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Studies on Ketene and Its Derivatives. XXXVIII.[1] Reaction of Diketene with Phenylhydrazones to give 4-Acetyl-2-phenylpyrazolidin-3-ones

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1,3-Dipolar cycloaddition of phenylhydrazones (I) with diketene to give 4-acetyl-2-phenylpyrazolidin-3-one derivatives (II) was investigated. Refluxing of diketene with phenylhydrazone of aromatic ketone and aldehyde, such as acetophenone phenylhydrazone (Ia), benzophenone phenylhydrazone (Ib), benzaldehyde phenylhydrazone (Ig), and cinnamicaldehyde phenylhydrazone (Ih) in acetic acid gave the corresponding substituted pyrazolidin-3-ones; *i.e.*, 4-acetyl-2,5-diphenyl (IIa), 4-acetyl-2,5,5-triphenyl (IIb), 1,4-diacetyl-2,5-diphenyl (IIg), and 1,4-diacetyl-2-phenyl-5-styryl (IIh) compounds. Similar treatment of aliphatic ketone phenylhydrazones, such as acetone phenylhydrazone (Ic), methylethylketone phenylhydrazone (Id), cyclopentanone phenylhydrazone (Ie), and cyclohexanone phenylhydrazone (If), afforded resinous products, but the reaction was carried out in benzene with a catalytic amount of acetic acid, 4-acetyl-5,5-dimethyl-2-phenylpyrazolidin-3-one (IIc), 4-acetyl-5-ethyl-5-methyl-2-phenylpyrazolidin-3-one (IId), 4-acetyl-2-phenylspiro(pyrazolidin-5,1′-cyclopentane)-3-one (IIe), and 4-acetyl-2-phenylspiro(pyrazolidin-5,1′-cyclohexane)-3-one (IIf) were obtained.

It is well known that phenylhydrazine reacts with diketene to give the phenylhydrazone of acetoacetic phenylhydrazide,[3,4] which, on heating in glacial acetic acid or aqueous mineral acid, affords 2-phenyl-5-methyl-3-pyrazolone or 1-phenyl-5-methyl-3-pyrazolone in good yield.[5] While investigating some potential uses of diketene, we studied its reaction with phenylhydrazones, and have found that 4-acetyl-2-phenylpyrazolidin-3-ones (II) can be obtained by a novel reaction involving the 1,3-dipolar cycloaddition, which is the subject of this paper.

When diketene was allowed to react with acetophenone phenylhydrazone (Ia) in acetic acid, colorless prisms of mp 114—115° were obtained. Elemental analysis and the mass spectrum established its empirical formula as an adduct of Ia and diketene, $C_{18}H_{18}O_2N_2$ (IIa). Its infrared (IR) spectrum indicated the presence of the carbonyl at 1715 (shoulder) and 1695 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum of IIa in deuteriochloroform consisted of two methyl groups (1.55 ppm, 3H, singlet and 2.47 ppm, 3H, singlet), a methine proton (4.13 ppm, 1H, singlet), and an NH proton (5.37 ppm, 1H, singlet). These spectral data are consistent with the structure of the adduct as 4-acetyl-5-methyl-2,5-diphenylpyrazolidin-3-one (IIa).

Reduction of IIa with sodium borohydride afforded 4-(α-hydroxyethyl)-5-methyl-2,5-diphenylpyrazolidin-3-one (IV). In its IR spectrum the acetyl carbonyl absorption, which had been observed in the spectrum of the starting material (IIa) at 1715 cm^{-1}, disappeared and the absorption due to the hydroxy group was observed at 3546 cm^{-1}. In the NMR spectrum of IV the signal of the methyl protons at 1.32 ppm presented as a doublet (J=6 cps). These spectral data indicated that the acetyl group of IIa was reduced to the secondary alcohol (IV). Treatment of IV with 10% sodium hydroxide gave 4-ethylidene derivative (V),

1) Part XXXVII: T. Kato, H. Yamanaka, Y. Yamamoto and T. Sakamoto, *Yakugaku Zasshi*, **90**, 613 (1970).
2) Location: *Aobayama, Sendai.*
3) F. Chick and N.T.M. Wilsmore, *J. Chem. Soc.*, **93**, 946 (1908).
4) F. Chick and N.T.M. Wilsmore, *J. Chem. Soc.*, **97**, 1978 (1910).
5) H.Z. Lecher, R.P. Parker and R.C. Conn, *J. Am. Chem. Soc.*, **66**, 1959 (1944).

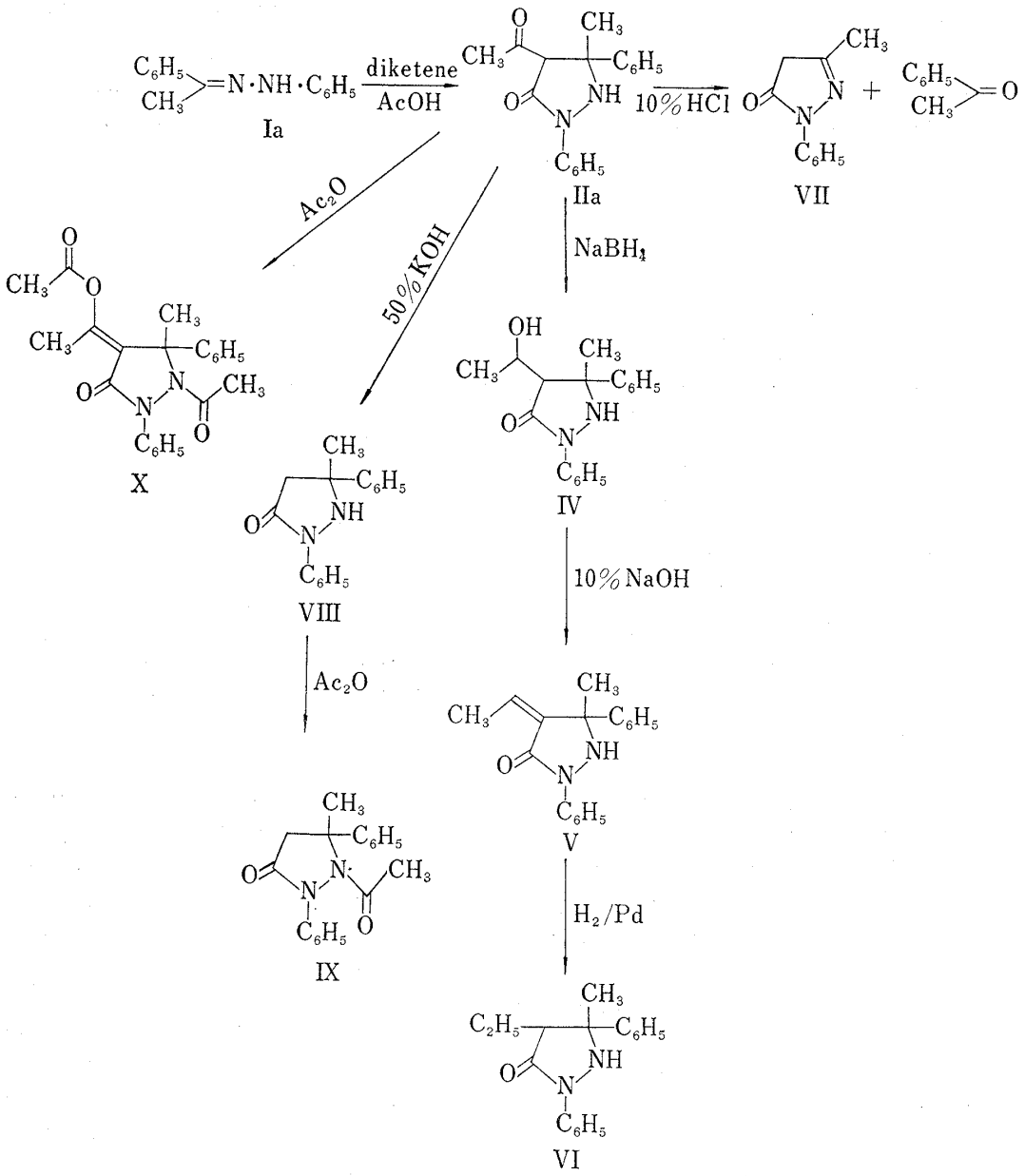


Chart 1

which was reduced to the 4-ethyl derivative (VI) upon catalytic reduction with palladium-Norit.

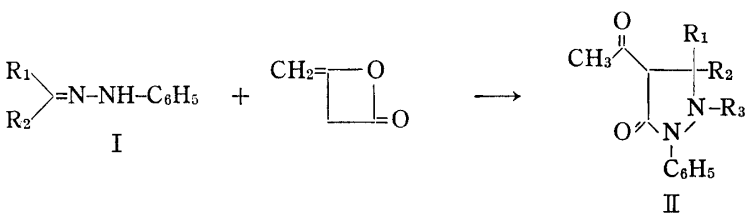
Acidic hydrolysis of IIa with 10% hydrochloric acid gave acetophenone and 2-phenyl-5-methyl-3-pyrazolone (VII). However, alkaline hydrolysis of IIa with 50% potassium hydroxide afforded the deacetylated product (VIII), which reacted with acetic anhydride to transform into 1-acetyl-5-methyl-2,5-diphenylpyrazolidin-3-one (IX). Acetylation of IIa with acetic anhydride gave the diacetyl compound (X).

Based upon these chemical behaviours the structure of 4-acetyl-5-methyl-2,5-diphenylpyrazolidin-3-one (IIa) is unequivocally given for this adduct.

Employing the same procedure given for Ia, the reaction of the phenylhydrazone of aromatic ketone such as benzophenone phenylhydrazone (Ib) with diketene in acetic acid gave 4-acetyl-2,5,5-triphenylpyrazolidin-3-one (IIb) in 40% yield.

Similar treatment of the phenylhydrazone of aliphatic ketone such as acetone phenylhydrozone (Ic) with diketene in acetic acid resulted in the formation of a resinous product,

TABLE I



No.	R_1	R_2	R_3	Solvent	Catalyst	mp (°C)	Yield (%)
IIa	C_6H_5	CH_3	H	AcOH	—	114—115	68
IIb	C_6H_5	C_6H_5	H	AcOH	—	129—130	40
IIc	CH_3	CH_3	H	benzene	AcOH (NEt_3)[a]	112—113	59 (14)
IId	CH_3CH_2	CH_3	H	benzene	AcOH (NEt_3)[a]	79—81	63 (30)
IIe	$-(CH_2)_4-$		H	benzene	AcOH	78—79	36
IIf	$-(CH_2)_5-$		H	benzene	AcOH (NEt_3)[a]	127—128	56 (45)
IIg	C_6H_5	H	CH_3CO	AcOH	—	168—170	60
IIh	$C_6H_5-CH=CH-$	H	CH_3CO	AcOH	—	149—150	48

No.	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N	IR $\nu_{max}^{CHCl_3}$ cm^{-1} CH_3CO-	$>N-CO-$	NMR ($CDCl_3$·TMS) ppm CH_3CO-	$>CH$	$>NH$
IIa	$C_{18}H_{18}O_2N_2$	73.45	6.16	9.52	73.02	5.97	9.56	1715	1695	2.47	4.13	5.35
IIb	$C_{23}H_{20}O_3N_2$	77.50	5.66	7.86	77.22	5.66	7.78	1705	1690	2.24	4.70	6.13
IIc	$C_{13}H_{16}O_2N_2$	67.22	6.94	12.06	67.15	6.77	11.85	1700	1685	2.34	3.50	4.93
IId	$C_{14}H_{18}O_2N_2$	68.27	7.37	11.37	68.11	7.04	11.31	1702	1683	2.33	3.53	4.86
IIe	$C_{15}H_{18}O_2N_2$	69.74	7.02	10.85	69.50	6.81	10.74	1700	1685	2.38	3.62	4.98
IIf	$C_{16}H_{20}O_2N_2$	70.56	7.40	10.29	70.36	7.43	10.49	1703	1685	2.34	3.52	4.87
IIg	$C_{19}H_{18}O_3N_2$	70.79	5.63	8.69	70.87	5.53	8.75	1709	1689	2.46	3.89 (d)	—
IIh	$C_{21}H_{20}O_3N_2$	72.39	5.79	8.04	72.39	5.48	7.94	1715	1685	2.42	3.67 (d)	—

a) Triethylamine was used as a catalyst in place of AcOH.
d: doublet

but when the reaction was carried out under the mild condition — *e.g.*, refluxing in benzene in the presence of a catalytic amount of acetic acid — the pyrazolidin-3-one derivatives (IIc—f) were obtained.

Table I summarizes the results of the reaction.

When the phenylhydrazone of aromatic aldehyde such as benzaldehyde phenylhydrazone (Ig) was allowed to react with diketene in benzene in the presence of triethylamine, the acetoacetate of Ig (IIIg) was obtained in good yield (84%). However, when the reaction was carried out in acetic acid, 1,4-diacetyl-2,5-diphenylpyrazolidin-3-one (IIg) was obtained in 60% yield.

It is of interest to note that the heating of IIIg in acetic acid at reflux afforded none of the cyclic product such as IIg, but gave Ig, acetone and carbon dioxide. This fact suggests that IIg is not formed *via* IIIg as an intermediate, but formed directly by 1,3-dipolar cycloaddition.

In the NMR spectrum of IIg signals of two acetyl groups and two methine protons are observed at 2.11 ppm (3H, singlet), 2.46 ppm (3H, singlet), 3.89 ppm (1H, doublet, J=0.9 cps),

and 6.03 ppm (1H, doublet, J=0.9 cps), respectively. The IR spectrum exhibits the characteristic carbonyl absorptions at 1709 and 1689 cm^{-1}.

Treatment of IIg with acetic anhydride gave the enolacetate (XI). Upon catalytic reduction of IIg with platinum dioxide in acetic acid 4-(α-acetoxyethyl)-2,5-diphenylpyrazolidin-3-one (XIV) and 4-(α-acetoxyethyl)-5-cyclohexyl-2-phenylpyrazolidin-3-one (XVII) were obtained. A similar reduction, in which tetrahydrofuran (THF) was used as a solvent in place of acetic acid, gave XIV and 1,4-diacetyl-5-cyclohexyl-2-phenylpyrazolidin-3-one (XVI).

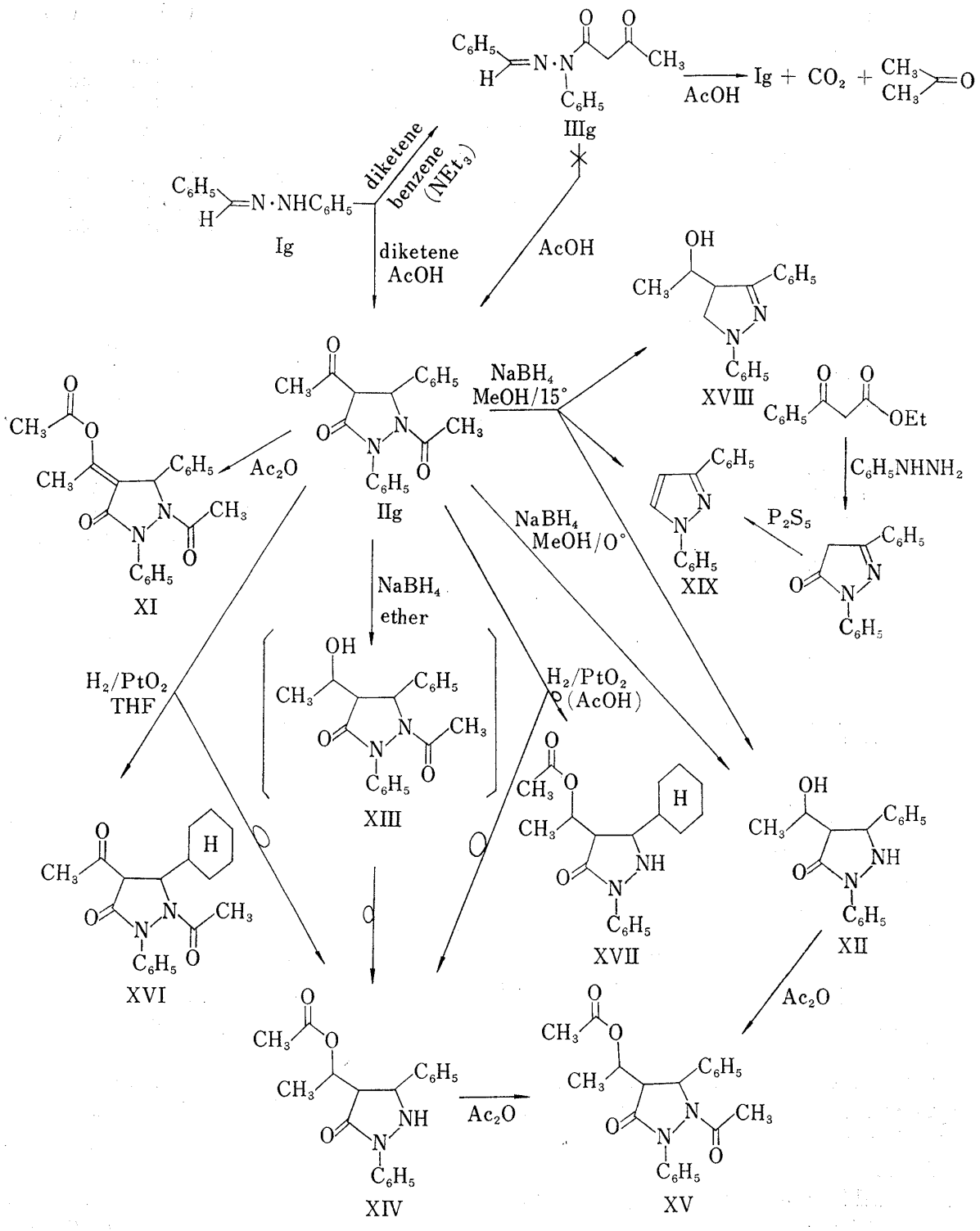
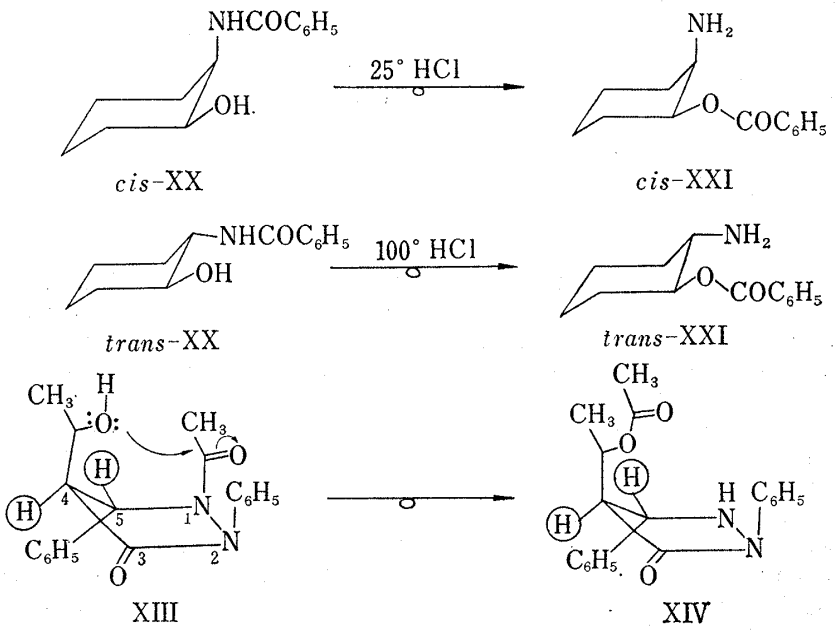


Chart 2

XIV was also obtained by the reduction of IIg with sodium borohydride in ether; *i.e.*, the reduction did not afford the N-acetyl derivative (XIII) but gave the O-acetyl product (XIV). Similar reduction in which methanol was used as a solvent instead of ether under ice-cooling gave 4-(α-hydroxyethyl)-2,5-diphenylpyrazolidin-3-one (XII) in 75% yield, however, when the reduction was carried out at room temperature IIg was reduced to 4-(α-hydroxyethyl)-1,3-diphenylpyrazoline (XVIII), 1,3-diphenylpyrazole (XIX), and XII. Because only a few references[6] are available concerning the reduction of the amide carbonyl with sodium borohydride, the reduction of IIg to give XVIII and XIX seems to be worthy of note.

As mentioned above, it is of interest to learn the intramolecular rearrangement of the acetyl group during the reduction of IIg with sodium borohydride in ether or catalytic reduction in THF.

The structural assignment of the rearranged product (XIV) was made as following; that is, in its NMR spectrum methyl protons (1.45 ppm, doublet, $J=7$ cps), ring protons at 4-position (3.36 ppm, quartet, $J=7$ and 9 cps) and 5-position (4.60 ppm, doublet, $J=9$ cps), and a methine proton of 4-hydroxyethyl group (5.37 ppm, multiplet) can be observed. The IR spectrum indicates the presence of an ester carbonyl at 1730, 1240, and 1210 cm^{-1}. In the mass spectrum the strong peak is presented at *m/e* 264 which is produced from a molecular ion (*m/e* 324) by the elimination of acetic acid. These spectral data are consistent with the O-acetate (XIV) but not with the isomeric N-acetyl structure (XIII).



XIII XIV

Chart 3

Concerning the rearrangement of the acetyl group, it is reported[7] that *cis*-2-benzamidocyclohexanol (*cis*-XX) is easily transformed into the 3-benzoyloxy isomer (*cis*-XXI) on treatment with hydrochloric acid at 25°, but the *trans* isomer (*trans*-XX) does not rearrange until the temperature rises to 100°. The reason for this was explained as following; that is, the *trans* isomer (*trans*-XX) takes more difficultly the co-planality form than the *cis* isomer (*cis*-XX) does.

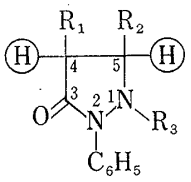
Similar mechanism will be given for the transformation of XIV; *i.e.*, though XIII was not isolated as an intermediate, the first stage of this reduction should be the formation of

6) S. Yamada, Y. Kikugawa and S. Ikegami, *Chem. Pharm. Bull.* (Tokyo), **13**, 394 (1965); Y. Kondo and B. Witkop, *J. Org. Chem.*, **33**, 206 (1968); Y. Kikugawa, S. Ikegami and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **17**, 98 (1969); Y. Kikugawa and S. Yamada, *Tetrahedron Letters*, **1969**, 699.

7) G. Fodor and J. Kiss, *Nature*, **164**, 917 (1947).

XIII, which has a sterically favourable *cis*-conformation between 1-acetyl and 4-α-hydroxyethyl group, and the next stage might well involve the six-membered cyclic rearrangement giving XIV under the same consideration as applied to the rearrangement of benzamidocyclohexanol (XX). This assumption was supported by the NMR spectral studies; that is, as shown in Table II the coupling constants found for H_4 and H_5 of the 1-acetyl devivatives (IIg, XV, XVI) show small values (0.9—1.5 cps). The smaller coupling constants can be attributed to the 1,4-*cis* configuration of 1-acetyl compound, in which the dihedral angle of H_4 and H_5 is nearly rectangular.[8]

TABLE II



No.	R_1	R_2	R_3	$J_{4,5}$ (cps)
IIg	CH_3CO	C_6H_5	CH_3CO	0.9
XII	$CH_3CH(OH)$	C_6H_5	H	10.2
XIV	$CH_3CH(OCOCH_3)$	C_6H_5	H	5.0
XV	$CH_3CH(OCOCH_3)$	C_6H_5	CH_3CO	1.3
XVI	CH_3CO	C_6H_{11}	CH_3CO	1.5
XVII	$CH_3CH(OCOCH_3)$	C_6H_{11}	H	9.0

Experimental

4-Acetyl-5-methyl-2,5-diphenylpyrazolidin-3-one (IIa)——A suspension of acetophenone phenylhydrazone (Ia) (4.2 g, 0.02 mole) and diketene (3.5 g, 0.04 mole) in 25 ml of AcOH was heated under reflux for 1 hr. The solution was condensed *in vacuo* to give a residue, which was washed with ether. Purification by recrystallization from cyclohexane–$CHCl_3$ gave colorless prisms, mp 114—115°. Yield, 4 g (68%). Mass Spectrum *m/e*: 294 (M^+), 211, 210 (base peak), 209, 118.

4-Acetyl-2,5,5-triphenylpyrazolidin-3-one (IIb)——As above, benzophenone phenylhydrazone (Ib) (5.5 g) was treated with diketene (10 g) in AcOH (20 ml) to give colorless plates (IIb), mp 129—130°. Yield, 3 g (40%).

4-Acetyl-5,5-dimethyl-2-phenylpyrazolidin-3-one (IIc)——1) To a solution of acetone phenylhydrazone (Ic) (3 g) in abs. benzene (10 ml) was added diketene (3.3 g) and a few drops of AcOH. After refluxing for 2.5 hr, the reaction mixture was condensed under reduced pressure to give a crystalline solid, which was purified by recrystallization from ether to give colorless needles of mp 111—113°. Yield, 2.7 g (59%).

2) A solution of Ic (2.2 g), diketene (2.4 g), and a small amount of NEt_3 in benzene (10 ml) was refluxed for 1.5 hr. The reaction mixture was condensed to dryness *in vacuo*, and the residue was purified by alumina chromatography using petroleum ether as a solvent to give 0.5 g (14%) of IIc, mp 112—113°, undepressed on admixture with a sample obtained in the above run.

4-Acetyl-5-ethyl-5-methyl-2-phenylpyrazolidin-3-one (IId)——1) Following the procedure given for the first run of IIc, methyl ethyl ketone phenylhydrazone (Id) (10.5 g) was treated with diketene (8.4 g) in 30 ml of benzene in the presence of AcOH (1 ml) to give colorless needles (IId), mp 79—81°. Yield, 10 g (63%). Mass Spectrum *m/e*: 246 (M^+), 217, 176 (base peak), 162, 93.

2) Following the procedure given for the second run of IIc, Id (2.5 g) was treated with diketene (10 ml) in the presence of a drop of NEt_3 to give 1.1 g (30%) of IId.

4-Acetyl-2-phenylspiro(pyrazolodin-5,1′-cyclopentane)-3-one (IIe)——As above, cyclopentanone phenylhydrazone (Ie) (1.7 g) was treated with diketene (1.7 g) in abs. benzene (8 ml) in the presence of AcOH (0.5 ml) to give colorless prisms (petroleum benzine–ether), mp 78—79°. Yield, 0.9 g (36%).

4-Acetyl-2-phenylspiro(pyrazolidin-5,1′-cyclohexane)-3-one (IIf)——As above, the reaction of cyclohexane phenylhydrazone (If) (1.9 g) with diketene (1.6 g) in benzene (10 ml) in the presence of AcOH (0.2 ml)

8) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

afforded colorless prisms (petroleum benzine–ether), mp 127—128°. Yield, 1.5 g(56%). Mass Spectrum *m/e*: 272 (M^+), 188 (base peak), 145, 93.

1,4-Diacetyl-2,5-diphenylpyrazolidin-3-one (IIg)——Following the procedure given for IIa, benzaldehyde phenylhydrazone (10.2 g) was treated with diketene (13.6 g) in AcOH (50 ml) giving colorless prisms (benzene), mp 168—170°. Yield, 10.5 g (60%). Mass Spectrum *m/e*: 322 (M^+), 280 (base peak), 237, 196, 78.

1,4-Diacetyl-2-phenyl-5-styrylpyrazolidin-3-one (IIh)——As above, cinnamic aldehyde phenylhydrazone (Ih) (2 g) was treated with diketene (2 g) in AcOH (10 ml) to give colorless prisms (cyclohexane–$CHCl_3$), mp 151—152°. Yield, 1.5 g (48%).

N-Acetoacetyl-N-phenyl-N′-benzylidenehydrazine (IIIg)——To a solution of Ig (3.8 g) in abs. benzene (20 ml) was added diketene (2 g) and a catalytic amount of Et_3N. The mixture was refluxed for 1 hr, and condensed *in vacuo* to give a crystalline substance. Recrystallization from petroleum benzine–ether gave colorless needles, mp 95°. Yield, 4.5 g (84%). *Anal.* Calcd. for $C_{17}H_{16}O_2N_2$ (IIIg): C, 72.84; H, 5.75; N, 9.99. Found: C, 73.06; H, 5.74; N, 9.92. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1718, 1669. NMR ($CDCl_3$, ppm): 2.34 (3H, singlet), 4.06 (2H, singlet), 7.0—7.7 (10H, multiplet).

N-Acetoacetyl-N-phenyl-N′-cinnamilidenehydrazine (IIIh)——As above, Ih (2.2 g) was treated with diketene (1.7 g) in benzene (15 ml) in the presence of Et_3N to give colorless prisms (petroleum benzine–ether), mp 138—139°. Yield, 2.7 g (90%). *Anal.* Calcd. for $C_{19}H_{18}O_2N_2$ (IIIh): C, 74.49; H, 5.92; N, 9.15. Found: C, 74.81; H, 6.05; N, 8.97. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1715, 1670, 1625. NMR ($CDCl_3$, ppm): 2.34 (3H, singlet), 4.00 (2H, singlet), 6.67—7.65 (13H, multiplet).

N-Acetoacetyl-N-phenyl-N′-ethylidenehydrazine (IIIi)——As above, the reaction of acetaldehyde phenylhydrazone (Ii) (2.7 g) with diketene (2.5 g) in benzene (15 ml) in the presence of AcOH (2 ml) afforded colorless plates (petroleum benzine–ether), mp 64—65°. Yield, 1.8 g (42%). *Anal.* Calcd. for $C_{12}H_{14}O_2N_2$ (IIIi): C, 66.03; H, 6.47; N, 12.84. Found: C, 66.01; H, 6.34; N, 12.89.
IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1720, 1662, 1630. NMR ($CDCl_3$, ppm): 1.86 (3H, doublet, $J=5$ cps), 2.30 (3H, singlet), 3.93 (2H, singlet), 6.61 (1H, quartet, $J=5$ cps), 7.0—7.7 (5H, multiplet).

A similar reaction in which Et_3N was used as a catalyst in place of AcOH afforded 1.5 g (34%) of IIIi.

4-(α-Hydroxyethyl)-5-methyl-2,5-diphenylpyrazolidin-3-one (IV)——To a suspension of IIa (1.5 g) in MeOH (30 ml) was added $NaBH_4$ (0.5 g) with ice-cooling. After stirring for 1 hr, the solvent was distilled off *in vacuo*. To the residue was added H_2O (20 ml), and the mixture was extracted with ether. The ether soluble fraction was dried, condensed to give a crystalline substance. Recrystallization from *n*-hexane–ether gave colorless needles (IV), mp 115—117°. Yield, 1.3 g (80%). *Anal.* Calcd. for $C_{18}H_{20}O_2N_2$ (IV): C, 72.95; H, 6.80; N, 9.45. Found: C, 72.57; H, 6.52; N, 9.56. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 3546, 3390, 1675. NMR ($CDCl_3$, ppm): 1.32 (3H, doublet, $J=6$ cps), 1.61 (3H, singlet), 2.96 (1H, doublet, $J=5$ cps), 3.40 (1H, broad), 4.35 (1H, multiplet), 4.97 (1H, broad), 7.1—8.1 (10H, multiplet).

4-Ethylidene-5-methyl-2,5-diphenylpyrazolidin-3-one (V)——A suspension of IV (1 g) in 10% NaOH (30 ml) was heated under reflux for 6 hr. After cooling, the reaction mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was dried, condensed to give a crystalline solid. Recrystallization from benzene gave colorless prisms (V), mp 135—136°. Yield, 0.8 g (85%). *Anal.* Calcd. for $C_{18}H_{18}ON_2$ (V): C, 77.67; H, 6.52; N, 10.07. Found: C, 77.76; H, 6.21; N, 10.14. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1678, 1645. NMR ($CDCl_3$, ppm): 1.63 (3H, doublet, $J=8$ cps), 1.77 (3H, singlet), 4.15 (1H, broad), 6.75 (1H, quartet, $J=8$ cps), 7.0—8.1 (10H, multiplet).

4-Ethyl-5-methyl-2,5-diphenylpyrazolidin-3-one (VI)——To a solution of V (0.6 g) in MeOH (15 ml) Pd-C (40%, 0.2 g) was added. The mixture was shaken in H_2 until 60 ml had been absorbed. The time required was about 2 hr. The catalyst was filtered off and the solvent was removed from the filtrate by evaporation under reduced pressure to give a crystalline substance. Recrystallization from petroleum ether gave colorless prisms, mp 82—84°. Yield, 0.5 g (82%). *Anal.* Calcd. for $C_{18}H_{20}ON_2$ (VI): C, 77.11; H, 7.19; N, 9.99. Found: C, 76.77; H, 6.98; N, 10.35. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 2995, 1688. NMR ($CDCl_3$, ppm): 1.10 (3H, triplet, $J=8$ cps), 1.34 (3H, singlet), 1.4—1.9 (2H, multiplet), 2.75 (1H, triplet, $J=8$ cps), 4.38 (1H, broad), 6.7—7.9 (10H, multiplet).

Hydrolysis of 4-Acetyl-5-methyl-2,5-diphenylpyrazolidin-3-one (IIa)——1) With 10% HCl: A suspension of IIa (2 g) in 10% HCl (30 ml) was heated under reflux for 2 hr. The mixture was extracted with ether. The ether fraction was condensed to give 0.7 g (82%) of acetophenone. The ether insoluble layer was neutralized with Na_2CO_3 to give a crystalline solid, which was purified by recrystallization to colorless plates (VII), mp 127—128°, undepressed on admixture with an authentic sample of 3-methyl-1-phenly-5-pyrazolone.[9] Yield, 1.1 g (92%).

2) With 50% KOH: A suspension of IIa (2 g) and 50% KOH (15 ml) was heated under reflux for 2 hr. The reaction mixture was acidified with 10% HCl, and extracted with $CHCl_3$. The $CHCl_3$ layer was dried, condensed to give a viscous oil, which was dissolved in petroleum benzine and stored in a refregirator for a week to give a crystalline solid. Recrystallization from ether–petroleum ether gave colorless prisms,

9) L. Knorr, *Ann.*, **238**, 147 (1887).

mp 66—68°. Yield, 1.4 g (82%). *Anal.* Calcd. for $C_{16}H_{16}ON_2$ (VIII): C, 76.16; H, 6.39; N, 11.10. Found: C, 76.07; H, 6.24; N, 11.27. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 3400, 1685. NMR ($CDCl_3$, ppm): 1.15 (3H, singlet), 2.62—3.24 (2H, quartet), 4.14 (1H, broad) 7.0—8.0 (10H, multiplet).

1-Acetyl-5-methyl-2,5-diphenylpyrazolidin-3-one (IX)——A solution of VIII (0.2 g) in Ac_2O (5 ml) was heated at reflux for 10 hr. The mixture was condensed *in vacuo* giving a crystalline solid. Recrystallization from ether–petroleum benzine gave colorless plates, mp 105—106°. Yield, 0.2 g (86%). *Anal.* Calcd. for $C_{18}H_{18}O_2N_2$ (IX): C, 73.45; H, 6.16; N, 9.52. Found: C, 73.38; H, 6.46; N, 9.51. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 2995, 1720, 1660. NMR ($CDCl_3$, ppm): 1.80 (3H, singlet), 2.06 (3H, singlet), 2.86—3.53 (2H, quartet), 7.0—7.7 (10H, multiplet).

1-Acetyl-4-(α-acetoxyethylidene)-5-methyl-2,5-diphenylpyrazolidin-3-one (X)——As above, IIa (1 g) was treated with Ac_2O (15 ml) to give colorless prisms (petroleum benzine–ether), mp 160—162°. Yield, 0.7 g (61%). *Anal.* Calcd. for $C_{22}H_{22}O_4N_2$ (X): C, 69.82; H, 5.86; N, 7.40. Found: C, 70.08; H, 5.98; N, 7.47. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1769, 1710, 1668, 1173. NMR ($CDCl_3$, ppm): 1.15 (3H, singlet), 1.76 (3H, singlet), 2.20 (3H, singlet), 2.50 (3H, singlet), 7.1—7.7 (10H, multiplet).

1-Acetyl-4-(α-acetoxyethylidene)-2,5-diphenylpyrazolidin-3-one (XI)——A solution of IIg (1 g) in Ac_2O (10 ml) was refluxed for 36 hr. The reaction mixture was condensed *in vacuo*, and a crystalline residue was purified by recrystallization from petroleum benzine–$CHCl_3$ to colorless needles, mp 135—136°. Yield, 1 g (90%). *Anal.* Calcd. for $C_{21}H_{20}O_4N_2$ (XI): C, 69.21; H, 5.53; N, 7.69. Found: C, 69.13; H, 5.47; N, 7.67. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1765, 1720, 1680, 1175. NMR ($CDCl_3$, ppm): 1.96 (3H, singlet), 1.99 (3H, singlet), 2.55 (3H, doublet, J=1.3 cps), 6.39 (1H, doublet, J=1.3 cps), 7.1—7.5 (10H, multiplet).

Catalytic Reduction of IIg——1) In AcOH: A suspension of IIg (1 g) and PtO_2 (0.1 g) in AcOH (20 ml) was shaken in H_2 for 48 hr. After the absorption of H_2 was completed, the catalyst was filtered off. The filtrate was evaporated *in vacuo*. The residue was purified by column chromatography on alumina and then on silica gel (elution with petroleum ether and ether) to afford 0.2 g (20%) of XVII and 0.3 g (30%) of XIV. The former, on recrystallization from *n*-hexane, gave colorless needles of mp 110—112°. XVII and the second product was recrystallized from ether to give colorless prisms, mp 132—133° (XIV). *Anal.* Calcd. for $C_{19}H_{20}O_3N_2$ (XIV): C, 70.35; H, 6.22; N, 8.64. Found: C, 70.06; H, 6.13; N, 8.81. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1730, 1695. NMR ($CDCl_3$, ppm): 1.45 (3H, doublet, J=7 cps), 1.78 (3H, singlet), 3.36 (1H, quartet, J=7 cps, J=9 cps), 4.00 (1H, broad), 4.60 (1H, doublet, J=9 cps), 5.37 (1H, multiplet), 7.1—8.1 (10H, multiplet). Mass Spectrum *m/e*: 324 (M^+), 264, 195 (base peak), 146, 131, 77. *Anal.* Calcd. for $C_{19}H_{26}O_3N_2$ (XVII): C, 69.09; H, 7.93; N, 8.48. Found: C, 69.34; H, 7.99; N, 8.85. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1730, 1688. NMR ($CDCl_3$, ppm): 0.6—2.0 (11H, multiplet), 1.32 (3H, doublet, J=6 cps), 1.91 (3H, singlet), 2.50 (1H, triplet, J=4 cps), 3.00 (1H, multiplet), 4.65 (1H, broad), 5.10 (1H, multiplet), 6.9—7.9 (5H, multiplet).

2) In THF: Similar reduction of IIg (2 g) with PtO_2 (0.1 g) as above, in which THF (50 ml) was used in place of AcOH, gave 0.5 g (25%) of XIV, and 0.2 g (10%) of XVI, colorless prisms (petroleum benzine) of mp 129—130°. *Anal.* Calcd. for $C_{19}H_{24}O_3N_2$ (XVI): C, 69.49; H, 7.39; N, 8.53. Found: C, 69.61; H, 7.08; N, 8.49. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1703. NMR ($CDCl_3$, ppm): 0.9—2.1 (11H, multiplet), 2.10 (3H, singlet), 2.43 (3H, singlet), 3.66 (1H, doublet, J=1.5 cps), 4.68 (1H, quartet, J=1.5 cps, J=6 cps), 7.0—7.7 (5H, multiplet).

Reduction of IIg with $NaBH_4$——1) In MeOH: To a solution of IIg (1.6 g) in abs. MeOH (30 ml) was added $NaBH_4$ (0.5 g) with ice-cooling. After being allowed to stand at room temperature overnight, the reaction mixture was condensed. The residue was extracted with ether. The organic layer was dried, condensed, and the residue was purified by chromatography on alumina using petroleum ether and ether as eluent. The petroleum ether eluted fraction was evaporated to give 0.1 g (9%) of XIX, colorless prisms of mp 84—85°, undepressed on admixture with an authentic sample of 1,3-diphenylpyrazole.[10] The petroleum ether–ether (2:1) eluted fraction gave 0.3 g of XVIII as pale green needles, mp 90—91°. The third fraction obtained from the ether elution gave 0.15 g (11%) of XII as colorless plates, mp 82—84°. *Anal.* Calcd. for $C_{17}H_{18}O_2N_2$ (XII): C, 72.32; H, 6.43; N, 9.92. Found: C, 71.93; H, 6.21; N, 10.01. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 3470, 1675. NMR ($CDCl_3$, ppm): 1.05 (3H, doublet, J=6 cps), 3.82 (1H, quartet, J=10.2 cps, J=7.8 cps), 4.08 (1H, multiplet), 4.40 (1H, doublet, J=10.2 cps), 4.50 (1H, broad), 7.0—8.0 (10H, multiplet). Mass Spectrum *m/e*: 282 (M^+), 264, 238, 196, 195 (base peak), 161. *Anal.* Calcd. for $C_{17}H_{18}ON_2$ (XVIII): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.47; H, 6.88; N, 10.62. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 3600, 1600. NMR ($CDCl_3$, ppm): 1.21 (3H, doublet, J=7 cps), 1.49 (1H, singlet), 3.6—4.5 (4H, multiplet), 6.7—7.9 (10H, multiplet).

The same reaction in which reaction time was shortened to 0.5 hr gave 1.2 g (85%) of XII.

2) In Ether: The mixture of IIg (1.6 g), $NaBH_4$ (0.5 g) and abs. ether (30 ml) was allowed to stand at room temperature for 3 days with stirring. The reaction mixture was condensed, and 10% AcOH (30 ml) was added. The mixture was extracted with $CHCl_3$. From the $CHCl_3$ extract 1.2 g (75%) of XIV and a small amount of XII were obtained.

4-(α-Acetoxyethyl)-1-acetyl-2,5-diphenylpyrazolidin-3-one (XV)——A solution of XIV (0.15 g) in Ac_2O (5 ml) was heated at reflux for 1 hr. Removal of Ac_2O *in vacuo* gave a crystalline solid. Recrystallization from petroleum benzine–$CHCl_3$ gave XV as colorless needles, mp 192—193°. Ylied, 0.12 g (70%). The

similar treatment of XII (0.2 g) with Ac_2O gave XV in 50% yield (0.15 g). *Anal.* Calcd. for $C_{21}H_{22}O_4N_2$ (XV): C, 68.83; H, 6.05; N, 7.65. Found: C, 69.09; H, 6.10; N, 7.53. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1735, 1730 (shoulder), 1690. NMR ($CDCl_3$, ppm): 1.48 (3H, doublet, $J=7$ cps), 1.94 (3H, singlet), 2.06 (3H, singlet), 2.97 (1H, quartet), 5.37 (1H, multiplet), 5.67 (1H, doublet, $J=1.3$ cps), 7.1—7.5 (10H, multiplet). Mass Spectrum *m/e*: 366 (M^+), 324 (base peak), 264, 249, 196, 195.

Reaction of IIIg with AcOH——A solution of IIIg (1.4 g) in AcOH (10 ml) was refluxed for 1 hr, during which time CO_2 was detected by passing the gas evolved into a $Ba(OH)_2$ solution. The mixture was heated gently in a water bath and the distillate was collected, to which 2,4-dinitrophenylhydrazine was added yielding yellow crystals of mp 128°, undepressed on admixture with an authentic sample of acetone 2,4-dinitrophenylhydrazone. The heating was continued under reduced pressure and AcOH was distilled off. The resulting residue was purified by passing it through an alumina column using petroleum ether as a solvent to give 0.6 g (61%) of Ig as colorless needles, mp 155—156° (EtOH).

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10) L. Knorr and P. Duden, *Ber.*, **26**, 115 (1893).