69     23039.
 23        40          4.76     0.43      5807.
 25        41         35.15     3.14     42879.
 26        42          5.19     0.46      6327.
 28        43          4.48     0.40      5463.
 35        50          4.07     0.36      4967.
 41        51         33.37     2.98     40703.
 44        52          5.61     0.50      6839.
 45        53         14.66     1.31     17887.
 46        54         12.49     1.11     15231.
 48        55         13.64     1.22     16639.
 49        56          2.62     0.23      3196.
 53        57          1.78     0.16      2168.
 60        63          1.81     0.16      2204.
 61        64          1.30     0.12      1584.
 63        65          7.03     0.63      8575.
 65        66          4.07     0.36      4967.
 71        67         30.27     2.70     36927.
 72        68          4.33     0.39      5279.
 75        69          2.60     0.23      3176.
 83        71          2.12     0.19      2584.
 89        75          1.25     0.11      1522.
 93        76          6.51     0.58      7943.
 97        77        100.00     8.93    121983.
102        78         13.56     1.21     16543.
105        79         11.73     1.05     14303.
107        80          3.43     0.31      4183.
109        81          8.60     0.77     10495.
112        82          6.14     0.55      7487.
113        83          1.63     0.15      1990.
121        89          1.87     0.17      2276.
123        90          1.61     0.14      1960.
126        91         11.49     1.03     14015.
128        92          5.94     0.53      7239.
132        93         21.38     1.91     26079.
134        94          4.72     0.42      5759.
135        95          3.40     0.30      4151.
137        96          1.40     0.12      1702.
144       102          1.68     0.15      2048.
145       103         14.22     1.27     17343.
148       104         42.18     3.77     51455.
149       105          5.81     0.52      7087.
151       106          5.86     0.52      7151.
171       115          4.38     0.39      5343.
173       116          2.77     0.25      3376.
177       117         48.32     4.31     58943.
180       118         11.52     1.03     14047.
184       119          8.87     0.79     10815.
189       120          5.17     0.46      6311.
190       121          7.21     0.64      8799.
192       122          1.14     0.10      1392.
198       127          1.70     0.15      2076.
201       128         12.76     1.14     15567.
```

BACKGROUND subtracted
70ev.

MS-1

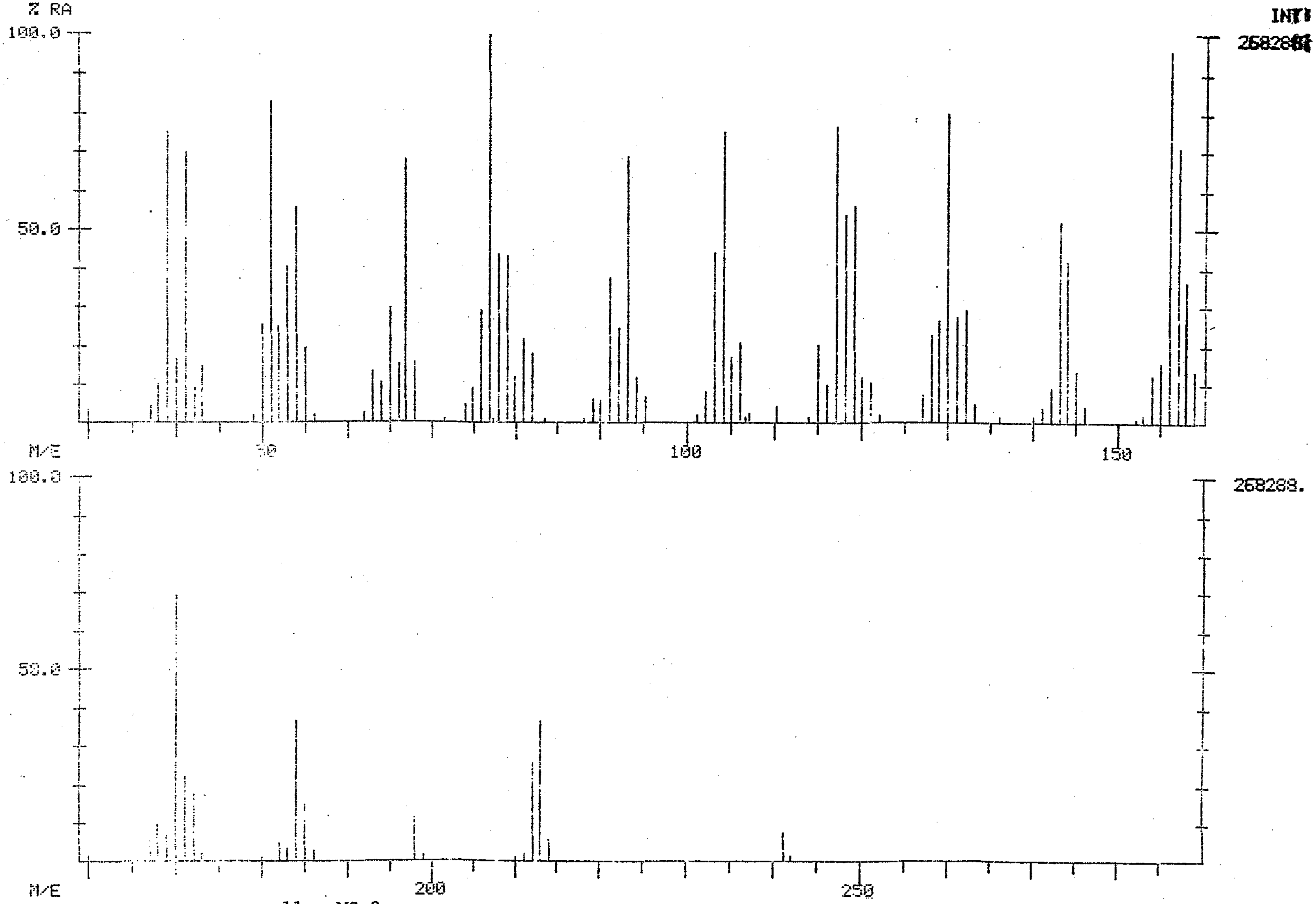
| PEAK NO. | NOMINAL MASS | % RA | % TI | INT |
|---|---|---|---|---|
| 204 | 129 | 23.87 | 2.13 | 29119. |
| 208 | 130 | 51.47 | 4.59 | 62783. |
| 211 | 131 | 10.31 | 0.92 | 12575. |
| 215 | 132 | 8.41 | 0.75 | 10255. |
| 216 | 133 | 2.34 | 0.21 | 2856. |
| 239 | 141 | 1.06 | 0.09 | 1290. |
| 242 | 142 | 3.61 | 0.32 | 4407. |
| 247 | 143 | 17.39 | 1.55 | 21215. |
| 250 | 144 | 16.82 | 1.50 | 20511. |
| 251 | 145 | 5.00 | 0.45 | 6103. |
| 252 | 146 | 1.46 | 0.13 | 1780. |
| 261 | 154 | 2.65 | 0.24 | 3232. |
| 263 | 155 | 3.30 | 0.29 | 4020. |
| 268 | 156 | 57.50 | 5.13 | 70143. |
| 272 | 157 | 21.98 | 1.96 | 26815. |
| 276 | 158 | 22.90 | 2.04 | 27935. |
| 280 | 159 | 8.92 | 0.80 | 10879. |
| 282 | 160 | 1.01 | 0.09 | 1226. |
| 291 | 167 | 1.95 | 0.17 | 2376. |
| 294 | 168 | 3.54 | 0.32 | 4319. |
| 297 | 169 | 2.41 | 0.21 | 2936. |
| 300 | 170 | 37.30 | 3.33 | 45503. |
| 303 | 171 | 13.46 | 1.20 | 16415. |
| 305 | 172 | 19.67 | 1.76 | 23999. |
| 306 | 173 | 3.27 | 0.29 | 3988. |
| 313 | 182 | 2.42 | 0.22 | 2952. |
| 314 | 183 | 2.23 | 0.20 | 2724. |
| 317 | 184 | 33.53 | 2.99 | 40895. |
| 321 | 185 | 11.95 | 1.07 | 14575. |
| 322 | 186 | 1.69 | 0.15 | 2064. |
| 335 | 198 | 4.79 | 0.43 | 5839. |
| 342 | 211 | 1.60 | 0.14 | 1954. |
| 345 | 212 | 25.37 | 2.26 | 30943. |
| 348 | 213 | 32.16 | 2.87 | 39231. |
| 350 | 214 | 4.84 | 0.43 | 5903. |
| 353 | 241 | 3.44 | 0.31 | 4191. |

MS-1

MASS SPECTRUM
DATE: 06/06/78 TIME: 1357
SAMPLE: W-IH-MS-2
PLOT THRESHOLD = 1.00

SAMPLE RUN: WE
CALIB. RUN: H114
BASE M/E: 77 TOTAL IONIZATION: 7335490.

SCAN 13
RET. TIME: 6:17



11. MS-2

10-Phenyl-10,11,12-triaza-$\Delta^{11}$-bicyclo[7.3.0]duodec-1-ene.

```
LOW RESOLUTION MASSES        SAMPLE RUN:  WE                SCAN    13
DATE: 06/06/78  TIME: 1357  CALIB. RUN:  H114              RET. TIME:      6:17
SAMPLE: W-IH-MS-2           BASE M/E:     77     TOTAL IONIZATION: 7336490.
LIST THRESHOLD =   1.70 % RELATIVE ABUNDANCE

PEAK      NOMINAL       %        %
 NO.        MASS        RA       TI          INT

 15          30        3.63     0.13       9743.
 28          37        4.40     0.16      11791.
 37          38       10.03     0.37      26911.
 44          39       75.00     2.74     201215.
 49          40       16.46     0.60      44159.
 55          41       69.85     2.55     187391.
 56          42        9.05     0.33      24287.
 57          43       14.60     0.53      39167.
 87          49        2.08     0.08       5583.
 91          50       25.38     0.93      68095.
104          51       83.02     3.04     222719.
115          52       24.86     0.91      66687.
117          53       40.03     1.46     107391.
119          54       55.63     2.03     149247.
127          55       19.27     0.70      51711.
131          56        2.10     0.08       5631.
158          62        2.68     0.10       7183.
161          63       13.33     0.49      35775.
171          64       10.68     0.39      28639.
178          65       29.53     1.08      79231.
183          66       15.17     0.55      40703.
192          67       67.65     2.47     181503.
200          68       15.41     0.56      41343.
236          74        4.88     0.18      13103.
238          75        9.20     0.34      24671.
246          76       29.06     1.06      77951.
252          77      100.00     3.66     268287.
259          78       43.61     1.59     116991.
265          79       43.08     1.58     115583.
271          80       12.05     0.44      32319.
279          81       21.40     0.78      57407.
287          82       18.01     0.66      48319.
303          89        6.25     0.23      16767.
312          90        5.93     0.22      15919.
319          91       37.50     1.37     100607.
325          92       24.48     0.90      65663.
333          93       68.61     2.51     184063.
339          94       11.92     0.44      31967.
346          95        6.63     0.24      17791.
378         101        2.11     0.08       5647.
381         102        8.29     0.30      22239.
384         103       43.99     1.61     118015.
390         104       74.90     2.74     200959.
396         105       17.15     0.63      46015.
402         106       20.73     0.76      55615.
408         107        2.42     0.09       6479.
424         110        4.26     0.16      11439.
449         115       20.25     0.74      54335.
455         116        9.95     0.36      26687.
460         117       76.43     2.80     205055.
465         118       53.63     1.96     143871.
472         119       56.01     2.05     150271.
477         120       11.86     0.43      31807.
```

MS-2

| PEAK NO. | NOMINAL MASS | % RA | % TI | INT |
|---|---|---|---|---|
| 484 | 121 | 10.50 | 0.38 | 28159. |
| 489 | 122 | 2.19 | 0.08 | 5879. |
| 500 | 127 | 7.24 | 0.26 | 19423. |
| 505 | 128 | 22.35 | 0.82 | 59967. |
| 509 | 129 | 26.10 | 0.95 | 70015. |
| 514 | 130 | 79.68 | 2.91 | 213759. |
| 518 | 131 | 27.19 | 0.99 | 72959. |
| 523 | 132 | 29.10 | 1.06 | 78079. |
| 528 | 133 | 4.83 | 0.18 | 12959. |
| 561 | 141 | 4.18 | 0.15 | 11215. |
| 565 | 142 | 8.85 | 0.32 | 23743. |
| 569 | 143 | 51.72 | 1.89 | 138751. |
| 573 | 144 | 41.65 | 1.52 | 111743. |
| 577 | 145 | 13.26 | 0.49 | 35583. |
| 580 | 146 | 4.31 | 0.16 | 11567. |
| 591 | 153 | 2.29 | 0.08 | 6135. |
| 595 | 154 | 12.29 | 0.45 | 32959. |
| 598 | 155 | 15.41 | 0.56 | 41343. |
| 600 | 156 | 96.18 | 3.52 | 258047. |
| 602 | 157 | 70.99 | 2.60 | 190463. |
| 605 | 158 | 36.50 | 1.33 | 97919. |
| 609 | 159 | 13.41 | 0.49 | 35967. |
| 628 | 167 | 5.43 | 0.20 | 14575. |
| 630 | 168 | 9.34 | 0.34 | 25055. |
| 632 | 169 | 6.52 | 0.24 | 17503. |
| 634 | 170 | 68.89 | 2.52 | 184831. |
| 636 | 171 | 22.30 | 0.82 | 59839. |
| 639 | 172 | 17.37 | 0.64 | 46591. |
| 640 | 173 | 2.28 | 0.08 | 6103. |
| 645 | 182 | 5.09 | 0.19 | 13653. |
| 646 | 183 | 3.35 | 0.12 | 8975. |
| 649 | 184 | 36.69 | 1.34 | 98431. |
| 651 | 185 | 14.84 | 0.54 | 39807. |
| 652 | 186 | 2.86 | 0.10 | 7679. |
| 664 | 198 | 11.19 | 0.41 | 30015. |
| 671 | 211 | 2.22 | 0.08 | 5943. |
| 673 | 212 | 25.95 | 0.95 | 69631. |
| 676 | 213 | 36.50 | 1.33 | 97919. |
| 678 | 214 | 5.81 | 0.21 | 15593. |
| 680 | 241 | 7.87 | 0.29 | 21119. |
| 681 | 242 | 1.78 | 0.07 | 4783. |

MS-2