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Studies on Acetylenic Compounds. LVI.[1,2] Syntheses of 4-Isoxazolin-3-ones and 1-Phenyl-3-hydroxypyrazoles

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The reactions of α-acetylenic esters with N-substituted hydroxylamines in the presence of strong bases afforded 2-substituted 4-isoxazolin-3-ones, which were also prepared from α-acetylenic acid chlorides and N-substituted hydroxylamines. 1-Phenyl-3-hydroxypyrazoles were obtained by the reaction of α-acetylenic esters with phenylhydrazine in the presence of alkoxides.

In the reactions of α-acetylenic esters or nitriles with bifunctional nucleophiles such as hydroxylamine[4] or phenylhydrazine,[5] the amino group of the nucleophile usually adds to the triple bond and then cyclization occurs to yield 2-isoxazolin-5-ones, 5-aminoisoxazoles, 1-phenylpyrazolin-5-ones or 1-phenyl-5-iminopyrazoles, respectively.

We have found that in the presence of excess alkali the amino group of hydroxylamine attacks the ester or nitrile group of α-acetylenic esters or nitriles in preference to the triple bond, to yield 3-hydroxy or 3-aminoisoxazoles.[6] In this paper we will describe that the reactions of N-substituted hydroxylamines and phenylhydrazine with α-acetylenic esters proceed in a similar manner to afford 4-isoxazolin-3-ones or 1-phenyl-3-hydroxypyrazoles under strongly basic conditions.

De Sarlo, *et al.* have shown that the reaction of methylhydroxylamine with ethyl phenylpropiolate (I) or methyl tetrolate (II) in pyridine gave 2-methyl-3-phenyl (III) or 2,3-dimethyl-3-isoxazolin-5-one (IV), respectively.[7] In the presence of one molar equivalent excess aqueous alcoholic sodium hydroxide, however, methylhydroxylamine reacted with I in a different manner to yield 2-methyl-5-phenyl-4-isoxazoline-3-on (V) of mp 114—115°, in 83% yield, which was identical with an authentic sample.[8] By the similar reaction of methylhydroxylamine and II, hygroscopic 2,5-dimethyl-4-isoxazolin-3-one (VI) of mp 37° and bp 71—74° (2 mmHg) was also obtained. The structure of VI was evidenced by its infrared (IR) spectrum (film) showing a lactam band at 1678 cm^{-1}, which excluded a 3-isoxazolin-5-one structure ($\nu_{c=o}$ 1730—1740 cm^{-1}).[7]

Reaction of I with phenyl hydroxylamine or cyclohexylhydroxylamine in the presence of aqueous alcoholic sodium hydroxide did not afford the expected 4-isoxazolin-3-ones, but the hydrolysis product of I, phenylpropiolic acid. However, non-aqueous reaction of I with phenylhydroxylamine in hot ethanol containing three molar equivalents of sodium ethoxide gave 2,5-diphenyl-4-isoxazolin-3-one (VII) of mp 86—87° (37%), which was identical with the sample prepared from N-phenyl-3,3-ethylenedioxy-3-phenylpropionhydroxamic

1) Part LV: M. Yoshimoto and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **19**, 46 (1971).
2) This work was presented at the 89th Annual Meeting of the Pharmaceutical Society of Japan in Nagoya, on 4th, April, 1969.
3) Location: *1-2-58, Hiromachi, Shinagawa-ku, Tokyo.*
4) References cited in ref. 6.
5) *a*) C. Moureu and I. Lazennec, *Compt. Rend.*, **142**, 1534 (1906); *b*) *Idem*, *Bull. Soc. Chim. France*, **35**, 843 (1906); *c*) *Idem*, *Compt. Rend.*, **143**, 1239 (1906).
6) I. Iwai and N. Nakamura, *Chem. Pharm. Bull.* (Tokyo), **14**, 1277 (1966).
7) F. De Sarlo, L. Fabbrini and G. Renzi, *Tetrahedron*, **22**, 2989 (1966).
8) S. Cabiddu, G. Gaudiano and A. Quilico, *Gazz. Chim. Ital.*, **92**, 501 (1962).

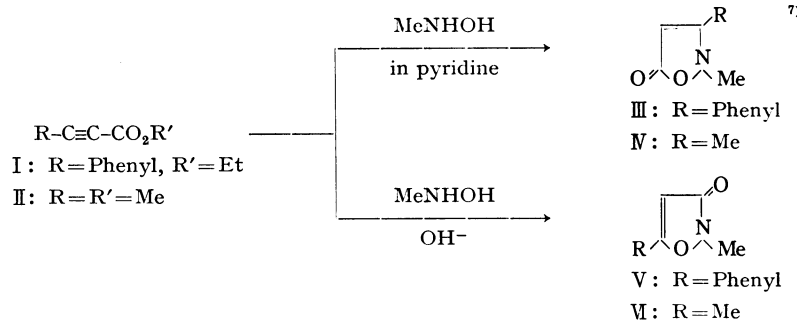


Chart 1

acid.[9] The reaction of cyclohexylhydroxylamine with I in *t*-butanol containing potassium *t*-butoxide (one molar equivalent) afforded two isomeric products, 2-cyclohexyl-5-phenyl-4-isoxazolin-3-one (VIII) of mp 75—76° (19%) and 2-cyclohexyl-3-phenyl-3-isoxazolin-5-one (IX) of mp 104—105° (17%). The structures of VIII and IX were assigned based on the IR spectra: a lactam band of VIII at 1664 and a lactone band of IX at 1745 cm^{-1}, respectively. The NMR spectra of VII and IX in deuteriochloroform also confirmed the structures: VIII showed an aromatic multiplet (5H) at 7.2—7.8, a singlet due to C_4-H of the isoxazoline ring (1H) at 5.98, a multiplet (1H, the methine proton adjacent to nitrogen) at 4.30 and broad signals due to cyclohexane protons at 2.1—0.8 ppm (10H); and IX showed an aromatic singlet (5H) at 7.52, a singlet due to C_4-H at 5.31, a multiplet at 3.55 (1H, methine proton adjacent to nitrogen) and broad signals due to cyclohexane ring (10H) at 2.0—0.8 ppm. On the other hand, heating the alcoholic solution of I and cyclohexylhydroxylamine in the absence of base gave an oily mixture of IX and 2-cyclohexyl-3-phenyl-3-ethoxyisoxazolidin-5-one (X) (4:11). The constitution of this mixture was inferred from its nuclear magnetic

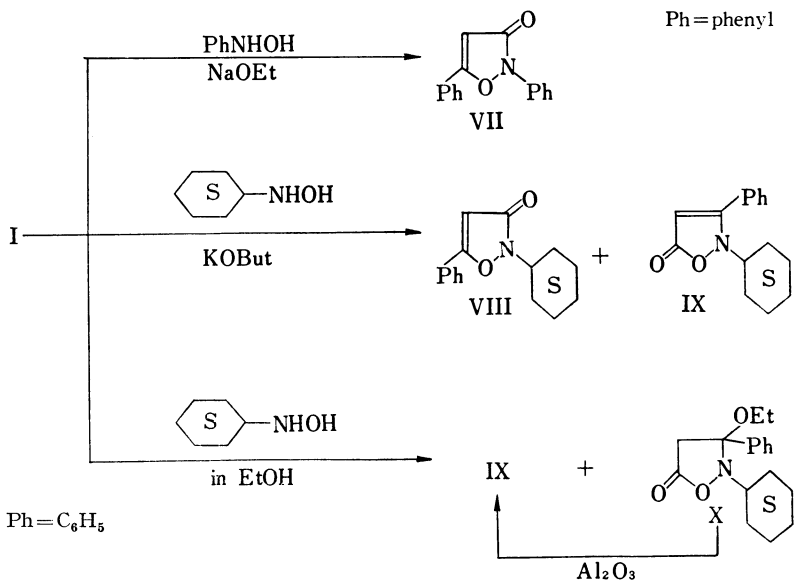


Chart 2

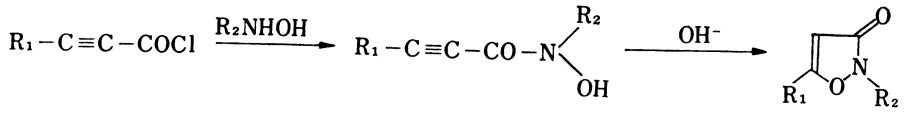
9) *a*) M. Mutter, C. Vogel and R. Bosshard, Japan Patent 40-6461 (1965); *b*) T. Yokobe, *Yakugaku Zasshi*, **89**, 1245 (1969).

resonance (NMR) spectrum in carbon tetrachloride, showing an aromatic singlet at 7.38 (5H), a singlet at 3.53 (2H, C_4-methylene protons of X), ethoxy signals at 4.11 (2H, q, J=7 Hz) and 1.24 ppm (3H, t, J=7 Hz), in addition to the above-mentioned signals due to IX. The cyclohexyl signals overlapped. The ratio of IX and X was measured by the integration of the two phenyl signals. On alumina chromatography, this mixture afforded pure IX in 84% yield. The reaction of II with cyclohexylhydroxylamine in the presence of potassium *t*-butoxide gave 2-cyclohexyl-5-methyl-4-isoxazolin-3-one (XI) of bp 84—86° (10^{-4} mmHg) in 17% yield.

Thus, 4-isoxazolin-3-ones can be prepared by the reaction of α-acetylenic esters with N-substituted hydroxylamines in the presence of strong bases. Since the yields were rather low, and in some cases (*e.g.*, the reaction of II with phenylhydroxylamine) this method was unsuccessful, the following reaction were carried out for the practical purpose.

Reaction of phenylpropiolyl chloride with phenylhydroxylamine (two equivalnts) in ether at 0° afforded quantitatively N,3-diphenylpropiolohydroxamic acid (XII), whose IR spectrum showed an acetylenic band at 2200 cm^{-1}. On treatment with 10% aqueous potassium hydroxide solution XII cyclized to give VII in 90% yield. This procedure was generally applicable and 4-isoxazolin-3-ones shown in Table I were obtained from various α-acetylenic acid chlorides in good yields. This method is an useful new route to N-aryl-4-isoxazolin-3-ones which have been prepared from β-ethylenedioxy acyl chlorides and N-arylhydroxylamines.[9]

Table I. 4-Isoxazolin-3-ones



R_1	R_2	Hydroxamic acid	4-Isoxazolin-3-one	Yield (%)
C_6H_5	C_6H_5	XII mp 68—71°	VII mp 86— 87°	90
Bu	C_6H_5	not purified	XIII bp 140—145° (0.0001 mmHg)	61
	C_6H_5	XIV mp 82—83.5°	XV mp 73— 75°	59
Me	C_6H_5	not purified	XVI mp 38— 39°	22[a]
C_6H_5		not purified	VIII mp 75— 76°	71

a) based on potassium tetrolate (See Experimental)

As for the reaction of I with phenylhydrazine in ethanol, it has been reported that 1,3-diphenylpyrazolin-5-one (XVII) of mp 137° is formed by addition of phenylhydrzaine to the triple bond followed by cyclization.[5a] Recently, Al-Jallo has shown[10] that the above reaction occurs at the refluxing temperature but at room temperature phenylhydrazine attacks the ester group to form phenylpropiolic acid hydrazide (XVIII), which, on heating over its melting point, cyclizes to 1,5-diphenyl-3-hydroxypyrazole (XIX) of mp 253°.[11]

We realized that the presence of a strong base also change the attacking site of phenylhydrazine, as in the case of hydroxylamines. When a mixture of I, phenylhydrazine and ethanol containing two molar equivalnt sodium ethoxide was refluxed, XIX of mp 252—253° was obtained in 42% yield. The yield was 79% when the reaction was carried out in

10) H.N. Al-Jallo, *Tetrahedron Letters*, **1970**, 875.
11) The reaction of the free propiolic acid with phenylhydrazine also gives XIX: F.G. Baddar, M.F. el-Newailhy and M.R. Salem, *J. Chem. Soc.* (*C*), **1969**, 836.

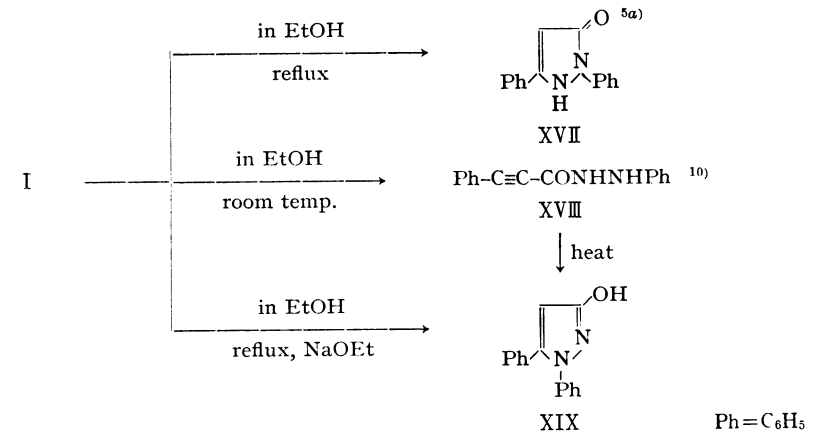


Chart 3

t-butanol using *t*-butoxide as the base. Similar reactions of methyl tetrolate (II) or ethyl propiolate with phenylhydrazine gave 1-phenyl-5-methyl-3-hydroxypyrazole (XX) of mp 165—165.5°[12] (55%) or 1-phenyl-3-hydroxypyrazole (XXI) of mp 153–155°[12] (73%), respectively. These 3-hydroxypyrazoles are known compounds and easily discriminated from 1-phenylpyrazolin-5-ones by comparison of the IR and NMR spectra.[13] These results show that phenylhydrazino anion ($C_6H_5NH\bar{N}H$) attacks the ester group in preference to the triple bond. There remains, however, the possibility that, under the basic conditions described, the alkoxide may add to the triple bond of the propiolic esters and the known reaction[5a] of the resulting alkoxyacrylic esters may afford 1-phenyl-3-hydroxypyrazoles.

Experimental[14]

2-Methyl-5-phenyl-4-isoxazolin-3-one (V)——To a mixture of methylhydroxylamine hydrochloride (4.01 g, 48 mmoles), sodium hydroxide (3.84 g, 96 mmoles), water (20 ml) and methanol (40 ml) was added dropwise a solution of ethyl phenylpropiolate (6.96 g, 40 mmoles) in methanol (20 ml) at 34—38° during the period of 15 min. The reaction mixture was allowed to stand for a night at room temperature (24—26°) and methanol was evaporated under reduced pressure. The residue was extracted twice with chloroform. The combined extracts were washed twice with water, dried over sodium sulfate, and the solvent evaporated, leaving white crystalline V (5.80 g, 83%). Recrystallization from benzene gave white needles of mp 114—115°.[8] *Anal.* Calcd. for $C_{10}H_9O_2N$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.81; H, 5.21; N. 7.96.

2,5-Dimethyl-4-isoxazolin-3-one (VI)——The similar reaction of methyl tetrolate as described above gave hygroscopic VI of mp 37° and bp 71—74° (2 mmHg) in 33.5% yield. IR ν_{max}^{liq} cm^{-1}: 1678 (C=O), 1631 (C=C). UV λ_{max}^{EtOH} mμ (ε): 231 (6130). NMR δ ppm (CCl_4): 5.42 (1H, q, J=0.8 Hz, C_4-H), 3.37 (3H, s, N-CH_3), 2.23 (3H, d, J=0.8 Hz, C_5-CH_3). *Anal.* Calcd. for $C_5H_7O_2N$: C, 53.09; H, 6.24; N, 12.38. Found: C, 53.20; H, 6.35; N, 12.52.

General Procedure for the Preparation of 4-Isoxazolin-3-ones——Method A): To a mixture of a N-substituted hydroxylamine (10 mmoles) and a solution of alkali metal alkoxide prepared from sodium or potassium (10—30 mmoles) and ethanol or *t*-butanol (10—15 ml) was added dropwise a solution of a propiolic ester (10 mmoles) in ethanol or *t*-butanol (5 ml) during 15 min. After refluxed for 2 hr, the reaction mixture was neutralized with acetic acid (equivalent to the amount of alkali metal employed), poured into 200 ml of water, and extracted three times with ether. The combined extracts were washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The residue was chromatographed on almuina or silica gel to give 4-isoxazolin-3-one.

12) R.H. Wiley and P. Wiley, "Heterocyclic Compounds, Vol. 20, Pyrazolones, Pyrazolidones and Derivatives," Interscience Publishers, New York, 1964, p. 246.
13) A.R. Katritzky and F.W. Maine, *Tetrahedron*, **20**, 299, 315 (1964).
14) All melting points were uncorrected. NMR spectra were taken by Varian A-60D Spectrometer, using tetramethylsilane as the internal standard.

Method B): To a solution or a suspension of a N-substituted hydroxylamine (10 mmoles) in ether (10 ml) was added dropwise a solution of a propiolyl chloride (5 mmoles) in ether (5 ml) during 30 min at 5—6° under ice-cooling. After stirred for 30 min at 5° and 2.5 hr at room temperature, the mixture was filtered. The ethereal solution was washed with 10% hydrochloric acid, water, dried over sodium sulfate and concentrated *in vacuo*, leaving a crude propiolohydroxamic acid. To a solution of the crude hydroxamic acid in methanol (5 ml) was added dropwise 10% aqueous sodium hydroxide solution (4 ml) during 15 min at 15—20°. After stirred for 2 hr at 22°, the mixture was poured into 50 ml of water. The precipitate was collected by filtration, washed with water, dried and recrystallized to give pure 4-isoxazolin-3-one.

2,5-Diphenyl-4-isoxazolin-3-one (VII)——A) The crude product (1.454 g) obtained from phenylhydroxylamine (1.09 g, 10 mmoles), sodium (0.69 g, 30 mmoles), ethyl phenylpropiolate (1.74 g, 10 mmoles) and ethanol (20 ml) was chromatographed on alumina (Woelm, grade II, 30 g). The first fraction eluted with hexane (300 ml) recovered unreacted phenylhydroxylamine (0.504 g). The following fraction eluted with benzene (600 ml) was collected and evaporated *in vacuo* to afford 0.866 g (36.5%) of VII, which was recrystallized from hexane to white needles of mp 86—87°.[9] IR ν_{max}^{Nujol} cm^{-1}: 1678 (C=O), 1634 (C=C). UV λ_{max}^{EtOH} $m\mu$ (ε): 274 (22200). NMR δ ppm (CCl_4): 7.9—7.0 (10H, aromatic m), 6.03 (1H, s, C_4-H). *Anal.* Calcd. for $C_{15}H_{11}O_2N$: C, 75.93; H, 4.67; N, 5.91. Found: C, 75.81; H, 4.72; N, 5.80.

B) Crude N,3-diphenylpropiolohydroxamic acid (XII) (1.18 g, 99%) was obtained from the reaction of phenylhydroxyl amine (1.09 g, 10mmoles) with phenylpropiolyl chloride (0.83 g, 5 mmoles). Recrystallization from petroleum ether–ether gave white prisms of pure XII, mp 58—61°. IR ν_{max}^{Nujol} cm^{-1}: 3150 (OH), 2200 (C≡C), 1610 (C=O). *Anal.* Calcd. for $C_{15}H_{11}O_2N$: C, 75.93; H, 4.67; N, 5.91. Found: C, 75.77; H, 4.61; N, 6.00. Crude XII (1.008 g, 4.21 mmoles) was converted to VII (0.905 g, 90%) as described in the general procedure.

2-Cyclohexyl-3-phenyl-3-isoxazolin-5-one (IX)——A mixture of cyclohexylhydroxylamine (2.30 g, 20 mmoles), ethyl phenylpropiolate (3.48 g, 20 mmoles) and ethanol (20 ml) was heated under reflux for 8 hr. After the solvent was evaporated *in vacuo*, the oily residue was dissolved in benzene–hexane (1:2) and chromatographed on alumina (Woelm, grade II, 110 g). The column was eluted successively with benzene–hexane (1:2, 200 ml; 1:1, 200 ml; 2:1, 300 ml) and chloroform (200 ml). The eluate was fractionated by every 100ml. Fractions NO. 4—23 were combined and evaporated to dryness, leaving crystalline IX (4.09 g, 84%). Recrystallization from hexane gave white plates of mp 104—105°. IR ν_{max}^{Nujol} cm^{-1}: 1745 (C=O). NMR δ ppm (CCl_4): 7.52 (5H, s, C_6H_5-), 5.31 (1H, s, C_4-H), 3.55 (1H, center, broad m, N–CH–), 0.8—0.2 (10 H, broad m, cyclohexyl protons). *Anal.* Calcd. for $C_{15}H_{17}O_2N$: C, 74.04; H, 7.05; N, 5.76. Found: C, 73.88; H, 7.15; N, 5.86.

2-Cyclohexyl-5-phenyl-4-isoxazolin-3-one (VIII)——A) The crude product obtained from cyclohexylhydroxylamine (3.45 g, 30 mmoles), potassium (1.17 g, 30 mmoles), ethyl phenylpropiolate (5.22 g, 30 mmoles) and *t*-butanol (45 ml) was dissolved in benzene–hexane (2:1) and introduced into a column containing alunmnia (Woelm, grade II, 250 g). Elution was with hexane (1400 ml), hexane–benzene (2:1, 300 ml; 1:1, 400 ml; 1:2, 300 ml), benzene (800 ml) and benzene–chloroform (2:1, 300 ml). The eluate was fractionated by 100 ml. Fractions NO. 5—7 afforded IX (0.826 g, 17%) of mp 104—105°. Fractions NO. 27—42 were combined and evaporated to dryness, leaving crude oily VIII (0.953 g, 19%), which crystallized on scratching. Rercystallization from hexane gave while prisms of mp 75—76°. IR ν_{max}^{Nujol} cm^{-1}: 1664 (C=O), 1626 (C=C). NMR δ ppm (CCl_4): 7.9—7.3 (5H, aromatic m), 6.00 (1H, s, C_4-H), 4.20 (1H, broad m, center, N-CH-), 2.4—1.0 (10H, broad m, cyclohexyl protons). *Anal.* Calcd. for $C_{15}H_{17}O_2N$: C, 74.04; H, 7.05; N, 5.76. Found: C, 73.83; H, 7.04; N, 5.82.

B) From cyclohexylhydroxylamine (1.51 g, 13.1 mmoles) and phenylpropiolyl chloride (1.08 g, 6.6 mmoles), IX of mp 75—76° (0.72 g, 45%) was obtained as described in the general procedure,

2-Cyclohexyl-5-methyl-4-isoxazolin-3-one (XI)——A) The crude product (6.7 g) obtained from cyclohexylhydroxylamine (6.88 g, 60 mmoles), potassium (2.34 g, 60 mmoles), methyl tetrolate (5.88 g, 60 mmoles) and *t*-butanol (90 ml) was chromatographed on silica gel (Kanto Kagaku, 900 g). Elution with benzene–chloroform (1:1) afforded XI of bp 84—85° (10^{-4} mmHg). Yield, 1.82 g (17%). IR $\nu_{max}^{liq.}$ cm^{-1}: 1678 (C=O), 1634 (C=C). UV λ_{max}^{EtOH} $m\mu$ (ε): 232 (11800). NMR δ ppm ($CDCl_3$): 5.50 (1H, q, J=1 Hz, C_4-H), 4.22 (1H, broad m, center, N-CH-), 2.24 (3H, d, J=1 Hz, -CH_3), 2.2—1.0 (10H, broad m, cyclohexyl protons). *Anal.* Calcd. for $C_{10}H_{15}O_2N$: C, 66.27; H, 8.34; N, 7.73. Found: C, 65.87; H, 8.40; N, 7.49.

2-Phenyl-5-buthyl-4-isoxazolin-3-one (XIII)——B) Crude N-phenylbutylpropiolohydroxamic acid (12.7 g, 93.8%) was obtained from phenylhydroxylamine (14.84 g, 13.6 mmoles) and 2-heptynoyl chloride (9.0 g, 6.8 mmoles). This hydroxamic acid (6.00 g) was treated with 10% aqueous sodium hydroxide solution as described in the general procedure. The crude product (5.00 g) was chromatographed on silica gel (Kanto Kagaku, 250 g). Elution with benzene gave XIII (3.64 g, 60.7%) as a yellow oil. Vacuum distillation (10^{-4} mmHg) caused degradation. IR $\nu_{max}^{liq.}$ cm^{-1}: 1685 (C=O), 1630 (C=C). UV λ_{max}^{EtOH} $m\mu$ (ε): 229 (11310), 265 (10340). NMR δ ppm ($CDCl_3$): 7.85—7.00 (5H, aromatic m), 5.54 (1H, t, J=0.8Hz, C_4-H), 2.8—2.4 (2H, m, C=C-CH_2-), 2.0—0.7 (7H, m, -$CH_2CH_2CH_3$). *Anal.* Calcd. for $C_{13}H_{15}O_2N$: C, 71.86; H, 6.95; N, 6.45. Found: C, 71.71; H, 7.18; N, 6.40.

Cyclohexylpropiolic Acid——To a solution of cyclohexanecarboxylic acid chloride (5.4 g, 3.6 mmoles) in benzene (60 ml) was added a solution of carboethoxymethylenetriphenylphosphorane (25.6 g, 7.2 mmoles)

in benzene (240 ml) at room temperature. After stirred for 4 hr, the reaction mixture was filtered and the benzene solution concentrated *in vacuo*. The residue was heated on an oil bath at 250° under reduced pressure (0.01 mmHg), and the pyrolyzed product was distilled through a side tube. The distillate was dissolved in petroleum ether, filtered and the solvent evaporated. Distillation of the residue gave ethyl cyclohexylpropiolate (3.57 g, 54%) of bp 115—120° (10^{-4} mmHg). IR ν_{max}^{liq} cm^{-1}: 2200 (C≡C), 1715, 1250 (CO_2Et). A solution of ethyl cyclohexylpropiolate (3.0 g, 17 mmoles) in ethanol (10 ml) was mixed with 10% aqueous sodium hydroxide solution (15 ml). After refluxed for 2 hr, the mixture was diluted with water and extracted with ether. The extract was dried over sodium sulfate, filtered and the solvent evaporated. Distillation of the residue gave cyclohexylpropiolic acid (1.95 g, 77%) of bp 135—140° (10^{-4} mmHg, bath temp.). IR ν_{max}^{liq} cm^{-1}: 2230 (C≡C), 1675 (C=O). *Anal.* Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.25; H, 8.10.

2-Phenyl-5-cyclohexyl-4-isoxazolin-3-one (XV)——B) Cyclohexylpropiolic acid chloride (5.45 g, 47.7 %) of bp 75—90° (1 mmHg) was prepared by heating the mixture of cyclohexylpropiolic acid (10 g, 6.5 mmoles), thionyl chloride (10 g, 8.5 mmoles) and benzene (15 ml) for 2 hr. The reaction of this acid chloride (5.00 g, 2.9 mmoles) and phenylhydroxylamine (6.33 g, 5.8 mmoles) as described in the general procedure gave N-phenylcyclohexylpropiolohydroxamic acid (XIV) (6.25 g, 87.5%). Recrystallization from ether–petroleum ether afforded white prisms of mp 82—83.5°. IR ν_{max}^{Nujol} cm^{-1}: 3100 (OH), 2260 (C≡C), 1610 (C=O). UV λ_{max}^{EtOH} $m\mu$ (ε): 270 (9370). *Anal.* Calcd. for $C_{15}H_{17}O_2N$: C, 74.04; H, 7.05; N, 5.76. Found: C, 73.97; H, 7.03; N, 5.76. Treatment of XIV (3.0 g) with 10% aqueous sodium hydroxide solution afforded 2-phenyl-5-cyclohexyl-4-isoxazolin-3-one (XV) (2.02 g, 67%). Recrystallization from hexane gave white prisms of mp 73—75°. IR ν_{max}^{Nujol} cm^{-1}: 1680 (C=O), 1630 (C=C). UV λ_{max}^{EtOH} $m\mu$ (ε): 229.5 (12170). NMR δ ppm ($CDCl_3$): 7.85—7.10 (5H, aromatic m), 5.50 (1H, d, J=1 Hz, C_4-H), 2.58 (1H, broad m, center, C=C-CH-), 2.25—1.10 (10H, m, cyclohexyl protons). *Anal.* Calcd. for $C_{15}H_{17}O_2N$: C, 74.04; H, 7.05; N, 5.76. Found C, 74.15; H, 7.11; N, 5.65.

2-Phenyl-5-methyl-4-isoxazolin-3-one (XVI)——B) To a solution of oxalyl chloride (3.91 g, 31 mmoles) in benzene (3 ml) was added portionwise potassium tetrolate (2.50 g, 20.5 mmoles). The mixture was warmed on an oil bath at 50—60° for 1.5 hr, cooled, filtered, and diluted with benzene to a volume of 20 ml. The solution of tetrolyl chloride thus obtained was mixed with a solution of phenylhydroxylamine (4.47 g, 41 mmoles) in ether (45 ml). Crude XVI (1.10 g) was obtained as described in the general procedure, and chromatographed on silica gel (Kanto Kagaku, 150 g). Elution with chloroform afforded pure XVI (0.80 g, 22% based on the amount of potassium tetrolate). Recrystallization from benzene–petroleum ether gave white prisms of mp 38—39° (lit. mp 33—36°[9]). IR ν_{max}^{Nujol} cm^{-1}: 1672 (C=O), 1637 (C=C). UV λ_{max}^{EtOH} $m\mu$ (ε): 227.5 (10490), 263.5 (10570). NMR δ ppm ($CDCl_3$): 7.0—7.9 (5H, aromatic m), 5.60 (1H, q, J=1 Hz, C_4-H), 2.30 (3H, d, J=1Hz, $-CH_3$). *Anal.* Calcd. for $C_{10}H_9O_2N$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.47; H, 5.36; N, 8.11.

1,5-Diphenyl-3-hydroxypyrazole (XIX)——To a mixture of phenylhydrazine (2.16 g, 20 mmoles) and a solution of potassium *t*-butoxide prepared from potassium (1.56 g, 40 mmoles) and *t*-butanol (400 ml) was added dropwise a solution of ethyl phenylpropiolate (3.48 g, 20 mmoles) in *t*-butanol (100 ml) during 10 min at room temperature. After the mixture was refluxed for 4 hr, the solvent was evaporated *in vacuo*. The residue was dissolved in water (40 ml) and washed with chloroform. The aqueous solution was neutralized by adding acetic acid (2.40 g, 40 mmoles), and the precipitated XIX (mp 248—251°, 3.74 g, 79%) was collected by suction filtration. Recrystallization from chloroform gave white needles of mp 252—253°. *Anal.* Calcd. for $C_{15}H_{12}ON_2$: C, 76.25; H, 5.12: N, 11.86. Found C, 76.10; H, 5.23; N, 11.73.

1-Phenyl-5-methyl-3-hydroxypyrazole (XX)——By the reaction of phenylhydrazine (5.04 g, 5 mmoles) with methyl tetrolate (4.90 g, 50 mmoles) in the presence of potassium *t*-butoxide prepared from potassium (3.90 g, 10 mmoles) and *t*-butanol (100 ml), XX was obtained and recrystallized from ethanol to white needles of mp 165—166.5°. Yield, 4.80 g (55%). The IR and NMR spectra of this sample was identical with those reported by Katritzky and Maine.[13] *Anal.* Calcd. for $C_{10}H_{10}ON_2$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.92; H, 5.68; N, 15.79.

1-Phenyl-3-hydroxypyrazole (XXI)——The similar reaction of ethyl propiolate (2.94 g, 30 mmoles) with phenylhydrazine (3.24 g, 30 mmoles) in the presence of potassium *t*-butoxide (60 mmoles) as described above afforded XXI (3.49 g, 73%). Recrystallization from chloroform gave white needles of mp 153—155°. NMR δ ppm ($(CD_3)_2CO$): 8.06 (1H, d, J=3 Hz, C_5-H), 7.9—7.1 (5H, aromatic m), 5.91 (1H, d, J=3 Hz, C_4-H). *Anal.* Calcd. for $C_9H_8ON_2$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.55; H, 5.09; N, 17.40.