ethanol to give 0.61 g (24%) of **8**: mp 167–168 °C; IR 5.84 μm; ^{1}H NMR (Me_2SO-d_6) δ 8.5–8.1 (d superimposed on m, 2, J = 10 Hz), 7.8–7.2 (m, 3), 6.80 (d, 1, J = 10 Hz).

Anal. Calcd for $C_{10}H_{16}N_2OS$: C, 59.4; H, 3.0; N, 13.9. Found: C, 59.5; H, 2.9; N, 14.1.

From 4. A mixture of NaOH (1.65 g, 41.3 mmol) and the ester **4** (10.0 g, 38.5 mmol) in 500 mL of water was heated at about 70 °C for 5 h, during which time most of the solid dissolved. The reaction mixture was cooled and filtered, and the filtrate was acidified with concentrated HCl. The resulting mixture was heated to boiling and then filtered while hot, and the collected solid was washed with water and dried in a vacuum oven to yield 4-oxo-4H-[1,3]thiazino[3,2-a]benzimidazole-2-carboxylic acid: 8.86 g (93%); mp 230–232 °C dec; IR 5.84 μm; ^{1}H NMR (Me_2SO-d_6) δ 8.3 (m, 1), 7.8–7.3 (m, 3), 7.27 (s, 1).

Anal. Calcd for $C_{11}H_6N_2O_3S$: C, 53.6; H, 2.5; N, 11.4. Found: C, 53.1; H, 2.5; N, 11.4.

This acid (5.00 g, 20.3 mmol) was suspended in 125 mL of Dowtherm A, heated to 250 °C, and then allowed to cool. The solution was diluted to 800 mL with hexane and cooled to precipitate a solid which was collected by filtration, washed with ether, and recrystallized from chloroform/hexane to give **8**: 2.35 g (57%; 53% overall); mp 167–168 °C; mixture melting point with the compound obtained from **7** is 167–168 °C; IR 5.84 μm; ^{1}H NMR (Me_2SO-d_6) δ 8.5–8.1 (d superimposed on m, 2, J = 10 Hz), 7.8–7.2 (m, 3), 6.80 (d, 1, J = 10 Hz).

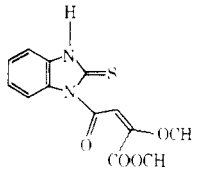
Anal. Calcd for $C_{10}H_6N_2OS$: C, 59.4; H, 3.0; N, 13.9. Found: C, 59.0; H, 3.0; N, 13.7.

Acknowledgment. The author is grateful to Professor R. F. Borch and Dr. C. M. Leir for useful discussions and suggestions.

Registry No.—**1**, 583-39-1; **2**, 69469-78-9; **3**, 69469-79-0; **4**, 68470-82-6; **7**, 69469-80-3; **8**, 55360-92-4; DMAD, 762-42-5; ethyl propiolate, 623-47-2; 4-oxo-4H-[1,3]thiazino[3,2-a]benzimidazole-2-carboxylic acid, 69469-81-4.

References and Notes

(1) A. McKillop, G. C. A. Bellinger, P. N. Preston, and A. Davidson, *Tetrahedron Lett.*, 2621 (1978).
(2) E. I. Grinblat and I. Y. Postovskii, *Zh. Obshch. Khim.*, **31**, 394 (1961); *J. Gen. Chem. USSR (Engl. Transl.)*, **31**, 357 (1961).
(3) J. W. Lown and J. C. N. Ma, *Can. J. Chem.*, **45**, 939 (1967).
(4) E. Winterfeldt and J. M. Nelke, *Chem. Ber.*, **100**, 3671 (1967).
(5) J. B. Hendrickson, R. Rees, and J. F. Templeton, *J. Am. Chem. Soc.*, **86**, 107 (1964).
(6) H. Nagase, *Chem. Pharm. Bull.*, **21**, 270 (1973).
(7) F. W. Short, B. C. Littleton, and J. L. Johnson, *Chem. Ind. (London)*, 705 (1971).
(8) A. F. Cameron, N. J. Hair, N. F. Elmore, and P. J. Taylor, *Chem. Commun.*, 890 (1970).
(9) V. Vögeli, W. von Philipsborn, K. Nagarajan, and M. D. Nair, *Helv. Chim. Acta*, **61**, 607 (1978).
(10) (a) A. W. Chow, D. R. Jakas, B. P. Trotter, N. M. Hall, and J. R. E. Hoover, *J. Heterocycl. Chem.*, **10**, 71 (1973); (b) H. Ogura, M. Kawano, and T. Itoh, *Chem. Pharm. Bull.*, **21**, 2019 (1973); (c) R. J. Alaimo, *J. Heterocycl. Chem.*, **10**, 769 (1973).
(11) L. V. Zav'yalova, N. K. Rozhkova, and K. L. Seitanidi, *Khim. Geterotsikl. Soedin.*, **11**, 47 (1975); *Chem. Heterocycl. Compd.*, **11**, 38 (1975).
(12) A referee has suggested that structure **2a** is a possible alternative for this compound. This possibility was investigated by running the condensation reaction in CD_3OD rather than CH_3OH since the enol ether of **2a** would be derived from the reaction solvent. The product which was isolated from CD_3OD was identical with that obtained from CH_3OH and shows no evidence in its ^{1}H NMR spectrum of any deuterium incorporation.



2a

(13) W. E. Truce, G. H. Klein, and R. B. Kruse, *J. Am. Chem. Soc.*, **83**, 4636 (1961).

Oxidation of Isoxazolidines with Peroxy Acids. Nitrones and N-Hydroxy-1,3-tetrahydrooxazines

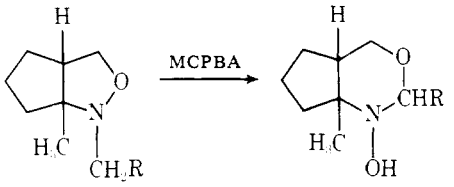
Norman A. LeBel,* Mary Ellen Post, and Dorothy Hwang

Department of Chemistry, Wayne State University, Detroit, Michigan 48202

Received October 16, 1978

N-Methylisoxazolidines, prepared by 1,3-dipolar cycloadditions of nitrones and olefins, are smoothly converted to N-hydroxy-1,3-tetrahydrooxazines by reaction with m-chloroperbenzoic acid. N-γ-Hydroxypropyl methylene nitrones are proposed intermediates. With N-benzylisoxazolidines, mixtures of 2-phenyl-1,3-tetrahydrooxazines and N-γ-hydroxypropyl C-phenyl nitrones are obtained. The preferred regiochemistry for nitrone formation involves the α-CH of the N-alkyl substituent as opposed to the isoxazolidine C_5-H. This reaction provides a useful supplement to syntheses based on nitrone cycloadditions.

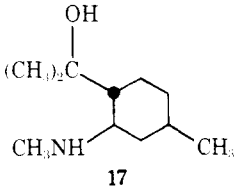
The reaction between nitrones and alkenes is one of the more versatile of 1,3-dipolar cycloaddition reactions, and the intramolecular counterpart can lead to a variety of interesting structures having useful synthetic potential.[1] The product isoxazolidines have, for the most part, been subjected to hydrogenolytic cleavage of the N–O bond, liberating 1,3-amino alcohols. Some years ago we described briefly two examples of the oxidative cleavage of polycyclic isoxazolidines.[2,3] We now report in detail on the scope and most probable mechanism for this useful reaction.



1, R = H
3, R = Ph

2, R = H
4, R = Ph

In a typical case, a solution of *cis*-1,6a-dimethylcyclopent[*c*]isoxazolidine (**1**)[4] in methylene chloride was treated with 1 molar equiv of m-chloroperbenzoic acid during the course of 1 h. After workup, the crystalline *cis*-1-hydroxy-7a-methylcyclopenta[*d*]tetrahydro-1,3-oxazine (**2**) was isolated in ~80% yield. The structure of **2** followed from an exact mass determination, its infrared spectrum (ν_{max} 3580 and 3250



17

0022-3263/79/1944-1819$01.00/0

(br) cm^{-1}), and its NMR spectrum, which showed, in particular, a low field AB quartet (δ 4.2, 4.4) for the N-CH_2-O methylene protons.

There are listed in Table I several additional examples of this reaction with *N*-methylisoxazolidines.

Chemical evidence for the structures of several of these *N*-hydroxy-1,3-tetrahydrooxazines was obtained. For example, heating **2** and **12** with dimedone in aqueous alcohol containing acid afforded the formaldehyde dimedone derivative in nearly quantitative yield; the hydroxylamino alcohols were not characterized. Lithium aluminum hydride reduction of **12** gave the known amino alcohol **17**, and catalytic hydrogenation of **16** in glacial acetic acid generated 1,3-diphenylpropane. In general, reaction of the *N*-hydroxy-1,3-tetrahydrooxazines with lithium aluminum hydride in ether or tetrahydrofuran with zinc and acetic acid and catalytic hydrogenation gave mixtures, of which one component was identified as the expected secondary amino alcohol (authentic samples were available from reduction of the isoxazolidines). Our mechanistic proposal envisions initial oxidation of isoxazolidine (cf. **1** or **3**) to the unstable *N*-oxide **18**, which can fragment to dipolar species **19**. Tautomerization and proton transfer (possibly by an intramolecular pathway, vide infra) would lead to the reactive methylene nitrone **20**, which is expected to undergo rapid ring closure to the product **2**.

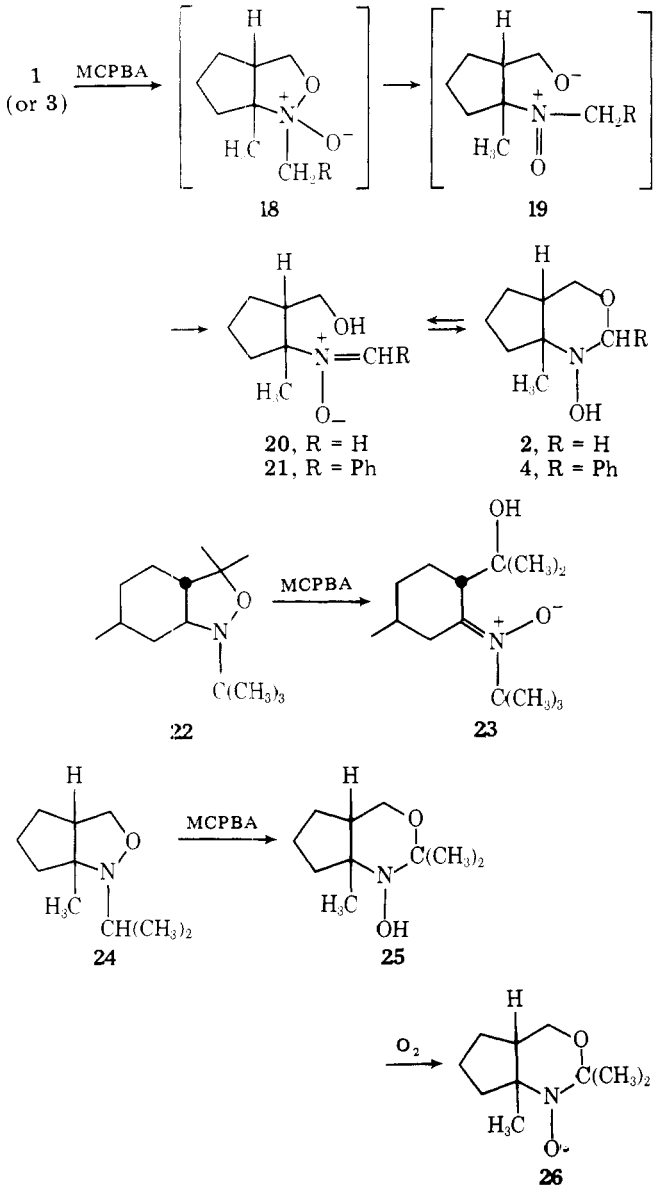
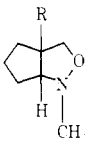
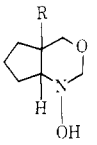
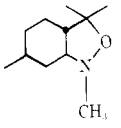
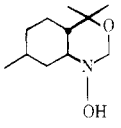
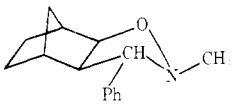
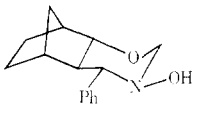
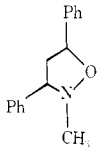
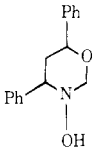


Table I. *N*-Hydroxy-1,3-tetrahydrooxazines from Isoxazolidines

isoxazolidine	product	yield, %[a]
		
5,[b] R = CH_3	6, R = CH_3	67
7,[c] R = Ph	8, R = Ph	73
9,[d] R = H	10, R = H	65
		76
11[d]	12	
		66
13[e]	14	
		75
15[f]	16	

[a] Actual yields are higher; the number given is for isolated material. [b] N. D. Ojha, Ph.D. Dissertation, Wayne State University, 1966. [c] R. J. Newland, *Diss. Abstr. Int. B.*, **35**, 3250 (1975). [d] Reference 4. [e] Reference 5. [f] References 5b and 6.

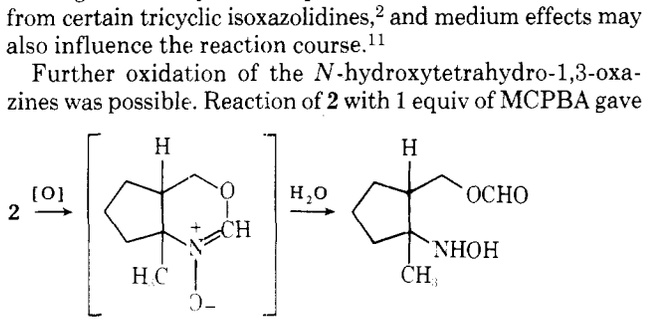
That nitrones are indeed intermediates in such reactions has been demonstrated in several ways. Oxidation of the *N*-benzyl analogue **3** of **1** was followed by rapid chromatography on alumina. Several fractions were collected. TLC analysis of the first fraction showed the presence of some benzaldehyde and a major component which was isolated and recrystallized. This product was the expected *N*-hydroxytetrahydro-1,3-oxazine **4** (stereochemistry uncertain) as shown by spectral analysis. The later chromatographic fractions contained a second major component, nitrone **21**, which could be trapped as a 1,3-dipolar adduct with methyl acrylate. When purified compounds **21** and **4** were rechromatographed or allowed to stand in solution for several hours, a mixture of the two in about a 1:1 proportion was observed. This behavior was quite unlike that of **2**, which was stable indefinitely.

When the peracid oxidation was carried out with *N-tert*-butyl-3,3,6-trimethyl-3a,4,5,6,7,7a-hexahydro-2,1-benzisoxazoline (**22**), it was possible to isolate the crystalline nitrone **23** in ~70% yield. Obviously proton transfer in the intermediate nitrosonium species must take place away from the *tert*-butyl group, and ring closure of **23** is unlikely. After steam distillation from aqueous acid, 3-methylcyclohexanone (from retro-aldol reaction of *trans*-2-(1-hydroxy-1-methylethyl)-5-methylcyclohexanone) was identified in the distillate and *N-tert*-butylhydroxylamine was present in the aqueous residue.

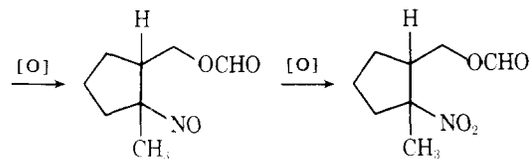
Similar treatment of the *N*-isopropylisoxazolidine **24** with 1 mol of MCPBA gave the *N*-hydroxytetrahydro-1,3-oxazine **25**, fully substituted at the positions α to the nitrogen. This method for production of 3-hydroxytetrahydro-1,3-oxazines appears to be far superior to those alternatives involving the addition of organometallic reagents to dihydro-1,3-oxazine *N*-oxides[7] or reduction of tetrahydro-1,3-oxazine *N*-oxyls.[8]

It is of particular interest to note (see Table I) that for all *N*-methylisoxazolidines conversion of intermediates such as **19** to methylene nitrones (cf. **20**) and subsequent ring closure to the *N*-hydroxytetrahydro-1,3-oxazines were favored over formation of the more highly substituted nitrones by proton transfer in the other direction (cf. **23**). Under the reaction conditions described herein, nitrone formation is highly regioselective toward the *N*-alkyl substituent.[9] This kinetic phenomenon may be implicating intramolecular proton transfer. This preferred regiochemistry was observed and noted when this reaction was utilized in an elegant synthesis of *dl*-cocaine; however, the hydroxy nitrone does not cyclize to a (bridged bicyclic) *N*-hydroxytetrahydro-1,3-oxazine.[10] The regioselectivity is not as pronounced in nitrone formation from certain tricyclic isoxazolidines,[2] and medium effects may also influence the reaction course.[11]

Further oxidation of the *N*-hydroxytetrahydro-1,3-oxazines was possible. Reaction of **2** with 1 equiv of MCPBA gave



27 **28**



29 **30**

an immediate blue-colored solution, which when worked up and examined by NMR, IR, and TLC was shown to contain a mixture of starting material **2** and hydroxylamino formate **28** (formed presumably by hydrolysis of the nitrone **27**). On the other hand, when **2** was oxidized with 2 mol of MCPBA, a mixture of nitroso formate **29** and its dimer was obtained. Finally, oxidation of **2** with excess MCPBA gave the nitro formate **30**. This behavior was expected.[7] Air oxidation of **25**, catalyzed by cupric acetate, generated the relatively unstable nitroxyl **26**.

Experimental Section

Melting points and boiling points are uncorrected. Microanalyses were performed by Midwest Microlabs, Inc., Indianapolis, Indiana.

Mass spectra were obtained with an AEI Model MS-902 double-focusing spectrometer at 70 eV ionization potential and 100 μA. The IR spectra were recorded with a PE Model 237B spectrophotometer, using 0.1-mm matched cells for solutions. The NMR spectra were recorded on a Varian Model T60A spectrometer; approximately 30% (w/v) solutions in the designated solvent were used with tetramethylsilane as the internal standard. VPC analyses were carried out on a HP Model 5750 dual flame ionization unit employing the columns and conditions specified.

General Procedure for Oxidation with *m*-Chloroperbenzoic Acid. Conversion of *cis*-1,6a-Dimethylcyclopent[*c*]isoxazolidine (1) to *cis*-1-Hydroxy-7a-methylcyclopenta[*d*]tetrahydro-1,3-oxazine (2). A solution of 2.14 g (10 mmol) of *m*-chloroperbenzoic acid (80%) in 90 mL of methylene chloride was added dropwise to a stirred, ice-bath cooled solution of 1.42 g (10 mmol) of isoxazolidine **1** in 10 mL of methylene chloride. The addition required 30 min, and stirring was continued for 1 h while the mixture was allowed to warm to room temperature. The mixture was passed through a column (¾ × 8 in.) containing alumina (Fisher Scientific, 80–200 mesh, ~70 g). Chloroform (200 mL) was passed through, and the total eluent was concentrated on a rotary evaporator to give 2 g of crude product **2**. Recrystallization from a mixture of ethyl acetate and hexane afforded 1.30 g (83%) of pure **2**: mp 112 °C; NMR (CCl_4) δ 1.27 (s, CH_3), 1.4–2.4 (br, 7 H), 3.60 (q, $J_{AB} \cong 14$ Hz, C–CH_2–O), 4.27 (q, $J_{AB} \cong 8$ Hz, O–CH_2–N), 7.27 (s, OH); IR 3580, 3230 (br) cm^{-1}; mass spectrum calcd for $C_8H_{15}NO_2$ 157.1102, found 157.1111.

***cis*-1-Hydroxy-4a-methylcyclopenta[*d*]tetrahydro-1,3-oxazine (6):** mp 86–87 °C; NMR (CCl_4) δ 0.90 (s, CH_3), 2.53 (br s, N–C–H), 3.42 (q, $J_{AB} \cong 11$ Hz, C–CH_2–O), 3.77 and 4.48 (dd, $J_{AB} \cong 8$ Hz, O–CH_2–N), 7.60 (br s, OH); IR (CCl_4) 3600, 3250 (br) cm^{-1}; mass spectrum calcd 157.1102, found 157.1124.

Anal. Calcd for $C_8H_{15}NO_2$: C, 61.12; H, 9.62; N, 8.91. Found: C, 61.30; H, 9.59; N, 8.81.

***cis*-1-Hydroxy-4a-phenylcyclopenta[*d*]tetrahydro-1,3-oxazine (8):** mp 142–143 °C; NMR ($CDCl_3$) δ 3.48 (br s, N–CH), 3.82 (s, C–CH_2–O), 4.15 and 4.77 (dd, $J_{AB} \cong 8$ Hz, O–CH_2–N), 6.27 (br s, OH), 7.38 (m, C_6H_5); IR ($CHCl_3$) 3580, 3210 (br) cm^{-1}; mass spectrum calcd for $C_{13}H_{17}NO_2$ 219.1258, found 219.1253.

***cis*-1-Hydroxycyclopenta[*d*]tetrahydro-1,3-oxazine (10):** unstable; NMR (CCl_4) δ 2.95 (br s, N–CH), 3.70 (s, C–CH_2–O), 3.77 and 4.50 (dd, $J \cong 7$ Hz, O–CH_2–N), 7.28 (br s, OH); IR (CCl_4) 3600, 3220 (br), 1245 cm^{-1}.

***trans,trans*-1-Hydroxy-4,4,7-trimethyloctahydro-3,1-benzoxazine (12):** hygroscopic; NMR (CCl_4) δ 0.95 (d, $J \cong 6$ Hz, CHC**H**$_3$), 1.13 and 1.18 (2s, $C(CH_3)_2$), 3.9–4.6 (m, 2 H, O–CH_2–N); mass spectrum, *m/e* 199 (M^+); IR (CCl_4) 3600, 3230 (br) cm^{-1}.

***exo*-3-Hydroxy-5,8-methano-4-phenyloctahydro-1,3-benzoxazine (14):** mp 120–121 °C; NMR ($CDCl_3$) δ 0.9–2.4 (9 H), 3.5–3.7 (N–C**H**Ph–CH and C–CH–O), 4.53 (q, $J_{AB} \cong 11$ Hz, O–CH_2–N), 7.40 (s, C_6H_5); IR ($CHCl_3$) 3585, 3250 (br), 1490, 1450 cm^{-1}.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.62; H, 7.77; N, 5.52.

3-Hydroxy-4,6-diphenyltetrahydro-1,3-oxazine (16): mp 161–162 °C; NMR (Me_2SO-d_6) δ 1.9 (br s, 1 H), 2.5 (s, 1 H), 3.3 (s, OH), 4.4–4.9 (m, 4 H), 7.3 (s, $2C_6H_5$); IR (CCl_4) 3600, 3275 (br), 1490, 1450 cm^{-1}.

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.29; H, 6.69; N, 5.54.

Oxidation of *cis*-1-Benzyl-6a-methylcyclopent[*c*]isoxazolidine (3) to a Mixture of 4 and 21. A sample of 0.23 g (1 06 mmol) of **3** in 10 mL of methylene chloride was reacted with 0.22 g (1.02 mmol) of MCPBA (80%) in the usual manner. The mixture was rapidly passed through a column containing alumina (12.5 g). Elution was with chloroform, and fractions of 25 mL were collected, concentrated, and examined by TLC (silica gel, 30% acetone in hexane). Traces of starting material **3** were detected in fraction 1. Fraction 2 was essentially pure *N*-hydroxy-7a-methyl-2-phenylcyclopenta[*d*]tetrahydro-1,3-oxazine (**4**) (mixture of diastereomers epimeric at C-3): NMR (CCl_4) δ 1.22 and 1.28 (s, CH_3), 3.6–4.0 (3 H, CH_2–O and OH), 4.80 and 4.97 (s, O–CHPh–N), ~7.3 (br, C_6H_5); IR ($CDCl_3$) 3580 cm^{-1} (OH), *no* 1600 cm^{-1} adsorption.

Fractions 3–5 contained mixtures of **4** and nitrone **21**, and fractions 6 and 7 were nearly pure **21**: NMR ($CDCl_3$) δ 1.7 (s, CH_3), 3.72 (br s, O–CH_2–CO), 4.6 (br s, OH), 7.3–7.7 (m, 4 H, meta and para C_6H_5, N=C**H**C_6H_5), 8.2–8.4 (m, 2 H, ortho C_6H_5); IR ($CDCl_3$) broad OH at 3300, 1580 and 1210 (nitrone) cm^{-1}.

The total recovery of products was 0.23 g (92%), of which 0.1 g was **21** (40%) and 0.13 g was **4** (52%).

Adduct from Nitrone 21 and Methyl Acrylate. The reaction mixture from 0.29 g (1.3 mmol) of **3** and 0.3 g (1.4 mmol) of MCPBA (80%) in 50 mL of methylene chloride was passed through a column containing 15 g of alumina (Fisher Scientific, 80–200 mesh), and chloroform was the eluent. The total eluent was concentrated to give 0.35 g of crude material (**4** and **21**), 25 mL of distilled methyl acrylate was added, and the mixture was heated at reflux on a steam bath for 20 h. Removal of the excess methyl acrylate at reduced pressure gave 0.43 g of a yellow oil, which was purified by passing it through a short column containing silica gel: NMR (CCl_4) δ 0.92 (s, C–CH_3), 3.73 (s, O–CH_3), ~3.5 (t, C–CH_2–O), 4.23 (m, 1 H, CH_2–C**H**(O)—$COOCH_3$), 4.58 (m, 1 H, CH_2–C**H**(N)–C_6H_5), 7.3 (br s, C_6H_5); IR (CCl_4) 3500 (br), 1750, 1455, 1443, 1370, 1220, 1180, 1090, 1030 cm^{-1}; mass spectrum calcd for $C_{18}H_{25}NO_4$ 319.1777, found 319.1797.

Hydrolysis of 12. Formation of Formaldehyde Dimedone. To a solution of 0.2 g of **13** in 4 mL of 50% aqueous ethanol was added 0.3 g of methone and one drop of 10% hydrochloric acid. The mixture was refluxed gently for 5 min and then cooled in an ice–water bath. The precipitated solid was collected on a filter and recrystallized from a mixture of ethanol and water, mp 190–192 °C (lit.[12] mp 191–191.5 °C for formaldehyde dimedone).

***trans,trans*-2-(1-Hydroxy-1-methylethyl)-*N*,5-dimethylcyclohexylamine (17) by Lithium Aluminum Hydride Reduction of 12.** A mixture of 0.1 g (0.5 mmol) of **13**, 0.1 g (2.9 mmol) of lithium aluminum hydride, and 20 mL of freshly distilled tetrahydrofuran was refluxed for 20 h. The solution was cooled, and 10% sodium hy-

droxide was added carefully with stirring until the gel settled rapidly. Ether (30 mL) was added, the layers were separated, and the organic phase was dried over magnesium sulfate and concentrated. The crude amino alcohol (0.1 g) was identical with an authentic sample[4] by TLC comparison (silica gel, acetone and 40% acetone in hexane) and VPC (15% E-20M Polyglycol on Chromosorb, 10 ft × ¼ in., 170 °C).

***N*-Methyl-*exo*-*cis*-3-(1-amino-1-phenylethyl)-2-norbornanol. A. Reduction of Isoxazolidine 13.** A solution of 1.2 g (5.2 mmol) of isoxazolidine **13** in 1 mL of glacial acetic acid was added to a stirred suspension of 1.2 g of zinc dust in 10 mL of 1:1 acetic acid–water. The mixture was stirred for 24 h at 75–80 °C, cooled, basified to pH >12 with 20% sodium hydroxide, and extracted with three 25-mL portions of ether. The combined extract was dried over magnesium sulfate and concentrated to give 0.66 g of oil which solidified in the freezer. Recrystallization from a mixture of ethyl acetate and hexane gave 0.4 g (33%) of amino alcohol: mp 93–94 °C; NMR ($CDCl_3$) δ 2.13 (s, CH_3–N).

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.58; H, 9.26; N, 6.08.

(*Z*)-*N*-[*trans*-2-(1-Hydroxy-1-methylethyl)-5-methyl-1-cyclohexylidene]-2-methyl-2-propanamine *N*-Oxide (23). When the oxidation procedure was applied to the *N*-*tert*-butylisoxazolidine **22**, the nitrone **23** was isolated in 70–80% yield; hygroscopic solid; mp 116–118 °C; IR (CCl_4) 3200 (br, OH), 1550 and 1180 (nitrone) cm^{-1}; NMR (CCl_4) δ 1.1 and 1.2 (s, $C(CH_3)_2$), 1.6 (s, $C(CH_3)_3$); mass spectrum, *m/e* 242 (M^+).

In a second preparation, a solution of 0.73 g (3.3 mmol) of **22** and 0.57 g (2.6 mmol) of MCPBA in 25 mL of methylene chloride was stirred for 1 h, and then 10 mL of concentrated hydrochloric acid was added slowly. The mixture was subjected to steam distillation, and the distillate was separated into layers. The methylene chloride layer was dried ($MgSO_4$) and concentrated to give ~0.4 g, which contained mostly 3-methylcyclohexanone as shown by VPC and by formation of the 2,4-dinitrophenylhydrazone (mp 160–161 °C, mmp 159–161 °C). The residue remaining after distillation was basified and extracted with methylene chloride. The extract was dried ($MgSO_4$) and concentrated to give 0.11 g of a mixture of *N*-*tert*-butylhydroxylamine (TLC, silica gel, 25% methanol in chloroform) and unreacted **22**.

***cis*-2,2,7a-Trimethylcyclopenta[*d*]tetrahydro-1,3-oxazinyl-1-oxy (26).** A solution of 0.54 g (2.5 mmol) of MCPBA (80%) in 23 mL of methylene chloride was added dropwise to a stirred, ice-cooled solution of 0.4 g (2.4 mmol) of **24** in 2 mL of methylene chloride over 1 h. After the cooling bath was removed, stirring was continued for 1 h; the colorless mixture was then extracted with two 10-mL portions of cold, saturated sodium bicarbonate solution and dried over potassium carbonate. The solution started to turn pale yellow, and the solvent was removed on a rotary evaporator to give 0.4 g of a solid contaminated with a light brown liquid. The solid was separated and washed quickly with cold pentane. ***cis*-1-Hydroxy-2,2,7a-trimethylcyclopenta[*d*]tetrahydro-1,3-oxazine (25)** was an unstable solid: mp 78–80 °C; NMR (CCl_4) δ ~1.3 (broad s, 9 H, $C(CH_3)_2$ and C–CH_3), 3.4 and 3.8 (q, $J_{AB} \cong 12$ Hz, $CHCH_2$–O, lines broadened); IR (CCl_4) 3600 (strong), 3450 (br), 1465, 1420, 1370, 1360, 1245 cm^{-1}.

The solid was taken up in 20 mL of methanol and stirred (under air) with 10 mg of cupric acetate monohydrate for 30 min at 25 °C. The solvent was evaporated under reduced pressure, and the product was extracted into pentane. Concentration gave 0.36 g of a brown oil, the **nitroxide 26:** the NMR spectrum showed broadened lines at approximately the same chemical shift as observed with **25;** mass spectrum calcd for $C_{10}H_{18}NO_2$ 184.1337, found 184.1344.

***cis*-[2-(Hydroxylamino)-2-methylcyclopentyl]methyl Formate (28), *cis*-(2-Nitroso-2-methylcyclopentyl)methyl Formate (29), and Dimer.** To a solution of 0.2 g (1.3 mmol) of tetrahydrooxazine **2** in 4 mL of methylene chloride at 0–5 °C, kept under a nitrogen atmosphere, was added dropwise with stirring a solution of 0.28 g (1.3 mmol) of MCPBA (80%) in 5 mL of methylene chloride. The cooling bath was removed, and the blue solution was allowed to stir for 1 h. After rapid filtration through an alumina column with a chloroform eluent in the usual manner (extraction with saturated sodium bicarbonate solution was equally effective), the combined eluent was concentrated on a rotary evaporator to give 0.2 g of a blue oil. Examination by TLC (silica gel, 20% acetone in hexane), NMR, and IR showed a mixture of starting material **2, 28,** and some **29.**

Further oxidation of the blue-colored mixture with 0.4 g of MCPBA was carried out for 1 h. Workup as described above gave 0.2 g of blue nitroso formate **29** (by TLC): NMR ($CDCl_3$) δ 1.0 (s, C–CH_3), 4.4 (d, $J \cong 7$ Hz, $CHCH_2$–O), 8.0 (s, OCHO).

After standing overnight in the refrigerator, colorless crystals of the dimer were present: IR ($CHCl_3$) 1725 (OC=O), 1550 (–NO monomer), 1270 (dimer), 1180 (C–O–C) cm^{-1}; NMR ($CDCl_3$) δ 1.6 (s, C–CH_3), 4.0 (d, $J \cong 7$ Hz, $CHCH_2$–O), 8.2 (s, OCHO).

Within 5 min at 25 °C a solution containing **29** and its dimer was observed. Similar results were obtained when the oxidation of **2** (0.2 g, 1.3 mmol) was carried out with 2 equiv of MCPBA (0.56 g, 80%, 2.6 mmol).

***cis*-(2-Nitro-2-methylcyclopentyl)methyl Formate (30).** A solution of 0.03 g (0.08 mmol) of the dimer of **29** in 3 mL of methylene chloride was added dropwise with stirring to a solution of 0.07 g (0.16 mmol) of MCPBA (80%) in 2 mL of methylene chloride maintained at 0–5 °C under nitrogen. The cooling bath was removed, and stirring was continued overnight. After the usual workup, 0.03 g of **30** was obtained as a pale yellow oil: IR 1735 (–OC(=O)H), 1540 (–NO_2) cm^{-1}; NMR (CCl_4) δ 1.73 (s, C–CH_3), 4.15 (d, $J \cong 7$ Hz, $CHCH_2$–O), 7.98 (s, OCHO).

1-*tert*-Butyl-3,3,6-trimethyl-3a,4,5,6,7,7a-hexahydro-2,1-benzisoxazoline (22). A solution of 7.2 g (47 mmol) of freshly distilled citronellal and 4.5 g (50 mmol) of *N*-*tert*-butylhydroxylamine in 200 mL of ether was stirred overnight with 75 g of anhydrous sodium sulfate. After filtration, the solvent was removed at reduced pressure and the residue was distilled to give 10.2 g (97%) of a pale yellow oil, bp 110–112 °C (0.65 torr), identified as ***N*-(3,7-dimethyl-6-octen-1-ylidene)-2-methyl-2-propanamine *N*-oxide:** NMR (CCl_4) δ 0.95 (d, $J \cong 6.5$ Hz, $CHCH_3$), 1.43 (s, $C(CH_3)_3$), 1.61 and 1.70 (2 br s, $C{=}C(CH_3)_2$), 1.97 (m, 2 H), 2.33 (m, 2 H), 5.11 (t of septets, $J = 7$ Hz, CH=C), 6.83 (t, $J = 6.5$ Hz, CH=N).

Anal. Calcd for $C_{14}H_{27}NO$: C, 74.61; H, 12.07; N, 6.21. Found: C, 74.78; H, 12.13; N, 5.96.

A solution of 100 g (0.44 mol) of the *N*-*tert*-butyl nitrone in 2 L of mesitylene was refluxed for 8 h. The dark brown solution was extracted with three 100-mL portions of 10% hydrochloric acid, and the combined extracts were washed with two 100-mL portions of ether and basified to pH 12 with 10% potassium hydroxide. The oil was extracted with three 100-mL portions of ether, and the combined extract was dried over potassium carbonate and concentrated at reduced pressure. The residue was distilled to give 40.4 g (40%) of isoxazolidine **22** (as a mixture of stereoisomers; about 65% trans,trans and 32% cis,trans), bp 60–65 °C (0.5 torr). A portion was redistilled for analysis.

Anal. Calcd for $C_{14}H_{27}NO$: C, 74.61; H, 12.07; N, 6.21. Found: C, 74.76; H, 12.05; N, 6.32.

The mesitylene layer from the above reaction was examined and found to contain the oxime of citronellal, formed presumably by a Cope-type elimination from the nitrone.

Hydrogenolysis of 16 to 1,3-Diphenylpropane. A solution of 0.70 g (2.7 mmol) of tetrahydrooxazine **16** in 8 mL of ethyl acetate was added to a suspension of 0.55 g of palladium–carbon catalyst in 40 mL of glacial acetic acid containing 2 drops of concentrated sulfuric acid. The mixture was hydrogenated in a Parr apparatus for 36 h at 55 psig. The mixture was filtered, concentrated to about 5 mL, basified with 15% NaOH solution, and extracted with several volumes of ether. The combined extract was washed once with saturated sodium bicarbonate, dried over anhydrous potassium carbonate, and filtered. Evaporation of solvent gave 0.61 g of a pale yellow liquid. The material was dissolved in pentane and filtered through a short alumina column with pentane as eluent. Removal of the solvent afforded 0.3 g of a liquid which was homogeneous by TLC (silica gel, ethyl acetate). It was identified as 1,3-diphenylpropane by comparisons of NMR and IR spectra.[13]

Acknowledgment. This work was supported, in part, by the National Science Foundation under Grant No. GP14114. We are indebted to Mr. L. Baczynsky of the Upjohn Co., Kalamazoo, Mich., for the exact mass determination of *N*-oxy **26.**

Registry No.—**1,** 69575-65-1; **2,** 69502-83-6; **3,** 69502-84-7; **4** isomer 1, 69502-85-8; **4** isomer 2, 69515-88-4; **5,** 69502-72-3; **6,** 69502-77-8; **7,** 69502-73-4; **8,** 69502-78-9; **9,** 69502-74-5; **10,** 69502-79-0; **11,** 69575-64-0; **12,** 69502-80-3; **13,** 69502-75-6; **14,** 69502-81-4; **15,** 69502-76-7; **16,** 69502-82-5; **17,** 69502-58-5; **21,** 69502-59-6; **21** methyl acrylate adduct, 69502-60-9; **22** isomer 1, 69502-61-0; **22** isomer 2, 69515-87-3; **23,** 69502-62-1; **24,** 69502-63-2; **25,** 69502-64-3; **26,** 69502-65-4; **28,** 69502-66-5; **29,** 69502-54-1; **29** dimer, 69508-42-5; **30,** 69502-55-2; methyl acrylate, 96-33-3; formaldehyde dimedone, 2181-22-8; methone, 126-81-8; *N*-methyl-*exo*-*cis*-3-(1-amino-1-phenylethyl)-2-norbornanol, 69502-56-3; 3-methylcyclohexanone, 591-24-2; 3-methylcyclohexanone 2,4-dinitrophenylhydrazones, 486-46-4; *N*-*tert*-butylhydroxylamine, 16649-50-6; citronellal, 106-

23-0; *N*-(3,7-dimethyl-6-octen-1-ylidene)-2-methyl-2-propanamine *N*-oxide, 69502-57-4.

References and Notes

(1) For recent reviews, see (a) D. S. C. Black, R. F. Crozier, and V. C. Davis, *Synthesis*, 205 (1975); (b) A. Padwa, *Angew. Chem., Int. Ed. Engl.*, **15**, 3 (1976); W. Oppolzer, *ibid.*, **16**, 10 (1977).
(2) N. A. LeBel and L. A. Spurlock, *J. Org. Chem.*, **29**, 1337 (1964).
(3) N. A. LeBel, *Trans. N.Y. Acad. Sci.*, **27**, 858 (1965).
(4) N. A. LeBel, M. E. Post, and J. J. Whang, *J. Am. Chem. Soc.*, **86**, 3759 (1964).
(5) (a) R. R. Fraser and Y. S. Lin, *Can. J. Chem.*, **46**, 801 (1968); (b) R. Grashey, R. Huisgen, and H. Leiterman, *Tetrahedron Lett.*, 9 (1960); (c) R. Huisgen, R. Grashey, H. Hauck, and H. Seidl, *Chem. Ber.*, **101**, 2043 (1968).
(6) R. Huisgen, R. Grashey, H. Hauck, and H. Seidl, *Chem. Ber.*, **101**, 2548 (1968).
(7) T. D. Lee and J. F. W. Keana, *J. Am. Chem. Soc.*, **97**, 1273 (1975); *J. Org. Chem.*, **41**, 3237 (1976). See also M. Guyot and M. Dvolaitzky, *J. Chem. Res. (M)*, 1734 (1977).
(8) A. Rassat and P. Ray, *Tetrahedron*, **30**, 3315 (1974).
(9) The *N*-isopropyl analogue of **15** is oxidized with MCPBA to afford the 2,2-dimethyl derivative of **16** as the major product, rather than the *N*-isopropyl nitrone from proton transfer toward the phenyl group: M. J. Cuba, unpublished observations.
(10) J. J. Tufariello and G. B. Mullen, *J. Am. Chem. Soc.*, **100**, 3638 (1978).
(11) In ref 2, a *N*-methylisoxazolidine was reacted with peracetic acid in acetic acid solvent, and aqueous acid hydrolysis afforded 8-oxobicyclo[3.2.1]-octan-2-ol in 40% yield. When the same isoxazolidine was oxidized with MCPBA in CH_2Cl_2, two major products were observed, one of which was the unstable *N*-hydroxytetrahydro-1,3-oxazine arising from a methylene nitrone.
(12) E. C. Horning and M. G. Horning, *J. Org. Chem.*, **11**, 95 (1946).
(13) D. L. Ransley, *J. Org Chem.*, **33**, 1517 (1968).

Structure Elucidation of Tetrazolo[5,1-*c*]benzo-*as*-triazine. An Interesting Ternary Equilibrium of Tetrazole–Azide Systems

András Messmer,* György Hajós, József Tamás, and András Neszmélyi

Central Research Institute for Chemistry of the Hungarian Academy of Sciences, H-1525 Budapest, Hungary

Received July 5, 1978

The title equilibrium has been studied by UV, MS, and NMR. The originally proposed angular structure tetrazolo[5,1-*c*]benzo-*as*-triazine (**3**) is the major component both in solution and in the solid state. By means of ^{13}C NMR spectroscopy, an interesting ternary equilibrium was detected in Me_2SO which involves **3** as the main component (64%), in addition to **2** (25%) and **4** present in smaller amounts (10%).

We have recently reported[1] that 3-hydrazinobenzo-*as*-triazine (**1**) can be converted by nitrous acid to tetrazolo[5,1-*c*]benzo-*as*-triazine (**3**) through the intermediate formation of 3-azidobenzo-*as*-triazine (**2**) (Scheme I). The tetrazole compound **3** proved to be stable in crystalline form, and its infrared spectrum recorded in potassium bromide showed no azide band. In solution, however, both azidobenzo-*as*-triazine (**2**) and tetrazolo[5,1-*c*]benzo-*as*-triazine (**3**) could be detected. Theoretically, another direction of ring closure toward the N-2 atom may be assumed in which case the linearly arranged tetrazolo[1,5-*b*]benzo-*as*-triazine (**4**) would form. This alternative was excluded since cyclization of **2** to **4** would involve the destruction of the benzenoid ring of the benzo-*as*-triazine moiety. In the case of the angular structure proposed by us, however, the aromatic sextet of the benzene ring of benzo-*as*-triazine is retained.

Several examples are known from the literature[2] where, in similar cases, the more benzenoid derivative is formed mainly or exclusively.

Shortly after our publication, Paudler et al.[3] found that the single-ring 3-azido-*as*-triazine derivatives **7** give rise to tetrazolo[1,5-*b*]-*as*-triazine compounds **8a** by a ring closure toward the N-2 atom. In no case was any cyclization toward the N-4 atom observed which would have resulted in tetrazolo[5,1-*c*]-*as*-triazine (**8b**), analogous to our case. On the basis of this observation, the above authors concluded that the structure of tetrazolobenzo-*as*-triazine (**3**), proposed by us, may not be correct and suggested reinvestigation of the problem.

Our original proposal for the structure of the tetrazole compound **3** was well supported by a simple UV study. The UV spectrum of the tetrazole compound in question was compared with that of the two possible tetrazoloisoquinolines: the angular tetrazolo[5,1-*a*]isoquinoline (**9**),[4] which occurs in solution only in the tetrazole form, and the linear tetrazolo[1,5-*b*]isoquinoline (**10**),[5] which is, in ethanol and dimethyl sulfoxide solutions, in equilibrium with the azide isomer

Scheme I