HCl. A yellow solid was extracted with ether and dried, yield 1.05 g (76%). Recrystallization from pentane and sublimation at low pressure gave the analytical sample of 1-α-nitraminoethyl-1-methoxy-2-bromocyclopentane, mp 105–106°, 112° dec.

Anal. Calcd for $C_8H_{15}N_2O_3Br$: C, 35.95; H, 5.66; N, 10.49. Found: C, 36.31; H, 5.72; N, 10.60.

The ir spectrum of the nitramine was taken in dilute carbon tetrachloride (cm^{-1}): NH, 3360; NO_2, 1580 and 1340. The nmr spectrum (CCl_4) follows: δ 4.83 (q, 1, J = 7 Hz), 4.17 (br, 1), 3.4 (s, 3), 1.33 (d, 3, J = 7 Hz). The uv spectrum was taken in 95% ethanol: λ_{max} 232 mμ (ε 8500).[5,20]

Registry No.—Ia, 23042-83-3; Ib, 23042-84-4; Ic, 23042-85-5; Id, 23042-86-6; Ie, 23042-87-7; If, 23042-88-8; Ig, 23042-89-9; IIa, 23042-90-2; IIb, 23042-91-3; IIc, 23042-92-4; IId, 23042-93-5; IIe, 23042-94-6; IIf, 23042-95-7; IIg, 23042-96-8; 1-acetylcyclopentene oxime, 23042-97-9; 1-acetylcyclohexene oxime, 23042-98-0; 1-acetylcycloheptene oxime, 23042-99-1; 1-acetyl-4-*t*-butylcyclohexene oxime, 23043-00-7; 1-α-nitraminoethyl-1-methoxy-2-bromocyclopentane, 23043-01-8.

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Fused-Ring Isoxazolines and Their Isomers[1]

KYONG PAE PARK, CHYNG-YANN SHIUE, AND LEALLYN B. CLAPP

Metcalf Chemical Laboratories, Brown University, Providence, Rhode Island 02912

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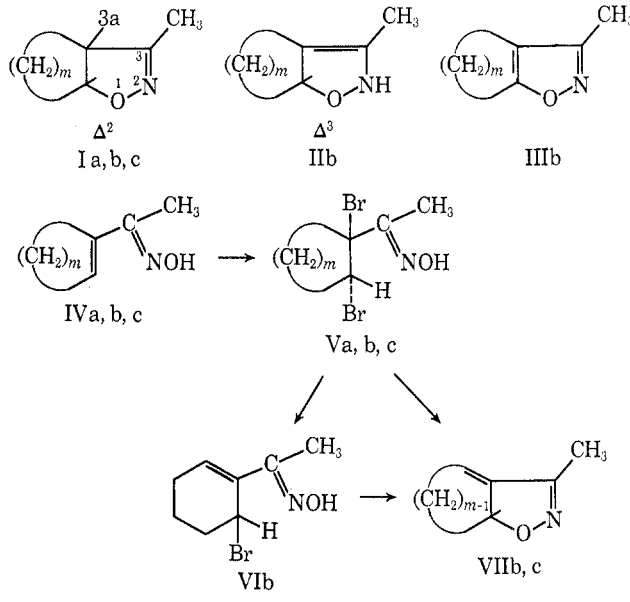
Δ²-Isoxazolines[2] are commonly synthesized from α,β-unsaturated carbonyl compounds by treatment with hydroxylamine. The extensive work of Barnes,[2] Blatt,[2] and von Auwers[2] has shown that the isoxazolines do not arise by direct cyclization (Michael self-addition) of the unsaturated oxime. No Δ³-isoxazoline with an unsubstituted NH[3] has been reported, but a Δ⁴-isoxazoline has recently been postulated as an intermediate in the pathway to an aziridine.[4,5]

We have synthesized a series of Δ²-isoxazolines I, the unsaturated isomeric oximes IV, and the unsaturated isomeric fused ring compounds III and VII. The cycloalkene added the elements of acetonitrile oxide[6,7] to give the Δ²-isoxazolines I. These isoxazolines do not add bromine at room temperature in a period of 24 hr. By oxidation with N-bromosuccinimide[8] Ib was converted in 67% yield to IIIb. The isoxazoline Ib was not oxidized to IIIb by chromic acid in acetic acid,[9] the usual reagent for converting the isoxazoline to an isoxazole. Compounds Ia and Ic gave 3a-bromo derivatives by action of N-bromosuccinimide, but IIIa was not formed by dehydrobromination, and IIIc was too unstable to isolate for analysis. Compound IIIc was identified by ir and nmr spectra (Table I).



Condensation of the 1-acetylcycloalkenes with hydroxylamine in the presence of pyridine gave the unsaturated oximes IV, isomers of I. Compounds IV added bromine (accepted as a *trans* addition) to give *trans*-dibromo derivatives V. The small dipole moment of Vb (0.59 D in benzene) is compatible with the *trans* structure. Acetone oxime, for example, has a dipole moment of 0.88 D.[10] *trans* elimination of HBr to give VIIb is also consistent with the proposed stereochemistry of Vb. Dehydrobromination of Vb with 1 mol of triethylamine in homogeneous medium yielded VIb, identified by nmr spectra and isolated as a glass. Compounds VIIb,c were obtained in a two-phase reaction by shaking solutions of Vb,c in carbon tetrachloride over sodium hydroxide pellets. Compound VIb was also converted to VIIb by the same method. However, compound Va did not undergo the dehydrobromination reactions carried out in a similar way. The allylic bromide VIb is a logical reactive precursor of VIIb. The nonreactivity of Va by comparison with Vb toward dehydrobromination is explained by Brown's I-strain theory.[11] A five-membered ring reluctantly forms an *endo* double bond which would be the case if VIa were a precursor to VIIa. On the other hand, a six-membered ring readily forms an *endo* double bond[11] (VIb) in the pathway to VIIb. Presumably the seven-membered-ring VIc would be subject to internal strain more closely resembling that of the six-membered ring than the five-membered ring. Compound VIc was not isolated but VIIc was isolated and identified.

(1) Support by Public Health Service Grant CA-07521 is gratefully acknowledged. The Varian A-60A nmr spectrometer and the mass spectrometer used in this research were purchased under a National Science Foundation Research Instrument Grant.

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TABLE I

PROPERTIES OF COMPOUNDS Ia–c, IIIb,c, IVa–c, Va–c, VIb, AND VIIb,c[a]

Compound	Mp or bp (mm), °C	Yield, %	Ir, cm^{-1}	Nmr, δ
Ia	53.5–55 (0.3)	37	1620, 1010, 950	1.8 (s, 3), 3.4 (br, 1), 4.9 (br, 1)
Ib	44.5–45.5 (0.14)	58	1620, 1015	1.92 (s, 3), 2.82 (q, 1), 4.25 (q, 1)
Ic	88–90 (3)	46	1625, 1160, 1035	1.8 (s, 3), 3.2 (q, 1), 4.57 (q, 1)
IIIb	37–38 (1)	67	1650, 1620	2.21 (s, 3), 2.48 (br, 2), 2.64 (br, 2)
IIIc			1640, 1620	2.08 (s, 3), 2.5–2.9 (br, 2), 2.2–2.5 (br, 2)
IVa	94–95.5	41	3610, 3200, 1630	9.8 (br, 1), 2.0 (s, 1), 6.0 (br, 1)
IVb	63–63.5	73	3610, 3300, 3050, 1640	9.94 (s, 1), 1.95 (s, 3), 6.11 (br, 1)
IVc	59–60	62	3590, 3270, 3040, 1640	1.97 (s, 3), 6.23 (br, 1)
Va	77–78.5	77	3600, 3200, 1650	2.1 (s, 3), 4.7 (br, 1)
Vb	118–119	100	3600, 3350	9.07 (s, 1), 2.07 (s, 3), 4.72 (br, 1)
Vc	100–101	44	3580, 3300, 1670	2.1 (s, 3), 4.81 (br, 1)
VIb		[b]		9.64 (s, 1), 2.00 (s, 3), 4.24 (br), 5.66 (br)
VIIb	54–55 (0.12)	65	1675, 1650, 1580	1.93 (s, 3), 4.46 (br, 1), 5.67 (br, 1)
VIIc	107–108		1670, 1530, 1080	2.13 (s, 3), 4.33 (br, 1), 6.1 (br, 1)

[a] Melting points are corrected. Analyses were satisfactory for all compounds reported except IIIb. Calcd: C, 70.04; H, 8.08; N, 10.21: Found: C, 69.33; H, 8.12; N, 9.83. [b] Obtained as a glass in 96% yield, assuming that the glass is pure.

Reversal of the order of adding reagents to 1-acetylcyclohexene to give the dibromo ketone and then Vb was not successful. Bromine was rapidly decolorized by addition to the unsaturated ketone, but, in the presence of pyridine, hydroxylamine rapidly gave tars with the dibromo ketone. Hydroxylamine hydrochloride alone gave no oxime nor were we successful with Subba Rao's[12] modification. Cromwell and Hess[13] found that a similar α-bromo ketone, 4-biphenyl 1-bromocyclohexyl ketone, gave nearly quantitative elimination of HBr with tertiary amines and even 68% elimination with alcoholic silver nitrate.

We synthesized compounds of type I and the isomeric compounds IV with the thought that one of the series IV might be in equilibrium with the tautomeric Δ^3-fused ring of type II. Catalytic hydrogenation of IVb suggests that the tautomer IIb may be present. In the presence of 10% palladium on carbon, compound IVb (IIb) is rapidly reduced to α-aminoethylcyclohexane. One mole of hydrogen is taken up at a faster rate than the next two, a behavior more consistent with structure IIb than IVb. The first mole of hydrogen added to IVb would be expected to give methyl cyclohexyl ketoxime. A sample of this ketoxime prepared independently from methyl cyclohexyl ketone did not add 2 mol of hydrogen under the same conditions in which IIb (IVb) added 3 mol of hydrogen. The alternate explanation that IVb adds the first mole of hydrogen in the 1,4 manner to give an ene-hydroxylamine (unknown) is not consistent with the instability such a structure would have. The ene-hydroxylamine should rearrange rapidly to methyl cyclohexyl ketoxime, which does not add hydrogen (*vide supra*) or add hydrogen rapidly to give α-aminoethylcyclohexane, but the second and third moles are added more slowly, not more rapidly than the first.

Other reactions described here and ir and nmr spectra, however, are compatible with the single structure IVb.

The experimental procedures are given below for the preparation of the series starting with Ib and IVb. Other members of each series were synthesized in a comparable manner. The properties of the resulting products are given in Table I.

Experimental Section

3-Methyl-Δ^2-hexahydro-1,2-benzisoxazole (Ib).—To a 500-ml round-bottomed flask, 100 ml of cyclohexene, 46.0 g (0.42 mol) of phenyl isocyanate, and 31.5 g (0.42 mol) of nitroethane were added. The solution was stirred while 10 drops of triethylamine in 10 ml of cyclohexene was added very slowly over a period of 0.5 hr. The reaction mixture was stirred at ambient temperatures for 0.5 hr more and was then refluxed for 2 hr. The reaction mixture was cooled and *sym*-diphenylurea was removed. The precipitate was washed with 100 ml of benzene in three portions, and the washings were added to the filtrate. The combined solution was washed twice with 100 ml of water, dried over anhydrous sodium sulfate, and put on a column containing 1 lb of alumina. The first 600 ml of carbon tetrachloride eluted 1.0 g of liquid which was about 60% Ib, 35% dimeric addition product, and a trace amount of dimethylfuroxan. Then 600 ml more of carbon tetrachloride eluted 18.0 g of liquid which was mostly Ib, crude yield 58%. This liquid was dissolved in 150 ml of pentane and washed with 50-ml portions of water until the organic phase became clear. This process removes dimethylfuroxan. The pentane solution was dried over anhydrous sodium sulfate, and pentane was removed on a rotating evaporator. The remaining oil was distilled at reduced pressure: bp 44.5–45.5° (0.14 mm); $n^{25}D$ 1.4810; d^{25}_4 1.033.

In the original work Mukaiyama and Hoshino[14] (and later Backman and Strom[7]) used only 0.5 mol of nitroethane with phenyl isocyanate in generating acetonitrile oxide *in situ*. We obtained better yields with an excess of phenyl isocyanate.

3-Methyl-$\Delta^{2,3a(7a)}$-tetrahydro-1,2-benzisoxazole (IIIb).—To 150 ml of carbon tetrachloride, 3.0 g (0.0216 mol) of Ib and 4.2 g (0.0236 mol) of N-bromosuccinimide were added and gently refluxed for 3 hr. Hydrogen bromide was liberated slowly. The solution was cooled, and precipitated succinimide was removed by filtration. The carbon tetrachloride solution was washed twice with 75 ml of 5% sodium hydroxide solution and then with water until the organic phase became clear. The carbon tetrachloride solution was dried over anhydrous sodium sulfate, and the solvent was removed on a rotating evaporator. The yield was 2.0 g, 67%. The analytical sample was distilled at reduced pressure: bp 37–38° (1 mm), $n^{25}D$ 1.4899. Compound IIIb was unstable upon standing and was analyzed on the day of preparation.

Reduction of Methyl 1-Cyclohexenyl Ketoxime (IVb).—

(12) K. S. R. Krishna Mohan Rao and V. B. Subba Rao, *Indian J. Chem.*, **6**, 66 (1968).

(13) N. H. Cromwell and P. H. Hess, *J. Amer. Chem. Soc.*, **82**, 136 (1960).

(14) T. Mukaiyama and T. Hoshino, *ibid.*, **82**, 5339 (1960).

Methyl 1-cyclohexenyl ketoxime IVb was prepared from 1-acetylcyclohexene[15] by a well-known procedure[16] with a yield of 73%.[17]

Compound IVb (128 mg, 0.92 m mol) was dissolved in 25 ml of 95% ethanol, and 20 mg of 10% palladium on carbon was added. The mixture was placed under 1 atm of hydrogen and stirred magnetically as hydrogen was absorbed. After an induction period of 12 min, 1 mol of hydrogen was taken up in 24 min and 2 mol at a distinctly slower rate in 2.5 hr. The hydrogen uptake stopped and the catalyst was removed. Removal of the solvent on a rotary evaporator left 80 mg of an oil which absorbed CO_2 from the air overnight to give a fine powder. Treatment with aqueous sodium hydroxide gave back the oil, and treatment with hydrochloric acid on another portion gave the hydrochloride of α-aminoethylcyclohexane. Recrystallization from ethanol–ethyl acetate gave the pure hydrochloride, mp 241.5° dec (lit.[18] mp 239–240°). An authentic sample of α-aminoethylcyclohexane hydrochloride (below) did not depress the melting point of this compound and gave identical infrared spectra.

An attempted hydrogenation of 130 mg of methyl cyclohexyl ketoxime, mp 60–61.5°,[19] with 19 mg of 10% palladium on carbon under the same conditions as described for compound IVb (above) resulted in an uptake of less than 0.5 mol in 16 hr. The partially reduced product was not further identified.

The authentic sample of α-aminoethylcyclohexane was prepared from 300 mg of methyl cyclohexyl ketoxime. The ketoxime was dissolved in 30 ml of absolute ethanol, and 5 g of sodium was added in pieces at a rate to keep the alcohol refluxing. Water was finally added and the amine was steam distilled. The hydrochloride (150 mg, 43%) was isolated and recrystallized from ethanol–ethyl acetate, mp 242–243° dec.

Methyl 2-(3-Bromo-1-cyclohexenyl) Ketoxime (VIb).—To a solution of 3.0 g (0.01 mol) of Vb[17] in 100 ml of carbon tetrachloride was added 1.02 g (0.01 mol) of triethylamine dropwise. Immediately, triethylamine hydrobromide was precipitated. The carbon tetrachloride solution was filtered. After reducing the volume of the filtrate to 25 ml using a rotating evaporator without heating, part of the solution was removed for an nmr spectrum of VIb. The low-field hydrogen on oxygen remained, and there was evidence of a trace amount of triethylamine from the easily identifiable ethyl hydrogens. The vinylic proton appeared at δ 5.66 and the allylic proton at δ 4.24. When the solvent was removed completely, an almost colorless glass of 2.10 g remained. The glassy solid was not as soluble in carbon tetrachloride as the starting compound. The nmr spectrum, as just described, was quite different from that of Vb or VIIb (Table I). However, profound decomposition occurred when an attempt was made to distil the glassy solid.

3-Methyl-$\Delta^{2,3a(4)}$-tetrahydro-1,2-benzisoxazole (VIIb).—In 100 ml of carbon tetrachloride 8.0 g (0.0268 mol) of Vb was dissolved, and to the solution was added 4.5 g of sodium hydroxide pellets. The heterogeneous reaction mixture was stirred for 1 hr, and then the precipitate and excess sodium hydroxide were removed by filtration. The filtrate was washed twice with 50 ml of water and dried over anhydrous sodium sulfate. The dried carbon tetrachloride yielded 2.85 g, 65%, of 3-methyl-$\Delta^{2,3a(4)}$-tetrahydro-1,2-benzisoxazole. The analytical sample was distilled at reduced pressure: bp 54–55° (0.12 mm), $n^{25}D$ 1.5174, d^{25}_4 1.0453.

When 2.0 g of VIb was suspended in carbon tetrachloride and treated with 4.5 g of sodium hydroxide pellets, as just described, 1.0 g of VIIb (identical ir and nmr spectra) was obtained.

Registry No.—Ia, 20936-78-1; Ib, 24010-91-1; Ic, 24010-92-2; IIIb, 24010-93-3; IIIc, 24010-94-4; IVa, 23042-97-9; IVb, 23042-98-0; IVc, 23042-99-1; Va, 24010-49-9; Vb, 24010-50-2; Vc, 24010-51-3; VIb, 24010-98-8; VIIb, 24010-99-9; VIIc, 24011-00-5.

(15) R. E. Christ and R. C. Fuson, *J. Amer. Chem. Soc.*, **59**, 893 (1937).
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Elimination of Methyl Mercaptan from N-Substituted N′-Cyano-S-methylisothioureas. Evidence for N-Cyanocarbodiimides[1a,b]

C. GORDON MCCARTY, JAMES E. PARKINSON, AND DONALD M. WIELAND[1c]

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506

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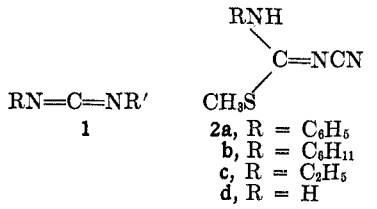
Although carbodiimides with a wide variety of substituents (R and R′ in **1**) have been prepared and characterized,[2] to our knowledge there is little, if any, recorded information on N-cyanocarbodiimides (R or R′ being CN in **1**). We report here evidence for the existence of N-cyanocarbodiimides in solutions resulting from the thermal or metal ion assisted elimination of methyl mercaptan from a series of N-substituted N′-cyano-S-methylisothioureas (**2a–2d**).

During the preparation of several compounds of the general formula **2** for another study,[3] it was found that they readily lose methyl mercaptan at their temperature of melting to yield viscous red oils or red glasses. The elimination of mercaptans from isothioureas was reported as early as 1881 by Will[4] and has been used by Ferris and Schutz[5] for the *in situ* generation of carbodiimides in solution. Ferris and Schutz facilitated the elimination by using a heavy metal ion to effect precipitation of an insoluble metal mercaptide and a base to serve as an acid acceptor. Their technique has been adopted in the present study.



Compounds **2a–2d** were conveniently prepared by the reaction of ammonia or the appropriate amine with dimethylcyanodithioimidocarbonate (**3**) which, in turn, was prepared by the method of Hantzsch and Wolvekamp.[6] The formulation of the isothioureas as shown in **2a–2d** is supported by their elemental analyses and spectral properties, some of which are summarized in Table I. Worthy of comment is the

TABLE I
INFRARED SPECTRA OF ISOTHIOUREAS 2a–2d

Compd	ν, cm⁻¹ (KBr) NH	C=N	C≡N
2a	3210	1520	2160, 2180
2b	3290	1550	2180
2c	3290	1550	2180
2d	3120, 3310	1530	2180, 2200

(1) (a) Support in part by NASA Grant NsG(T)-21 is gratefully acknowledged. (b) Abstracted from the M.S. Thesis of J. E. Parkinson and the Ph.D. Thesis of D. M. Wieland, West Virginia University, 1969. (c) NASA Trainee, 1965–1968.
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