# Reactions of azines with heterocumulene compounds(2) : Addition of azine to isocyanate

| | |
|---|---|
| その他（別言語等）のタイトル | アジン類とヘテロキュムレン化合物との反応(2) : アイジンのイソシアナートへの付加 |
| 著者(英語) | Sadayoshi Satsumabayashi, Hiroshi Nakano, Shinichi Motoki |
| journal or publication title | Bulletin of Nippon Dental University. General education |
| volume | 8 |
| page range | 87-96 |
| year | 1979-03-25 |
| URL | http://doi.org/10.14983/00000173 |

Reactions of Azines with Heterocumulene Compounds. II.

# Addition of Azine to Isocyanate

Sadayoshi SATSUMABAYASHI

Nippon Dental University, Tokyo　Fujimi, Chiyoda-ku, Tokyo

Hiroshi NAKANO

Dainichi Finechemicals Co. Ltd.　Ryouke 4-3, Kawaguchi-shi

Shinichi MOTOKI

Science University of Tokyo　Kagurazaka, Shinjuku-ku, Tokyo

(Received October 23, 1978)

# アジン類とヘテロキュムレン化合物との反応 Ⅱ

# アジンのイソシアナートへの付加

日本歯科大学歯学部　薩摩林　貞　美
大日精化工業技術部　中　野　　洋
東京理科大学理学部　元　木　信　一

カルボニル化合物とヒドラジンとの縮合により得られるアジンは分子内に構造 C=N−N=C をもち，一種の共役系化合物とみなされる。しかし，C=C−C=C や C=C−C=O と異なり，通常の不飽和化合物との反応で，ジールスアルダー型付加生物を得たという報告もなく，また反応形式も明確にされていない。著者等はこのアジンの反応特異性に興味をもち，既に報告したように，ヘテロキュムレンの一種であるジフェニルケテン(**2**)との反応をおこなってみた。この反応においても，アジンの特異性が現れ，脂肪族アジンの場合は1：2の付加により1,3-オキサジノン(**5**)が，芳香族アジンの場合1：1の付加により2-アゼチジノン(**4**)が生成したが，共に共役系としての性質を示さない。今回，アジンのこうした反応性を更に探求するため，ヘテロキュムレンとしてイソシアナートをもちいアジンと反応させ，種々の知見を得たので報告する。

アジン1モルとシアン酸2モルとが1,3-2,4-ビス付加をし，複素縮合環を形成することは Bailey らにより発見され criss-cross 付加と名づけられた。その後アジンとマレイン酸無水物等との同様な付加反応が報告されたが，アジンとしてはベンズアルドアジンがもちいられ，その他の芳香族アジンや脂肪族アジンをもちいての研究はほとんど報告されていない。

本研究においては，脂肪族アルドアジンとしてまずアセトアルドアジン(**1a**)をもちい，メチルイソシアナート(**3a**)とオートクレイブ中約 140°C で反応させた。得られた液状生成物は，元素分析・マススペクトルからクリスクロス体ではなく1：1-付加体であり，更に赤外・核磁気解析の結果2-ピラゾリン誘導体(**8a**)であることが判明した。他の

脂肪族アルドアジン（**1b, 1c**）も同様に反応し **8b, 8c** が得られた。これらの反応は，**1a-c** がまず熱により転移環化し，生成した H-N 部分が **3a-b** の N=C 結合に付加する機構で進行すると考えられる。

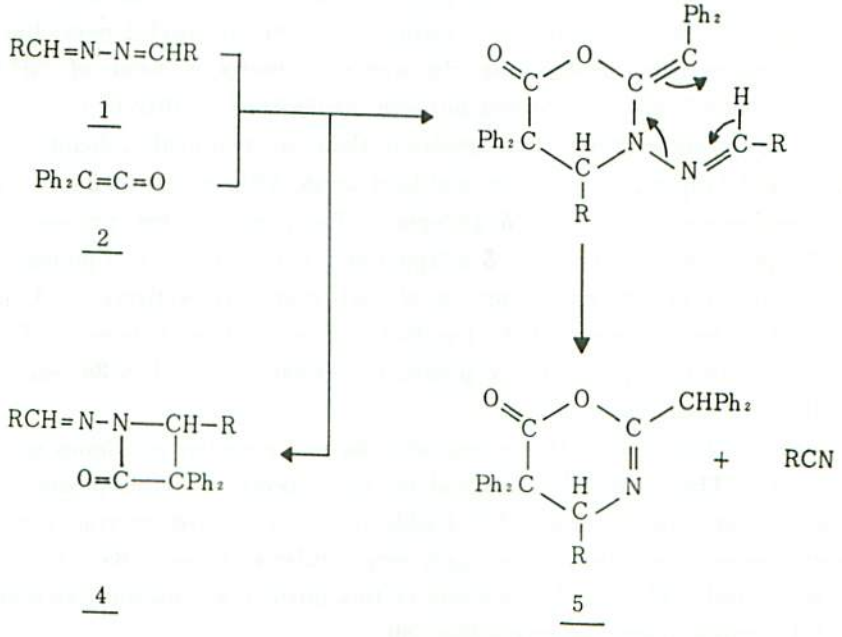
一方，芳香族アルドアジン（**1d-g**）は **1a-c** と同様な条件下 **3a-b** と反応し白色結晶体となる。元素分析・マス・赤外・核磁気解析の結果，これらいずれも 1：2-付加体，1，2-トリアゾロトリアゾール（**9a-e**）であることがわかった。**1a-c** の場合は転移しうる H が存在するのに対し，**1d-g** はこうした H をもたない。このため自己環化がおこりえず2モルの **3a-b** を 1,3-2,4-付加し，**9a-e** を生成するものと考えられる。

上記のように，アルデヒドアジンはヘテロキュムレンと比較的容易に反応するが，ケトンアジン（**1h**）は反応性が劣り，**3a-e** と反応しない。しかし **1h** も **2** とはエーテルの沸点で付加反応をおこし，**1d-g** と **3a-b** との反応同様にクリスクロス付加体となる。このことから，イソシアナートのヘテロキュムレンとしての反応性は，ケテンより相当に劣ることがわかる。

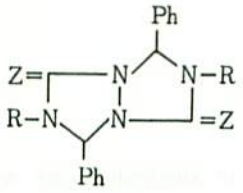
Reactions of Azines with Heterocumulene Compounds. II.

# Addition of Azine to Isocyanate

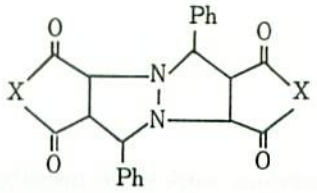
In previous work [1] we investigated the reaction of aldehyde azine with diphenylketene, a sort of heterocumulenes, and found that the reaction product depend on the structure of azine, that is, (a) in the reaction with aromatic aldehyde azine, diphenylketene (**2**) gave 2-azetidinone derivative (**4**); (b) in the reaction with aliphatic aldehyde azine, the ketene **2** gave 1, 3-oxazinone derivative (**5**), formed by the elimination of 1 mole of nitrile from the adduct of 2 mole of **2** and 1mole of the azine. Then, we studied the reactions of aldehyde azines with methyl isocyanate (**3a**) or phenyl isocyanate, and of ketone azine with **2**.



The reaction of one mole of benzaldazine with two moles of cyanic, thiocyanic acid or phenyl isocyanate in the manner of a 1, 3-2, 4-bis-addition yielding triazolotriazole derivative (**6**) was first investigated by Bailey and co-workers[2], and this reaction was termed Criss-Cross addition. Benzaldazine also reacted with other dienophile, such as maleic anhydride[3] or N-substituted maleinimide[4] to afford criss-cross 1 : 2-adduct (**7**).




**6**

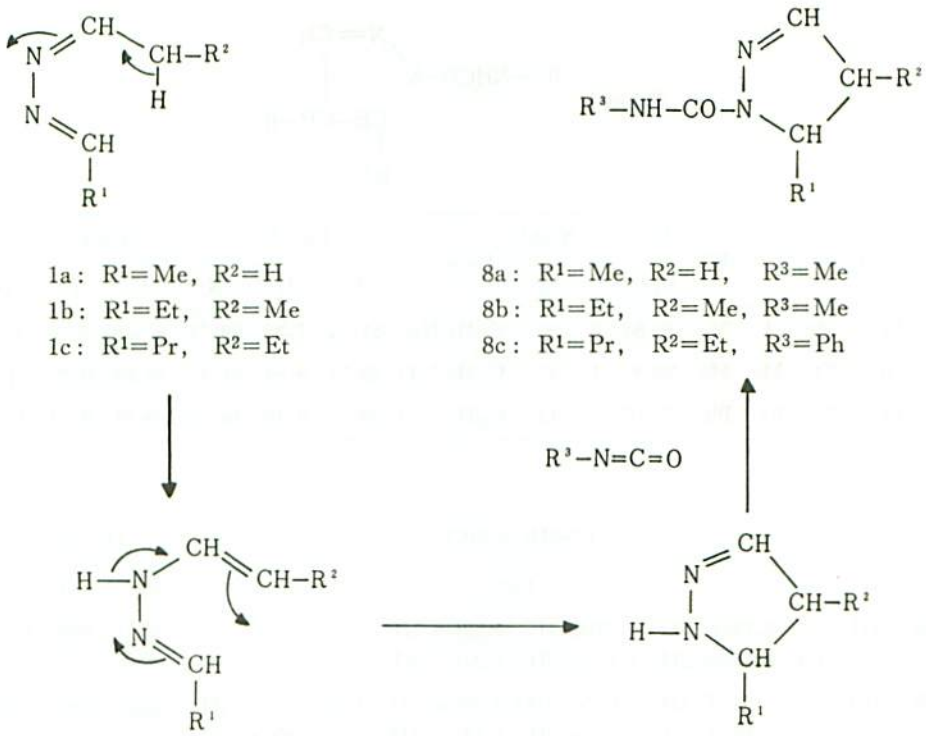



**7**

In contrast to the above 1, 3-2, 4-bisaddition of isocyanate to azine, the reaction of aliphatic aldehyde azine with isocyanate take a different course and yields 1 : 1-adduct.

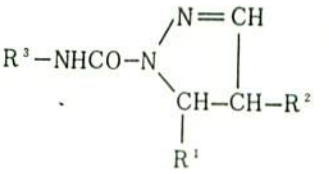
When acetaldehyde azine (**1a**) and methyl isocyanate (**3a**) were heated at 140°C in an autoclave for 5 hr, an oil product was obtained by distillation. Analysis and mass spectroscopy established the composition as a 1 : 1-adduct $C_6H_{11}N_3O$. Spectral data suggested the structure as 1-methylcarbamoyl-5-methyl-2-pyrazoline (**8a**). The infrared spectrum displays the characteristic absorption bands of -NH-CO- at 3300 and 1665cm$^{-1}$, and of a carbon nitrogen double bond at 1642cm$^{-1}$. Moreover, in the nuclear magnetic resonance spectrum, there are two methyl doublets centred at $\delta$ 1.24 and 2.76ppm, a methylene multiplet as an ABX system at $\delta$ 2.10–3.40ppm, and a methine sextet centred at $\delta$ 4.22ppm. The remaining two protons appeared at $\delta$ 6.24ppm as a quartet and at $\delta$ 6.74ppm as a triplet are due to a proton attached to a unsaturated carbon and a proton of -NH- group, respectively. A possible pathway for the formation of 1 : 1-adduct is concluded as follows. The self-cyclization of **1a** take place to give pyrazoline derivative, and then **3a** reacts to the pyrazoline intermediate.

Propionaldehyde azine (**1b**) reacted with **3a** under similar conditions to give an oil product. The analytical values and the mass spectrum of this product were in good agreement with the expected 1 : 1-adduct, and its infrared spectrum and nuclear magnetic resonance spectrum were again very similar to those of **8a**. On the basis of these spectral evidences, the structure of this product was assigned as 5-ethyl-4-methyl-1-methylcarbamoyl-2-pyrazoline (**8b**).




The reaction of aromatic isocyanate with **1a** was also examined and a reddish oil was obtained. A product, however, could not be isolated in a pure state from this viscous reaction mixture because of its high boilidg point. Then, in place of **1a**, butyraldehyde azine (**1c**) was used in the reaction with aromatic isocyanate. When phenyl isocyanate (**3b**) and **1c** were heated under the conditions similar to the reaction of **1a** with **3a**, a crystalline product was obtained. The infrared bands at 3310, 1655 and 1615cm$^{-1}$ indicate the presence of a NH group, a carbonyl group and a C=N group. respectively. There are five aromatic protons in the region of $\delta$ 7.80-7.10ppm as multiplet, two methyl triplets centred at 0.94 and 1.00ppm, a group of multiplet for six protons at 1.90–1.30 which altogether represents three $CH_2$ groups each attached to a saturated carbon centre. The remaining four protons appeared as a doublet at 6.88, as a singlet at 6.51, and as two multiplete at 3.95 and 2.65ppm are assigned to olefinic proton, to amide proton, and to methine protons, respectively. The values of elemental analysis and mass spectrum were in accord with the calculated values of the fromula $C_{15}H_{21}N_3O$. On the basis of these evidences, the structure of the crystalline adduct was confirmed to be 1–phenylcarbamoyl–4–ethyl–5–propyl–2–pyrazoline (**8c**). The results of the

**Table 1.**

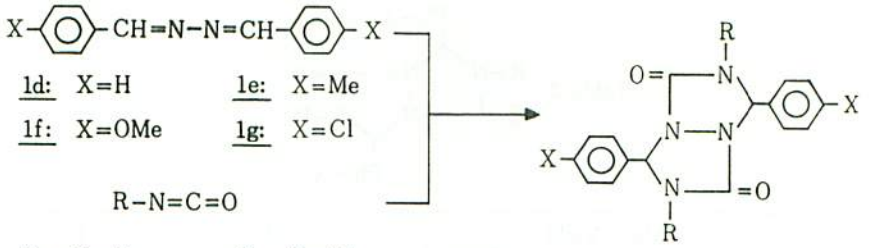


| Compd | $R^1$ | $R^2$ | $R^3$ | Mp or Bp/torr | Yield % | Formula | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **8a** | Me | H | Me | 85-85°/2 | 56 | $C_5H_{11}N_3O$ | 51.04 | 7.85 | 29.77 | 50.78 | 8.11 | 30.01 |
| **8b** | Et | Me | Me | 98-99°/1 | 41 | $C_8H_{15}N_3O$ | 56.78 | 8.94 | 24.83 | 56.55 | 9.20 | 24.99 |
| **8c** | Pr | Et | Ph | 73-76° | 12 | $C_{15}H_{21}N_3O$ | 69.46 | 8.16 | 16.21 | 69.21 | 8.33 | 16.50 |

| | MS m/e | $^1$H-NMR ($CDCl_3$) δ, ppm | IR ($cm^{-1}$) NH | CO | C=N |
|---|---|---|---|---|---|
| **8a** | 141 | 6.74(t, 1H) 6.24(q, 1H) 4.22(m, 1H) 3.40-2.10(m, 2H) 2.76(d, 3H) 1.24(d, 3H) | 3300 | 1665 | 1642 |
| **8b** | 169 | 6.58(d, 1H) 6.03(q, 1H) 3.76(m, 1H) 3.06-2.55(m, 1H) 2.77(d, 3H) 1.74(m, 2H) 1.14(d, 3H) 0.83(t, 3H) | 3320 | 1660 | 1645 |
| **8c** | 259 | 7.80-7.10(m, 5H) 6.88(d, 1H) 6.51(s. 1H) 3.95(m, 1H) 2.65(m, 1H) 1.90-1.30(m, 6H) 1.00(t, 3H) 0.94(t, 3H) | 3310 | 1655 | 1625 |

reactions of aliphatic aldehyde azines with isocyanates are summarized in Table 1.

Aromatic aldehyde azine was used instead of aliphatic azine and was allowed to react with **3a** or **3b**. Treatment of benzaldehyde azine (**1d**) with **3a** in an autoclave for 5 hr at 140°C gave a white solid. By the information of elementary analysis and mass spectroscopy, the solid was found to be a 1 : 2 addition product of **1d** with **3a**. The infrared band at 1730$cm^{-1}$ indicate the presence of saturated five membered ring ketone, and no absorption exhibit in the N-H region at about 3300$cm^{-1}$ or C=N region at 1650$cm^{-1}$. The nuclear magnetic resonance spectrum show absorptions at δ 7.51-7.25ppm assignable to aromatic protons, at 6.07 corresponding to methine which is situated among two nitrogen atoms and a phenyl group, at 2.79ppm due to methyl protons attached to nitrogen atom, in area ratio of 5 : 1 : 3. These spectral data suggested the structure of the reaction product of **1d** with **3a** as 5, 3'-diketo-4, 4'-dimethyl-3, 5'-diphenylhexahydro-1, 2-triazolotriazole (**9a**).




3a : R=Me
3b : R=Ph

9a : R=Me, X=H 9b : R=Ph, X=H
9c : R=Ph, X=Me 9d : R=Ph, X=OMe
9e : R=Ph, X=Cl

The azine **1d** reacted also with phenylisocyanate (**3d**) in refluxing xylene for 10 hr to give an white solid. The nuclear magnetic resonance spectrum of this product closely resemble to that of **9a**, except that the signals of aromatic protons apper at δ 7.60–7.04ppm and the absorptions of methyl protons disappear. The values of elemental analysis and mass spectrum were well in accord with the calculated values of the 1 : 2-adduct. Therefore, the structure of this product was confirmed to be triazolotriazole derivative (**9b**). The mass spectrum of **9b** exhibits the parent peak at m/e 466 and other peaks at m/e 327 (M–119) and 208 (M–2× 119), arising from the loss of phenyl isocyanate from the parent ion and further fragmentation of the ion of 327 by the loss of phenyl isocyanate. These are coincided with the fact that 1, 3–2, 4–biscycloaddition product of azine is readily cleaved as follows[4) 5)].

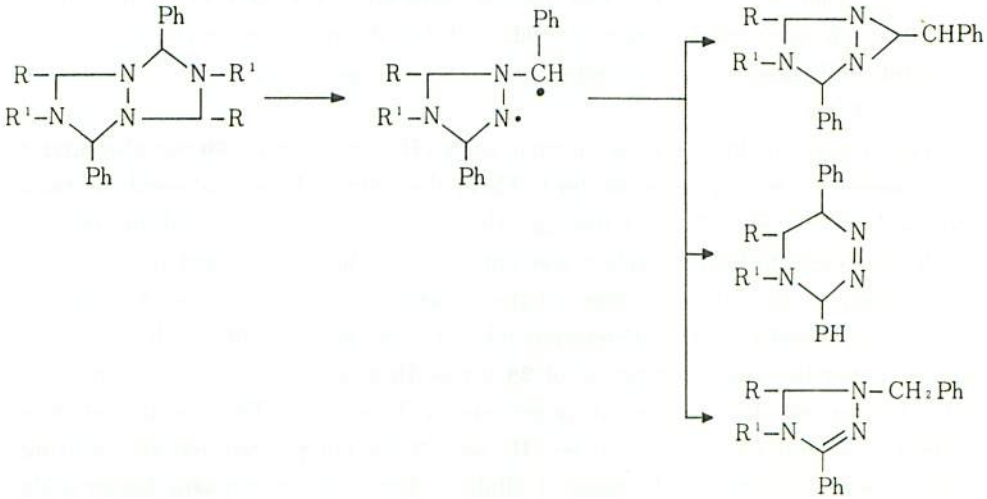
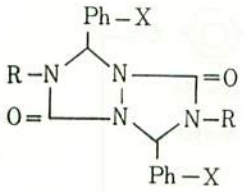


Table 2.

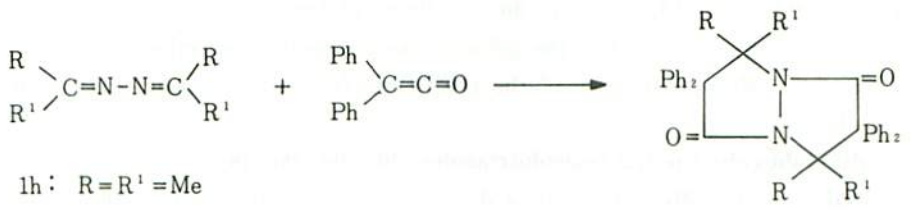



| Compd | R | X | Mp °C | Yield % | Formula | Calcd, % C | H | N | Found, % C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **9a** | Me | H | 174–5 | 46 | $C_{18}H_{18}N_4O_2$ | 67.06 | 5.63 | 17.38 | 66.81 | 5.92 | 17.50 |
| **9b** | Ph | H | 257–8 | 48 | $C_{28}H_{22}N_4O_2$ | 75.32 | 4.97 | 12.55 | 75.17 | 5.17 | 12.42 |
| **9c** | Ph | Me | 264–5 | 45 | $C_{30}H_{26}N_4O_2$ | 75.93 | 5.52 | 11.81 | 75.69 | 5.76 | 12.10 |
| **9d** | Ph | OMe | 238–9 | 28 | $C_{30}H_{26}N_4O_4$ | 71.13 | 5.17 | 11.06 | 70.84 | 5.33 | 10.88 |
| **9e** | Ph | Cl | 245–7 | 39 | $C_{28}H_{20}N_4O_2Cl_2$ | 65.25 | 3.92 | 10.87 | 65.03 | 4.15 | 11.12 |

| | MW | MS m/e | $^1$H-NMR ($CDCl_3$) δ, ppm | | | IR C=O |
|---|---|---|---|---|---|---|
| **9a** | 322.4 | 322 | 7.51–7.25(m, 10H) | 6.07(s, 2H) | 2.79(s, 6H) | 1728 |
| **9b** | 446.5 | 446 | 7.60–7.04(m, 20H) | 6.84(s, 2H) | | 1725 |
| **9c** | 474.5 | 474 | 7.60–6.96(m, 18H) | 6.80(s, 2H) | 2.28(s, 6H) | 1725 |
| **9d** | 506.5 | 506 | 7.60–7.17(m, 18H) | 6.98(s, 2H) | 3.71(s, 6H) | 1720 |
| **9e** | 515.4 | 514, 516 | 7.60–7.00(m, 18H) | 6.79(s, 2H) | | 1728 |

Other aromatic aldehyde azines, such as p-methyl-(**1e**), p-methoxy-(**1f**), and p-chloro-benzaldehyde azine (**1g**) also reacted with **3b** to give 3, 5′–di (p-methylphenyl)-(**9c**), 3, 5′–di (p-methoxyphenyl)-(**9d**) and 3, 5′–di (p-chlorophenyl)–5, 3′–diketo–4, 4′–diphenylhexahydro–1, 2–triazolotriazole (**9e**), respectively. The results are shown in Table 2.

The reaction of ketone azine, acetone azine (**1h**), with **3a** or **3b** was also carried out, however, no product was obtained. Then, the azine **1h** was allowed to react with diphenyl ketene (**2**) in refluxing ether for 5 hr, and a crystalline product which was found to be 1 : 2–adduct was obtained. The infrared and nuclear magnetic resonance spectral data suggested the structure of this product as 3, 5′–diketo–5, 5, 3′, 3′–tetramethyl–4, 4, 4′, 4′–tetraphenyl–1, 3–diazolodiazole (**10**). It was then conceived that the addition reaction of **2a** across **1b** proceded in the 1, 3–2, 4–position as in the case of the reaction of isocyanate with azine. The similar addition reaction of methyl ethyl ketone azine (**1i**) with **2** did not proceed and the starting meterials were recovered. In place of aliphatic ketone azine, aromatic ketone azine



1h : R=R¹=Me

1i : R=Me, R' =Et

10 : R=R¹=Me

such as acetophenone azine and benzophenone were also used in the reaction with **2**, but the reaction did not take place at all. In view of the formation of the compound **10**, it is evidence that the ketene **2** is more reactive as the heterocumulenes than the isocyanate **3a** or **3b**.

## Experimental

The Mass spectra were obtained on a Hitachi RMU-7M spectrometer (ionnizing potential : 70eV; chamber temperature : 150°C). The Infrared spectra were measured in potassium bromide disc or liquid films using a Hitachi 285 Grating Infrared spectrometer. The Nuclear Magnetic Resonance spectrawere recorded with a JNM-PMX 60 NMR spectrometer at room temperature. Carbon tetrachloride and chloroform-d were used as solvents, and tetramethylsilane was used as an internal reference. The chemical shifts were recorded in $\delta$ values and were followed by the splitting patern : s, singlet ; d, doublet ; t, triplet ; q, quartet ; m, multiplet.

**Materials.** The condensation reaction of the carbonyl compound with hydrazine hydrate to yield azine **1** was carried out in refluxing diethyl ether. Diphenyl ketene (**2**) was prepared by the method given in Org. Syn[6]. Methyl isocyanate (**3a**) and phenyl isocyanate (**3b**) were obtained commercially.

**1-Methylcarbamoyl-2-pyrazoline Derivatives (8a, 8b).** A mixture of 0.2mol of the azine (**1a** or **1b**), 0.4mol of **3a** and 100ml of benzene was heated in an autoclave for 5hr at 140°C. The mixture was then cooled and distilled to give an oil. In order to obtain a pure product, this oil was fractionally redistilled. The results are presented in Table 1.

**1-Phenylcarbamoylcarbamoyl-2-pyrazoline Derivative (8c).** A solution of 0.2mol of **1c** and 0.2mol of **3b** in 100ml of benzene was heated at 200°C for 10hr in an autoclave. After most of the solvent was removed, the residue was recrystallized from hexane to give **8c**.

**4, 4'-Dimethyl-3, 5'-diphenyl-5, 3'-diketohexahydro-1, 2-triazolotriazole (9a).**

A mixture of 0.1mol of **1d**, 0.3mol of **3a** and 100ml of benzene was heated for 5hr at 140°C in an autoclave. After the solvent was removed, dried ether was added to the mixture. Recrystallization of the precipitate from ligroin gave the results shown in Table 2.

**5,3'-diketohexahydro-1,2-triazolotriazoles (9b, 9c, 9d, 9e).** A mixture of 0.1mol of **1d**, 0.2mol of **3b** and 100ml of dried xylene was refluxed for 10hr under a nitrogen atmosphere, and the solvent was removed by distillation under reduced pressure. The residue was recrystallized from carbon tetrachloride to separate the product **9b** and the starting materials.

Other aromatic aldehyde azine (**1e**, **1f** or **1g**) also gave the corresponding triazolotriazole derivative (**9c**, **9d** or **9e**). Their physical constants, yields, and spectral data are shown in Table 2.

**3,5'-Diketo-1,3-diazolodiazole Derivative (10).** A solution of 0.05mol of **1h** and 0.1mol of **2** in 100ml of dried ether was refluxed for 5hr under nitrogen atmosphere and the solvent was removed. The residue was added to hexane to precipitate the crude product. Recrystallization from ligroin gave **10**: yield 47%; mp 153-4°C; ir bands at 1745cm$^{-1}$; nmr ($CDCl_3$) $\delta$ 7.67-6.83 (m, 20H), 1.67 (s, 3H), 1.45 (s, 6H), 1.38 (s, 3H); ms 500 (M), 485 (M-$CH_3$), 306 (M-$Ph_2C{=}C{=}O$).

Anal. Calcd for $C_{34}H_{32}N_2O_2$: C, 81.57; H, 6.44; N, 5.60. Foundr C, 81.42; H, 6.57; N, 5.59.

## References

1) S. Satsumabayashi, S. Motoki and H. Nakano, J. Org. Chem., **41**, 156, (1976).
2) J.R. Bailey and A.T. McPherson, J. Amer. Chem. Soc., **39**, 1322, (1917).
3) J.K. Stille and R.A. Morgan, J. Polym. Sci., 2397, (1965).
4) M. Harig and T.W. Jauregg, Helv. Chim. Acta, **40**, 852, (1957), **52**, 1672, (1969).
5) W. Bartmann, Chem. Ber., **100**, 2938, (1967).
6) L.I. Smith and H.H. Hoehn, Organic Syntheses, Coll. Vol. III 356, (1955).