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1,3-Oxazines and Related Compounds. II.[1] Ring Contraction Reaction of 1,3-Oxazin-4-one Derivatives into 1,2,4-Triazoles and Pyrazoles[2]

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The reaction of 6-methyl-2-phenyl-4*H*-1,3-oxazin-4-one (**1**) with hydrazine hydrate, methylhydrazine and phenylhydrazine was found to yield the corresponding 1,2,4-triazoles **3a**, **2b** and **3c** in 91, 52 and 76.5% yield, respectively.

Whereas, **1** was treated with the respective sulfates of hydrazine, methylhydrazine and phenylhydrazine to be transformed into the corresponding pyrazoles **9a**, **9b** and **9c** in 73.4, 61 and 42% yield, respectively.

Analogously, the reaction of **14a, b** with phenylhydrazine yielded the corresponding 1,2,4-triazole **15a, b.**

Keywords——ring contraction reaction; 1,3-oxazines; 1,2,4-triazoles; pyrazoles; 1,3-oxazinium salt

It has been reported that 1,3-oxazin-4-one derivatives undergo the ring transformation reaction with appropriate nucleophiles into various N-heterocycles such as pyridines,[4] pyrindines,[5] and pyrimidines.[6] In the course of our continuing study, it was found that the reaction of 1,3-oxazin-4-one derivatives with hydrazines lead to the ring contraction into 1,2,4-triazoles and pyrazoles, which is described in the present paper.

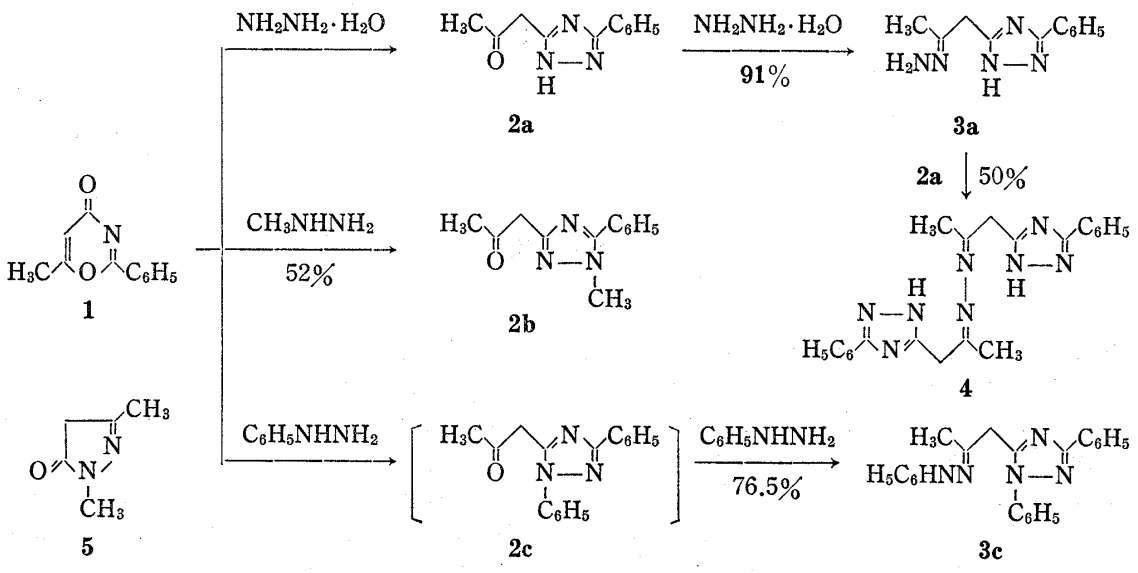


Chart 1

1) Preceding paper forms Part I of this series: Y. Yamamoto and Y. Azuma, *Heterocycles*, **6**, 1817 (1977).
2) A part of this work was presented at the 96th Annual Meeting of the Pharmaceutical Society of Japan, Nagoya, April, 1976, Abstracts of Papers, II, p. 130.
3) Location: *4-4-1 Komatsushima, Sendai 983, Japan.*
4) T. Kato, Y. Yamamoto, and M. Kondo, *Chem. Pharm. Bull.* (Tokyo), **23**, 1873 (1975).
5) T. Kato, Y. Yamamoto, and M. Kondo, *Heterocycles*, **3**, 293 (1975).
6) *a*) T. Kato and Y. Yamamoto, *Chem. Pharm. Bull.* (Tokyo), **15**, 1334 (1967); *b*) T. Kato, H. Yamanaka, Y. Yamamoto, and M. Kondo, *Yakugaku Zasshi*, **92**, 886 (1972).

The reaction of 6-methyl-2-phenyl-4*H*-1,3-oxazin-4-one (**1**)[7] with an equimolar amount of hydrazine hydrate in 95% ethanol afforded 3-acetonyl-5-phenyl-1*H*(2*H*)-1,2,4-triazole (**2a**), $C_{11}H_{11}N_3O$, mp 128°, in 35% yield.

Structure **2a** was assigned on the basis of the following data. Its infrared spectrum (IR) (KBr) showed a NH stretching band at 3400 cm^{-1} and a carbonyl band at 1715 cm^{-1}. The proton magnetic resonance spectrum (PMR) ($CDCl_3$) gave two singlets at δ 2.24 (3H) and 4.05 (2H) assigned to the methyl and methylene protons of the acetonyl group, and a multiplet at δ 7.2—8.3 (5H) originating from the aromatic protons.

Use of two equivalents of hydrazine hydrate resulted in formation of the hydrazone (**3a**) of **2a**, $C_{11}H_{13}N_5$, mp 115°, in 91% yield. During purification of **3a** by recrystallization, a small amount of **4**, $C_{22}H_{22}N_8$, mp 205° (dec.), was formed, whose spectral data were in accord with the proposed structure.

The phenylhydrazone **3c**, $C_{23}H_{21}N_5$, mp 177° (dec.), was exclusively formed by the reaction of **1** with two equivalents of phenylhydrazine, even with an equivalent of the latter. Proof of the structure of **3c** was achieved on the basis of the following spectral and chemical evidences (Chart 2).

Treatment of **3c** with titanium trichloride in dry dimethoxyethane according to the method reported by McMurry[8] generated a 66% yield of the ketone **2c**, $C_{17}H_{15}N_3O$, mp 71—72°. Subsequent reduction of **2c** with sodium borohydride in methanol at room temperature furnished the alcohol **6**, $C_{17}H_{17}N_3O$, bp 176° (0.08 Torr), in 50% yield. The ultraviolet spectrum (UV) of **6** was very similar to that of 5-methyl-1,3-diphenyl-1,2,4-triazole (**7**) prepared by the known procedure.[9]

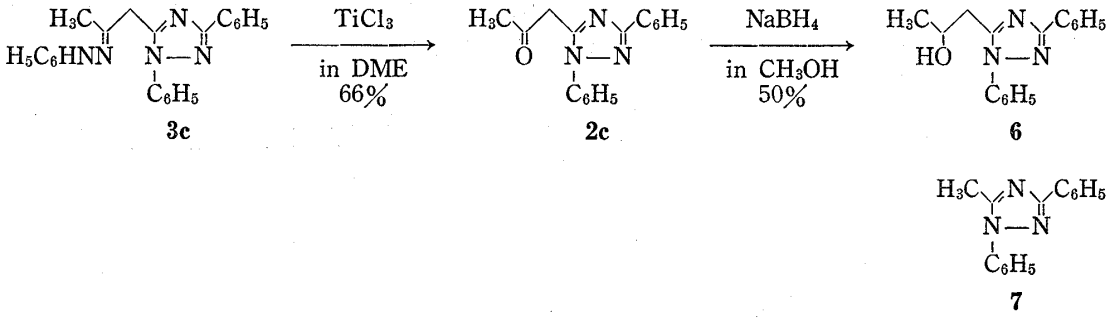


Chart 2

Similar treatment of **1** with a molar equivalent of methylhydrazine gave the ketone **2b**, $C_{12}H_{13}N_3O$, bp 168° (0.3 Torr), in 52% yield. However, using two equivalents of methylhydrazine resulted in formation of 1,3-dimethyl-5-pyrazolone (**5**),[10] and attempts for isolation of the expected triazole failed.

The position of the N-methyl group of **2b** was determined by comparison of the PMR spectrum with those of 1,5-dimethyl-3-phenyl-1,2,4-triazole (**8a**),[11] 1,3-dimethyl-5-phenyl-1,2,4-triazole (**8b**)[11] and **2a**. The most notable feature in the spectrum of **2b** is the broad multiplet due to the ring protons of phenyl group. The multiplicity is very similar to that of **8b** as shown in Fig. 1. In addition, the conversion of **2b** to **8b**, which was accomplished by treatment of **2b** with hydroiodic acid, provided further evidence for the structure of **2b**.

7) **1** was prepared in 70% yield by an improved prodedure (reported yield;[6a] 16%), see Experimental section.
8) J.E. McMurry and M. Silvestri, *J. Org. Chem.*, **40**, 1502 (1975).
9) M. Fujimori, H. Haruki, and E. Imoto, *Nippon Kagaku Zasshi*, **89**, 900 (1968).
10) E.C. Taylor and K.S. Hartke, *J. Am. Chem. Soc.*, **81**, 2456 (1959).
11) M.R. Atkinson and J.B. Polya, *J. Chem. Soc.*, **1954**, 3319.

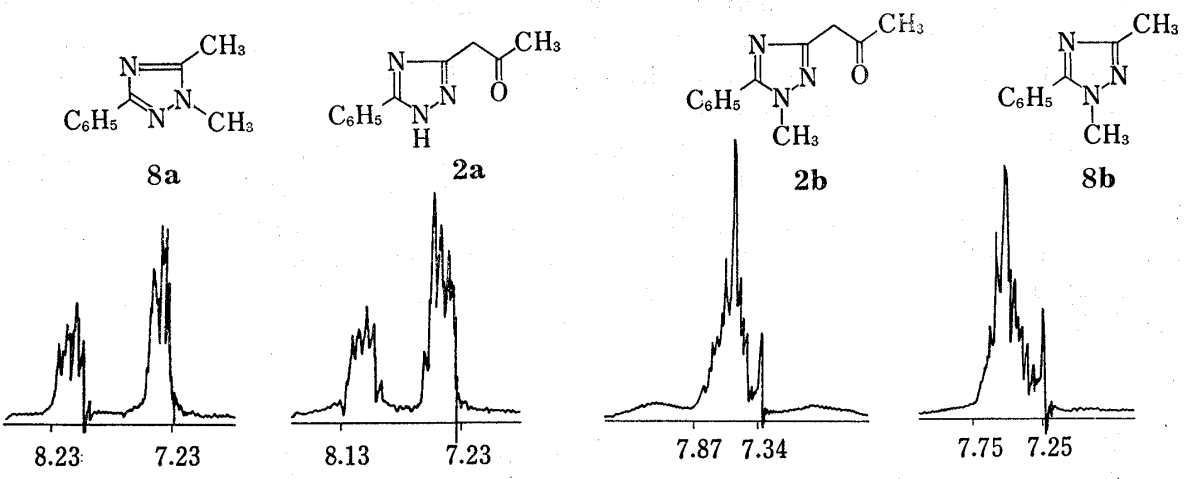
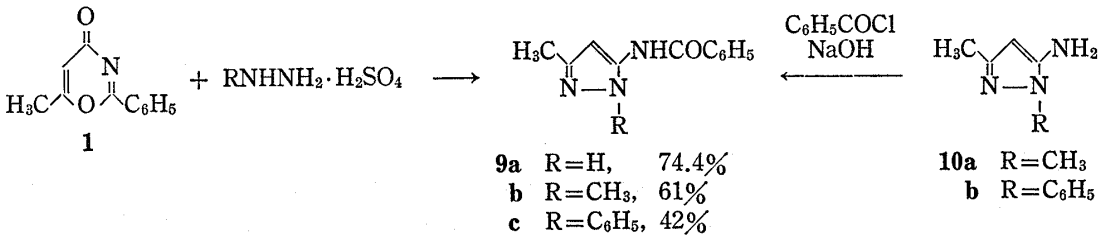


Fig. 1

In contrast with the case of hydrazine hydrate, hydrazine sulfate was allowed to react with **1** in 80% ethanol under reflux to give rise to 3-benzamido-5-methylpyrazole (**9a**) in 74.4% yield. Similarly, heating of **1** with the sulfates of methylhydrazine and phenylhydrazine yielded the corresponding pyrazole **9b** and **9c** in 61% and 42% yield, respectively.

The structural confirmation of **9b** and **9c** was carried out by comparison of their IR spectra with those of the respective authentic samples synthesized by benzoylation of 5-amino-1,3-dimethylpyrazole (**10a**) and 5-amino-3-methyl-1-phenylpyrazole (**10b**) obtained by Taylor's method.[10]



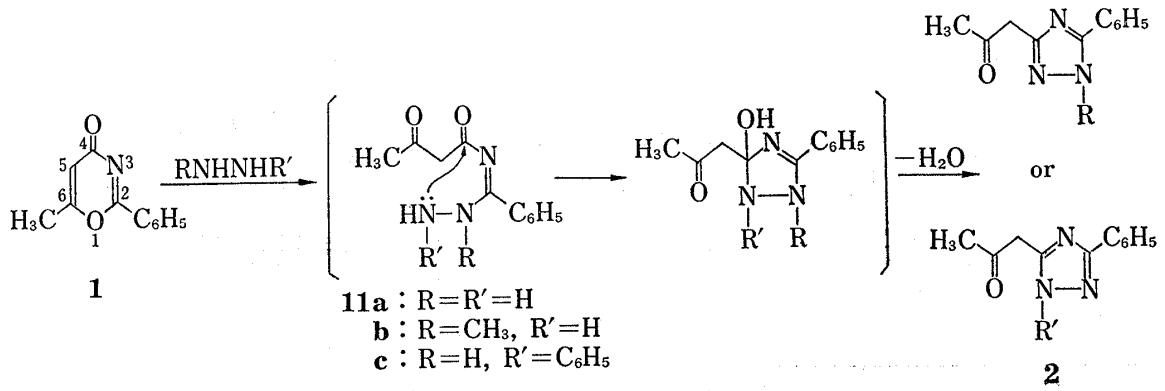
1

9a R=H, 74.4%
b R=CH₃, 61%
c R=C₆H₅, 42%

10a R=CH₃
b R=C₆H₅

Chart 3

These results evidently propose the mechanism that the ring contraction reaction proceeds in two steps: the first involves the ring opening by cleavage of either $C_{(2)}$–O bond or $C_{(6)}$–O bond of the 1,3-oxazine ring into an open-chain intermediate, and the second is the ring closure of the intermediate to the triazole or the pyrazole.



1

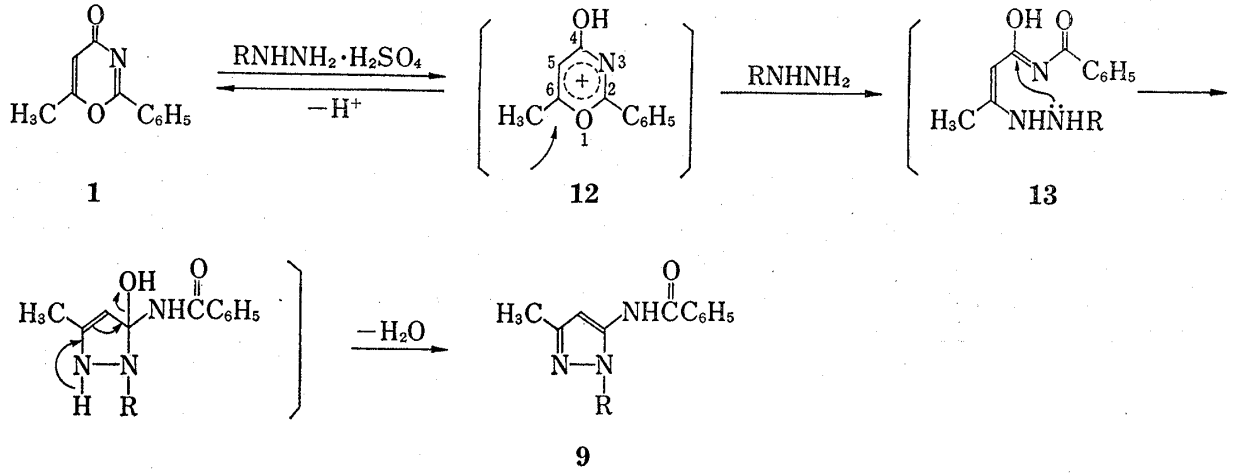
11a : R=R′=H
b : R=CH₃, R′=H
c : R=H, R′=C₆H₅

2

Chart 4

Thus, in the contraction reaction of **1** into the 1,2,4-triazole the initial attack on the 2-position by a hydrazine base seems to be much preferred rather than on the 6-position, and causes the cleavage of $C_{(2)}$–O bond leading to the intermediate **11** and the subsequent ring closure of **11** into the 1,2,4-triazole **2**.

Meanwhile, the mechanism for conversion into the pyrazole can be explained as follows; in the presence of the hydrazine sulfate, **1** is presumably in equilibrium with the 1,3-oxazinium salt **12** as shown in Chart 5, although the equilibrium concentration of **12** is expected to be lower than that of **1**. The oxazinium salt **12** undergoes the nucleophilic attack predominantly the 6-position[12] leading to the formation of the intermediate **13**, which recyclizes to the pyrazole **9**.



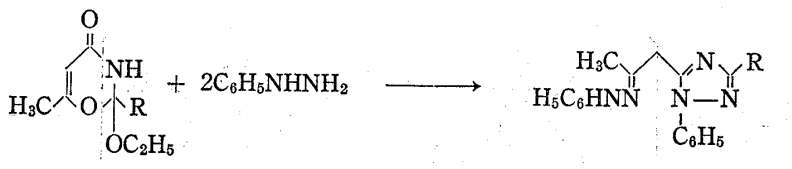
1 **12** **13** **9**

Chart 5

It is notable that treatment of N-acetoacetylbenzamide, obtained by hydrolysis of **1**, with hydrazine bases provided neither the triazole nor the pyrazole, but only benzamide.

It is of interest that the reaction of **1** with phenylhydrazine sulfate in the presence of sodium acetate resulted in formation of the triazole **3c** in 30% yield, whereas sulfates of hydrazine and methylhydrazine were allowed to react with **1** at the same conditions to yield the corresponding pyrazole **9a** and **9b** in 42% and 40% yield, respectively.

Analogously, the reaction of 2-benzyl-2-ethoxy-3,4-dihydro-6-methyl-2*H*-1,3-oxazin-4-one (**14a**)[6a] and 2-ethoxy-3,4-dihydro-2,6-dimethyl-2*H*-1,3-oxazin-4-one (**14b**)[6b] with two equivalents of phenylhydrazine afforded the corresponding triazole **15a** and **15b** in 78% and 38% yield, respectively (Chart 6).



14a R=$C_6H_5CH_2$
b R=CH_3

15a R=$C_6H_5CH_2$, 78%
b R=CH_3, 35%

Chart 6

12) It is established that the attack of nucleophilic reagents takes place preferentially at the 6-position of 1,3-oxazinium salts: for a review, see R.R. Schmidt, *Synthesis*, **1972**, 333.

Experimental[13]

Improved Method for Preparation of 6-Methyl-2-phenyl-4H-1,3-oxazin-4-one (1)——To a solution of benziminoethylether (37.5 g, 0.25 mol) in dry benzene (35 ml) was added dropwise diketene (44 g, 0.54 mol) with stirring. The solution was refluxed for 3 hr and then allowed to stand at room temperature for 2 hr. The precipitate formed was collected by filtration and recrystallized from benzene to give **1** (29 g) as colorless prisms, mp 139—140°. A few drops of acetic acid was added to the filtrate. The resulting solution was refluxed for 1 hr and evaporated under reduced pressure. The remaining semisolid was washed with benzene, and recrystallized from benzene to give 4 g of colorless prisms (**1**). Total yield: 33 g (70%). The IR spectrum was identical with that of an authentic sample.

3-Acetonyl-5-phenyl-1*H*(2*H*)-1,2,4-triazole (2a)——a) A solution of **1** (1 g, 5.3 mmol) and 85% hydrazine hydrate (0.31 g, 5.3 mmol) in 95% ethanol (20 ml) was allowed to stand for 2 hr at room temperature. The solvent was evaporated at reduced pressure by an aspirator. The resulting solid was washed with a small amount of ether and recrystallized from ether to give 0.38 g (35%) of **2a** as colorless needles of mp 128°. *Anal.* Calcd. for $C_{11}H_{11}N_3O$ (**2a**): C, 65.67; H, 5.47; N, 20.89. Found: C, 66.18; H, 5.45; N, 21.17. IR ν_{max}^{KBr} cm^{-1}: 3400 (NH), 1715 (C=O). PMR ($CDCl_3$) δ: 2.24 (3H, s, CH_3), 4.05 (2H, s, CH_2), 7.2—8.3 (5H, m, ring protons), 11.4 (1H, b, NH). UV λ_{max}^{EtOH} nm (log ε): 244 (4.15). MS *m/e*: 201 (M^+), 159, 104. 2,4-Dinitrophenylhydrazone: mp 248° (methanol). *Anal.* Calcd. for $C_{17}H_{15}N_7O_4$: C, 53.54; H, 3.94; N, 25.72. Found: C, 53.54; H, 3.78; N, 25.87.

b) The hydrazone **3a** (0.5 g) was treated with 36% formaldehyde (6 ml) and concentrated hydrochloric acid (2 ml) in dioxane (20 ml) according to Severin's procedure[14] to give 0.05 g (10%) of **2a**, mp 128°. The IR spectrum was identical with that of a sample obtained in the above run.

3-(5-Phenyl-1,2,4-triazole)acetone Hydrazone (3a)——a) The hydrazone **3a** was obtained from **1** (1 g, 5.3 mmol) and 0.62 g (10.6 mmol) of 85% hydrazine hydrate by similar procedure as described above, as colorless needles, mp 115° (benzene). Yield: 1.04 g (91%). *Anal.* Calcd. for $C_{11}H_{13}N_5$ (**3a**): C, 61.39; H, 6.04; N, 32.55. Found: C, 61.46; H, 6.12; N, 32.87. IR ν_{max}^{KBr} cm^{-1}: 3300 and 3150 (NH), 1670 and 1610 (C=N). PMR [$CDCl_3$–d_6-DMSO (2:1)] δ: 1.76 (3H, s, CH_3), 3.63 (2H, s, CH_2), 5.57 (2H, b, NH_2), 7.1—8.3 (5H, m, ring protons), 8.8 (1H, b, NH). UV λ_{max}^{EtOH} nm (log ε): 243 (4.21), 310 (3.44). MS *m/e*: 215 (M^+), 199, 184, 172, 159, 104.

b) A solution of **2a** (0.5 g, 2.5 mmol) and 85% hydrazine hydrate (0.15 g, 2.5 mmol) in 95% ethanol (10 ml) was stirred for 1 hr at room temperature. The solvent was removed under reduced pressure. Recrystallization of the residual solid from benzene gave **3a** (0.29 g, 54%), mp 115°. During recrystallization of **3a**, a small amount of **4** was obtained as insoluble material. The IR spectrum was identical with that of a sample obtained in the above run.

3-(5-Phenyl-1,2,4-triazole)acetone Azine (4)——a) A solution of **1** (1 g, 5.3 mmol) and 85% hydrazine hydrate (0.47 g, 8 mmol) in 95% ethanol (20 ml) heated under reflux for 2 hr and evaporated *in vacuo*. Recrystallization of the residual solid from 95% ethanol gave **4** (0.55 g, 52%) as colorless minute needles, mp 205° (dec.). *Anal.* Calcd. for $C_{22}H_{22}N_8$ (**4**): C, 66.33; H, 5.53; N, 28.14. Found: C, 66.09; H, 5.69; N, 28.18. IR ν_{max}^{KBr} cm^{-1}: 3420 (NH), 1640 (C=N). PMR ($CDCl_3$) δ: 1.89 (3H, s, CH_3), 2.21 (3H, s, CH_3), 3.91 (4H, s, $2\times CH_2$), 7.3—8.1 (10H, m, ring protons). MS *m/e*: 398 (M^+), 315, 240, 200, 172, 159, 104.

b) Heating a solution of **2a** (0.25 g, 1.24 mmol) and **3a** (0.27 g, 1.24 mmol) in 95% ethanol (10 ml) under reflux for 1 hr followed by evaporation *in vacuo* gave yellow solid, which was recrystallized from 95% ethanol to provide **4** (0.25 g, 50%), mp 205° (dec.). The IR spectrum was identical with that of a sample obtained in the above run.

3-Acetonyl-1-methyl-5-phenyl-1,2,4-triazole (2b)——A solution of **1** (5 g, 26.7 mmol) in absolute ethanol (50 ml) was cooled with an ice bath. To the solution was added dropwise methylhydrazine (1.3 g, 28.3 mmol) with stirring. The reaction solution was kept below 0° for 3 hr with stirring, and evaporated under reduced pressure by an aspirator. Distillation of the residual liquid gave two fractions: (1) 1,3-dimethyl-5-pyrazolone (**5**), bp 120—140° (0.3 Torr), 0.15 g; (2) 3-acetonyl-1-methyl-5-phenyl-1,2,4-triazole (**2b**), 3.1 g, bp 158—160° (0.3 Torr), which was contaminated with a small amount of the pyrazolone **5**. Redistillation of the fraction 2 gave pure **2b** (3 g, 52%), bp 168° (0.3 Torr). *Anal.* Calcd. for $C_{12}H_{13}N_3O$ (**2b**): C, 66.98; H, 6.05; N, 19.53. Found: C, 66.88; H, 6.04; N, 19.53. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1713 (C=O). PMR ($CDCl_3$) δ: 2.27 (3H, s, CH_3), 3.85 (2H, s, CH_2), 3.93 (3H, s, N–CH_3), 7.4—7.8 (5H, m, ring protons). MS *m/e*: 215 (M^+), 173, 158, 104.

5-(1,3-Diphenyl-1,2,4-triazole)acetone Phenylhydrazone (3c)——a) A solution of **1** (1 g, 5.3 mmol) and phenylhydrazine (1.2 g, 11 mmol) in 95% ethanol (20 ml) was heated under reflux for 1 hr. The precipitate

13) All melting points are uncorrected. IR spectra were taken with a Shimadzu IR-400 spectrophotometer. UV spectra were recorded on a Hitachi Model 200-20 spectrophotometer. Mass spectra were measured on a Hitachi RMU-6MG instrument. PMR spectra were recorded on a Hitachi R-24B NMR spectrometer. Chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane as an internal standard. Abbreviation used: s=singlet, d=doublet, m=multiplet, and b=broad.

14) T. Severin and R. Adam, *Chem. Ber.*, **108**, 88 (1975).

formed was taken up by filtration and recrystallized from 95% ethanol to give 1.1 g of **3c** as colorless prisms, mp 177° (dec.). Additional 0.4 g was obtained by evaporation of the filtrate followed by recrystallization. Total yield: 1.5 g (76.5%). *Anal.* Calcd. for $C_{23}H_{21}N_5$ (**3c**): C, 75.18; H, 5.76; N, 19.06. Found: C, 75.05; H, 5.96; N, 19.03. IR ν_{max}^{KBr} cm^{-1}: 3220 (NH), 1600 (C=N). PMR [$CDCl_3$–d_6-DMSO (1:1)] δ: 1.97 (3H, s, CH_3), 3.86 (2H, s, CH_2), 6.7—8.3 (15H, m, ring protons), 8.5 (1H, b, NH). UV λ_{max}^{EtOH} nm (log ε): 259 (4.48). MS *m/e*: 367 (M^+), 275, 260, 248, 234, 91.

b) A mixture of **1** (1 g, 5.3 mmol), phenylhydrazine sulfate [$(PhNHNH_2)_2 \cdot H_2SO_4 \cdot 2H_2O$] (1.87 g, 5.3 mmol) and sodium acetate (0.9 g, 10.6 mmol) in 95% ethanol (20 ml) was refluxed for 1 hr and evaporated *in vacuo*. The residue was made alkaline with 10% Na_2CO_3 solution and extracted with chloroform. The chloroform extracts were recrystallized from ethanol to give **3c** (0.59 g, 30%), mp 174—176°. The IR spectrum was identical with that of a sample obtained in the above run.

5-Acetonyl-1,3-diphenyl-1,2,4-triazole (2c)——A solution of **3a** (4 g, 11 mmol) in dry dimethoxyethane (100 ml) was placed in 300-ml three-necked flask equipped with a stirrer. A brisk stream of dry nitrogen was passed through the system. The flow of nitrogen was reduced to a slow stream, and to the solution was added dropwise 31 ml of 16% aqueous solution of titanium trichloride with stirring. The reaction mixture was refluxed for 30 min, then cooled, diluted with water (10 ml), and extracted with ether. The ether layer was washed with water and saturated brine, then dried over anhydrous $MgSO_4$, filtered, and concentrated in a rotary evaporator under reduced pressure. Distillation of the remaining liquid gave **2c** (2 g, 66%) as colorless liquid, bp 178—180° (0.15 Torr), mp 71—72° (*n*-pentane). *Anal.* Calcd. for $C_{17}H_{15}N_3O$ (**2c**): C, 73.64; H, 5.41; N, 15.16. Found: C, 73.53; H, 5.24; N, 14.53. IR ν_{max}^{neat} cm^{-1}: 1720 (C=O). PMR ($CDCl_3$) δ: 2.28 (3H, s, CH_3), 3.98 (2H, s, CH_2), 7.3—8.2 (10H, m, ring protons). UV λ_{max}^{EtOH} nm (log ε): 250 (4.14).

5-(2-Hydroxypropyl)-1,3-diphenyl-1,2,4-triazole (6)——To a solution of **3c** (1 g, 3.6 mmol) in methanol (10 ml) was added sodium borohydride (70 mg, 1.8 mmol). The reaction mixture was stirred for 30 min at room temperature, diluted with water, then neutralized with diluted hydrochloric acid, and condensed under reduced pressure. The remaining liquid was extracted with ether. Evaporation of the ether layer followed by distillation gave the alcohol **6**, bp 176° (0.08 Torr). Yield: 0.5 g (50%). IR ν_{max}^{neat} cm^{-1}: 3350 (OH), 1600 (C=N). PMR ($CDCl_3$) δ: 1.28 (3H, d, J=7 Hz, CH_3), 2.78—2.95 (2H, m, $C\underline{H}_A\underline{H}_BCH_X$), 4.02—4.52 (1H, m, $CH_A\underline{H}_BC\underline{H}_X$), 7.4—8.3 (10H, m, ring protons). UV λ_{max}^{EtOH} nm (log ε): 250 (4.35). β-Naphthylurethane: mp 152—153° (benzene). *Anal.* Calcd. for $C_{28}H_{24}N_4O_2$ (β-naphthylurethane): C, 75.00; H, 5.35; N, 12.50. Found: C, 74.76; H, 5.30; N, 12.43. IR ν_{max}^{KBr} cm^{-1}: 3400, 1715, 1600.

1,5-Dimethyl-3-phenyl-1,2,4-triazole (8a)——According to the method reported by Atkinson,[11] **8a** was prepared in 44% yield from benzimidoylmethylhydrazine and acetic anhydride. For **8a**: mp 116° (lit. mp 117°); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1520, 1500; PMR ($CDCl_3$) δ: 2.39 (3H, s, CH_3), 3.71 (3H, s, N–CH_3), and signals from phenyl group are shown Fig. 1.

1,3-Dimethyl-5-phenyl-1,2,4-triazole (8b)——According to the method reported by Atkinson,[11] **8b** was prepared in 48% yield from N-acetylbenzamide and methylhydrazine sulfate. For **8b**: mp 67° (lit. mp 66—68°); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1510, 1480; PMR ($CDCl_3$) δ: 2.41 (3H, s, CH_3), 3.89 (3H, s, N–CH_3), and signals from phenyl group are shown in Fig. 1.

Deacetylation of 2b to 1,3-Dimethyl-5-phenyl-1,2,4-triazole (8b)——A mixture of **2b** (0.6 g) in 57% hydroiodic acid (3 ml) was refluxed for 2 hr, and added additional 57% hydroiodic acid (1.5 ml). The resulting solution was continued to reflux for 1 hr, then poured onto cracked ice, made alkaline with 10% Na_2CO_3 solution, and extracted with chloroform. The chloroform layer was dried, filtered, and evaporated to yield a mixture of **8b** and **2b**. The mixture could be separated by column chromatography on alumina. Elution with ether-petroleum ether (3:1) gave **8b** (0.1 g, 20%), mp 66—68° and **2b** (0.2 g). The IR spectrum was identical in every respect with that of a sample prepared in the above run.

3-Benzamido-5-methylpyrazole (9a)——a) A mixture of **1** (2 g, 10.7 mmol) and hydrazine sulfate (1.4 g, 10.7 mmol) in 88% ethanol (40 ml) was refluxed for 1 hr. The solvent was then removed in a rotary evaporator. The residual liquid was made alkaline with 10% Na_2CO_3 solution. The precipitate formed was collected and recrystallized from methanol to give **9a** (1.6 g, 74.4%), mp 227° (dec.), as colorless needles. *Anal.* Calcd. for $C_{11}H_{11}N_3O$ (**9a**): C, 65.67; H, 5.47; N, 20.89. Found: C, 65.47; H, 5.51; N, 21.21. IR ν_{max}^{KBr} cm^{-1}: 3250 (NH), 1680 (C=O). PMR [$CDCl_3$–d_6-DMSO (1:1)] δ: 2.28 (3H, s, CH_3), 6.38 (1H, s, $C_{(4)}$–H), 7.4—8.1 (5H, m, ring protons), 10.5 (1H, b, NH), 12.0 (1H, b, NH). MS *m/e*: 201 (M^+), 173, 105, 77.

b) A mixture of **1** (1 g, 5.3 mmol), hydrazine sulfate (0.7 g, 5.3 mmol) and sodium acetate (0.88 g, 10.6 mmol) in 80% ethanol (20 ml) was refluxed for 1 hr and condensed under reduced pressure. The residual liquid was made alkaline with 10% Na_2CO_3 solution. The precipitate formed was collected and recrystallized from methanol to give **9a** (0.45 g, 42%), mp 225—227° (dec.). The IR spectrum was identical with that of a sample obtained in the above run.

5-Benzamido-1,3-dimethylpyrazole (9b)——a) A mixture of **1** (2 g, 10.7 mmol) and methylhydrazine sulfate (1.54 g, 10.7 mmol) in 88% ethanol (40 ml) was refluxed for 1 hr. By similar procedure given for **9a**, **9b** (1.4 g, 61%) was obtained as colorless prisms, mp 140°. *Anal.* Calcd. for $C_{12}H_{13}N_3O$ (**9b**): C, 66.97; H, 6.04; N, 19.53. Found: C, 67.03; H, 6.48; N, 19.88. IR ν_{max}^{KBr} cm^{-1}: 3230 (NH), 1670 (C=O). PMR ($CDCl_3$) δ: 2.15 (3H, s, CH_3), 3.58 (3H, N–CH_3), 5.96 (1H, s, $C_{(4)}$–H), 7.3—7.8 (5H, m, ring protons), 8.8 (1H, b, NH). MS *m/e*: 215 (M^+), 105, 77.

b) The pyrazole **9b** was synthesized from 5-amino-1,3-dimethylpyrazole (**10a**)[10] (0.5 g) and benzoyl chloride (0.63 g) using Schotten-Baumann condition. Recrystallization of the crude product from benzene gave colorless prisms (**9b**, 0.3 g, 33%), mp 132—134°. The IR spectrum was identical with that of a sample obtained in the above run.

c) A mixture of **1** (1 g, 5.3 mmol), methylhydrazine sulfate (1.54 g, 10.7 mmol) and sodium acetate (1.75 g, 21.3 mmol) in 80% ethanol (30 ml) was refluxed for 1 hr, and then condensed under reduced pressure. The residue was made alkaline with 10% Na_2CO_3 solution and extracted with ether. The ether extracts were recrystallized from ether to give **9b** (0.46 g, 40%), mp 138—140°. Evaporation of the ether layer afforded benzamide (60 mg), mp 128—130°. The IR spectra were identical with those of authentic samples.

5-Benzamido-3-methyl-1-phenylpyrazole (9c)——A mixture of **1** (2 g, 10.7 mmol) and phenylhydrazine sulfate [$(PhNHNH_2)_2 \cdot H_2SO_4 \cdot 2H_2O$] (2.2 g, 6.3 mmol) in 88% ethanol (30 ml) was heated at 55° (bath temperature) for 8 hr. By similar procedure given for **9a**, **9c** (1.24 g, 42%) was obtained as colorless prisms, mp 110° (ether). *Anal.* Calcd. for $C_{17}H_{15}N_3O$ (**9c**): C, 73.65; H, 5.42; N, 15.16. Found: C, 73.70; H, 5.46; N, 15.11. IR ν_{max}^{KBr} cm^{-1}: 3170 (NH), 1680 (C=O). PMR ($CDCl_3$) δ: 2.33 (3H, s, CH_3), 6.61 (1H, s, $C_{(4)}$–H), 7.4—7.8 (10H, m, ring protons), 8.1 (1H, b, NH). MS *m/e*: 277 (M^+), 105, 77.

b) The pyrazole **9c** was synthesized from 5-amino-3-methyl-1-phenylpyrazole (**10b**)[19] (0.5 g) and benzoyl chloride (0.45 g) using Schotten-Baumann condition. Recrystallization of the crude product from ether gave colorless prisms (**9c**, 0.24 g, 30%), mp 107°. The IR spectrum was identical with that of a sample obtained in the above run.

5-(3-Benzyl-1-phenyl-1,2,4-triazole)acetone Phenylhydrazone (15a)——A solution of 2-benzyl-2-ethoxy-3,4-dihydro-6-methyl-2*H*-1,3-oxazin-4-one (**14a**)[6a] (1 g, 4 mmol) and phenylhydrazine (0.86 g, 8 mmol) in 99% ethanol (30 ml) was allowed to stir at room temperature for 36 hr. The precipitate formed was taken up by filtration and recrystallized from methanol to give **15a** (1 g) as colorless prisms, mp 207° (dec.). The filtrate was evaporated *in vacuo* and the residual solid was recrystallized from methanol to give additional 0.2 g. Total yield: 1.2 g (78%). *Anal.* Calcd. for $C_{24}H_{23}N_5$ (**15a**): C, 75.59; H, 6.04; N, 18.37. Found: C, 75.38; H, 5.99; N, 18.48. IR ν_{max}^{KBr} cm^{-1}: 3220 (NH), 1600 (C=N). PMR (d_6-DMSO) δ: 1.91 (3H, s, CH_3), 3.76 (2H, s, CH_2), 4.04 (2H, s, CH_2), 6.9—7.6 (15H, m, ring protons). UV λ_{max}^{EtOH} nm (log ε): 274 (4.30). MS *m/e*: 381 (M^+), 289, 274, 248, 170, 91.

5-(3-Methyl-1-phenyl-1,2,4-triazole)acetone Phenylhydrazone (15b)——A solution of 2-ethoxy-3,4-dihydro-2,6-dimethyl-2*H*-1,3-oxazin-4-one (**14b**)[6a] (1 g, 6 mmol) and phenylhydrazine (1.26 g, 12 mmol) in 99% ethanol (30 ml) was allowed to stir at room temperature for 36 hr and evaporated under reduced pressure. The resulting solid was recrystallized from ether to give **15b** (0.62 g, 35%) as colorless prisms, mp 154°. *Anal.* Calcd. for $C_{18}H_{19}N_5$ (**15b**): C, 70.82; H, 6.23; N, 22.95. Found: C, 70.92; H, 6.22; N, 22.89. IR ν_{max}^{KBr} cm^{-1}: 3250 (NH), 1600 (C=N). PMR ($CDCl_3$) δ: 1.90 (3H, s, CH_3), 2.40 (3H, s, CH_3), 3.75 (2H, s, CH_2), 7.0—7.6 (10H, m, ring protons). UV λ_{max}^{EtOH} nm (log ε): 274 (4.27). MS *m/e*: 305 (M^+), 213, 198, 172, 91.

Reaction of N-Acetoacetylbenzamide with Hydrazine Hydrate——A solution of N-acetoacetylbenzamide (0.5 g, 2.4 mmol), prepared in 69% yield by treatment of **1** with a few drops of 10% NaOH solution in 95% ethanol at room temperature, and 85% hydrazine hydrate (0.14 g, 2.4 mmol) in 95% ethanol (10 ml) was refluxed for 1 hr. The solvent was removed under reduced pressure. The residue was washed with ether. The ether insoluble solid was recrystallized from 95% ethanol gave 3-methyl-5-pyrazolone (0.1 g, 42%), mp 213—214° (lit.[15] mp 215°), as colorless prisms, whose IR spectrum was identical with that of an authentic sample. Evaporation of the ether washings gave benzamide (0.28 g, 96%), mp 127—128°, undepressed on admixture with an authentic sample.

Reaction of N-Acetoacetylbenzamide with Methylhydrazine——A solution of N-acetoacetylbenzamide (0.5 g, 2.4 mmol) and methylhydrazine (0.11 g, 2.4 mmol) in 95% ethanol (10 ml) was allowed to stir for 1 hr at room temperature. By similar procedure 1,3-dimethyl-5-pyrazolone (82 mg, 30%), mp 115° (lit.[10] mp 117°), and benzamide (0.22 g, 75%) were obtained, which showed nondepression on a mixed melting point determination with respective authentic samples.

Reaction of N-Acetoacetylbenzamide with Phenylhydrazine——A solution of N-acetoacetylbenzamide (0.5 g, 2.4 mmol) and phenylhydrazine (0.26 g, 2.4 mmol) in 95% ethanol (10 ml) was refluxed for 30 min. By similar procedure 3-methyl-1-phenyl-5-pyrazolone (0.1 g, 24%), mp 126° (lit.[16] mp 124—127°), and benzamide (0.25 g, 85%) were obtained, which showed nondepression on a mixed melting point determination with respective authentic samples.

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