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Optical Rotatory Dispersion Studies. CXVIII.[1] Aliphatic *C*-Nitroso Compounds[2]

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Methods for synthesizing the unique blue *C*-nitroso chromophore attached to secondary aliphatic carbon atoms have been improved and the optical properties of this group in important steric environments (steroids and terpenoids) have been measured. The isolation of the pure blue monomers can be achieved in a few cases only, but measurement of circular dichroism spectra of the total reaction mixture gives absorption bands with value in diagnosing the orientation of the chromophore, since none of the other components absorbs in the visible region.

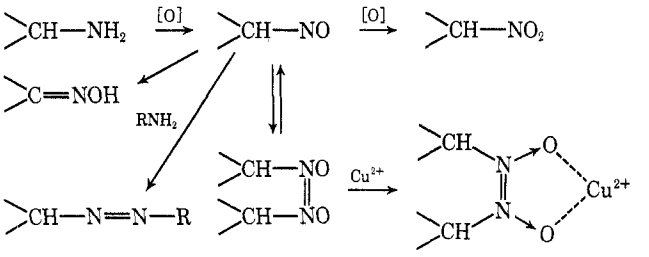
Part A

Monomeric aliphatic *C*-nitroso compounds are virtually unique in organic chemistry because of their deep color which results from absorption at 660–700 mμ.[4] Because of their ease of detection, nitroso derivatives were widely studied prior to 1920[5] but principally as tertiary *C*-nitroso compounds, which are incapable of tautomerization. Primary and secondary representatives have received only scant study because of difficulties in handling these very reactive (normally only transient) species.

The nitroso chromophore can be derived from aliphatic and alicyclic oximes,[4-6] amines,[4,7] and olefins[4,8] (by reaction with NOCl). Since none of these groups is readily amenable to optical investigations, whereas the long wavelength absorption of the nitroso function is readily distinguishable and may be measured in the presence of any other organic chromophore, we decided to examine the feasibility of employing *C*-nitroso compounds as "chromophoric derivatives."[9]

Nonhalogenated *C*-Nitroso Derivatives.—Those *C*-nitroso derivatives attached to a carbon atom carrying no further heteroatoms were synthesized by the sequence ketone → oxime → amine → nitroso. Following standard methods, the oxime reductions were carried out using sodium in alcohol to yield equatorial amines and by hydrogenation to yield axial amines.[10-12]

Nitroso monomers can be generated by oxidation of a primary amine,[7] but great care must be exercised, since, as summarized in the following scheme, overoxidation yields nitro derivatives, dimerization is facile, and tautomerization to oximes also can occur when the carbon carries a hydrogen atom[13] and the presence of



inorganic ions such as Cu^{2+} appears to lead to colored chelated forms of the nitroso dimer.

Results

Even with the improved methods of synthesis, it proved difficult in practice to get spectra with reproducible intensities because of the reactivity of the nitroso monomers, but qualitatively reproduction of the Cotton effects created no difficulties. Despite the manipula-

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(1) For part CXVII, see G. Barth, W. Voelter, H. S. Mosher, E. Bunnenberg, and C. Djerassi, *J. Amer. Chem. Soc.*, **92**, 875 (1970).

(2) Financial assistance (Grant No. AM-12758) from the National Institutes of Health is gratefully acknowledged.

(3) National Institutes of Health Postdoctoral Fellow, Stanford University, 1968–1969.

(4) B. G. Gowenlock and W. Luttke, *Quart. Rev. (London)*, **12**, 321 (1958).

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(6) D. C. Iffland and G. X. Criner, *J. Amer. Chem. Soc.*, **75**, 4047 (1953).

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(8) W. A. Tilden and J. J. Sudborough, *J. Chem. Soc.*, **63**, 479 (1893).

(9) C. Djerassi, *Proc. Chem. Soc.*, 314 (1964).

(10) C. W. Shoppee, R. J. W. Cremlyn, D. E. Evans, and G. H. R. Summers, *J. Chem. Soc.*, 4364 (1957).

(11) C. W. Shoppee, D. E. Evans, H. C. Richards, and G. H. R. Summers, *ibid.*, 1649 (1956).

(12) E. B. Hershberg, E. P. Oliveto, and R. Rauser, *Chem. Ind. (London)*, 1477 (1958).

(13) C. H. Robinson, L. Milewich, and P. Hofer, *J. Org. Chem.*, **31**, 524 (1966).

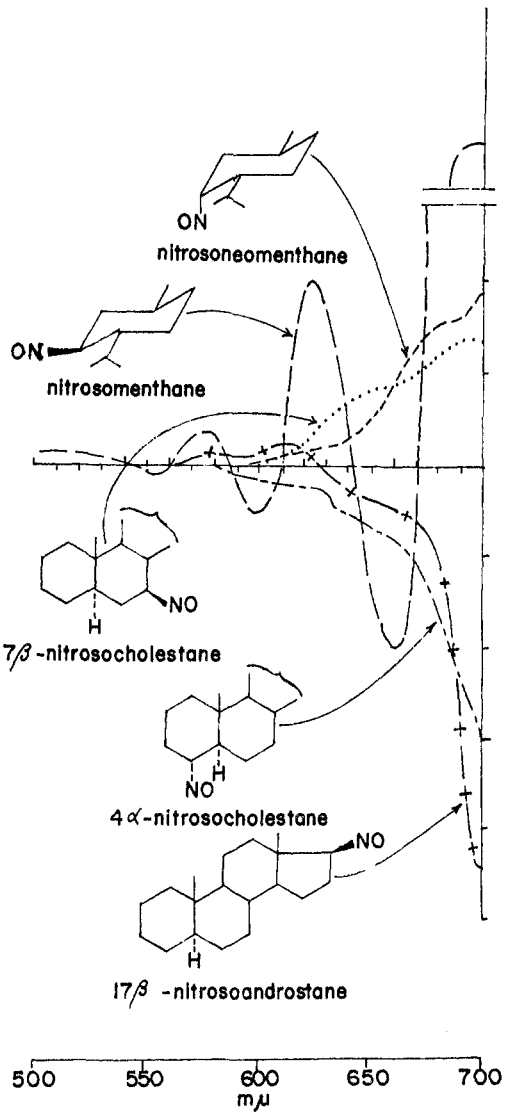
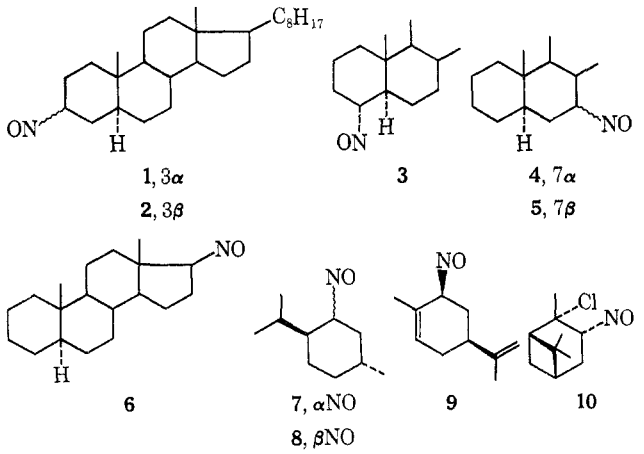


Figure 1.—Circular dichroism of nitroso derivatives in dichloromethane solution (amplitude differences between curves do not reflect molecular ellipticity differences).

tive complications, spectra of a representative group of optically active nitroso derivatives were obtained. The results are shown in Table I and a selection of spectra in Figure 1.



The spectra demonstrate that the nitroso chromophore is influenced by an optically active environment and can show sign inversions and differences in peak shape. Based on these findings, the *C*-nitroso chromophore holds definite promise for the conversion of amines to a readily observable, optically active group with a CD spectrum characteristic of the amine's environment. No amplitude information is determinable for the circular dichroism absorptions in Table I as the monomeric compounds are too unstable for isolation. Estimates of concentration from ultraviolet absorption studies were foiled by the inability to measure the absorption due to the weakness of the chromophore and our inability to concentrate the highly reactive monomers.

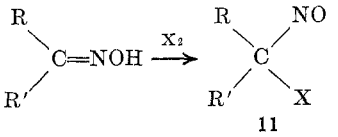
TABLE I

CIRCULAR DICHROISM OF OPTICALLY ACTIVE *C*-NITROSO COMPOUNDS

Compd	Sign	Position, mμ
3α-Nitrosocholestane[a] (1)	−	685
3β-Nitrosocholestane (2)	+	700
	−	675
4α-Nitrosocholestane[a] (3)	−	700
7α-Nitrosocholestane[a,b] (4)	+	690
	+	640
7β-Nitrosocholestane[a,b] (5)	+	695
	Inflection	650
17β-Nitroso-5α-androstane (6)	−	700
	−	650
	+	620
Nitrosomenthane (7)	+	690
	−	660
	+	625
	−	600
	+	575
	−	555
Nitrosoneomenthane (8)	+	700
	+	680
	+	625
Nitrosocarvodiene[c] (9)	−	700
	−	630
α-Pinene nitrosochloride (10)	+	695
	+	620

[a] The amines used to synthesize these derivatives were kindly supplied by Professor C. W. Shoppee, University of Sydney. [b] 7α- and 7β-nitrosocholestanes can be readily distinguished by their shorter wavelength CD absorptions; 7β shows minimum at 322 and maximum at 280 mμ, whereas 7α shows maximum at 330 and minimum at 294 mμ. [c] Synthesized from carvone *via* carvylamine.

α-Halogeno-*C*-nitroso Compounds.—The production of blue products (formulated as **11**) from oximes by the addition of bromine or chlorine has been known since the last century.[4] The bulkiness of the halogen atom represses dimerization and isomerization to oximes is inhibited in these compounds by the lack of a tautom-



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X = Br, Cl, NO_2

erizable hydrogen atom. Since such α-halonitroso derivatives promised to overcome many of the difficulties associated with their unsubstituted counterparts covered in the previous section, a series of them was subjected to CD analysis.

The steroidal nitrosobromides were synthesized from the corresponding oxime by careful treatment of a cold

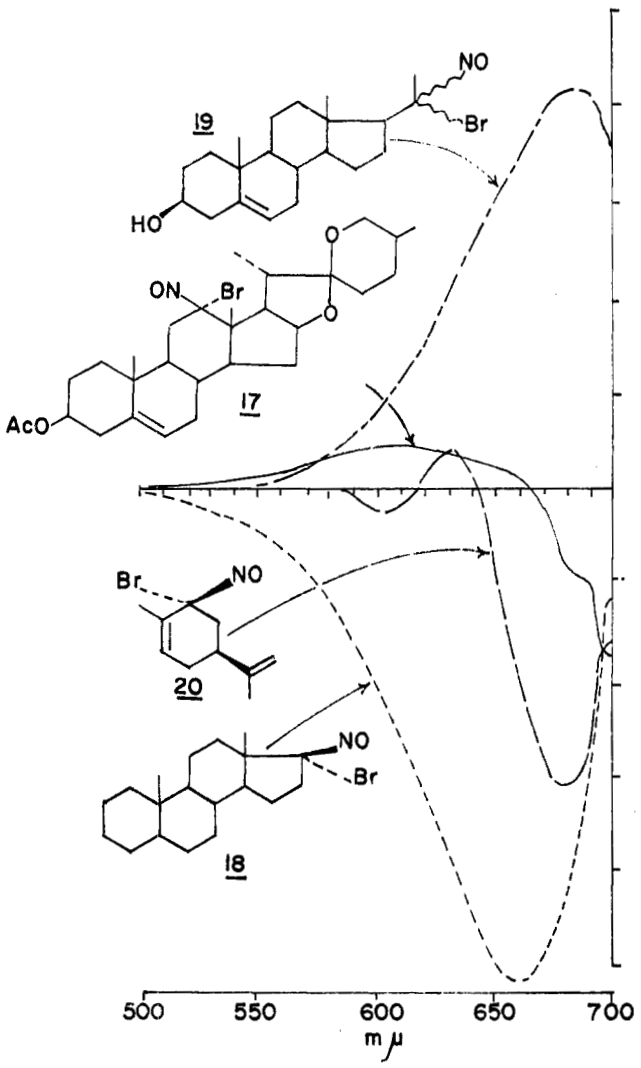


Figure 2.—Circular dichroism of geminal nitrosobromide derivatives in ethanol solution (amplitude differences between curves do not reflect molecular ellipticity differences).

pyridine–ethanol solution with a cold suspension of *N*-bromosuccinimide in ethanol. Spectra were run within 10 min of the addition and the solutions were filtered and maintained at 0° before measurement.

Bromination of oximes at the 7, 11, 12, 17, and 20 positions gave blue nitroso compounds, whose absorption band was readily discernible in the CD spectrometer. Normal work-up procedures, however, yielded colorless (and, in the case of C-20, rearranged) products. Cholestan-3-one ketoxime however yielded stable crystalline monomeric material on work-up. This material was isolated as deep blue crystals, unique for a steroid. Because of facile decomposition, however, even this compound could not be obtained in analytical purity.

The stereochemistry of these compounds is undoubtedly that in which the halogen atom occupies an axial position as the synthesis requires that the halogen approach the double bond of the oxime, and it is well known[14] that such approach is from the axial side in similar functional groups such as ketones.

CD Results.—Table II and Figures 2 and 3 show typical CD measurements for the products. The

(14) T. F. Gallagher and T. H. Kritchevsky, *J. Amer. Chem. Soc.*, **72**, 882 (1950).

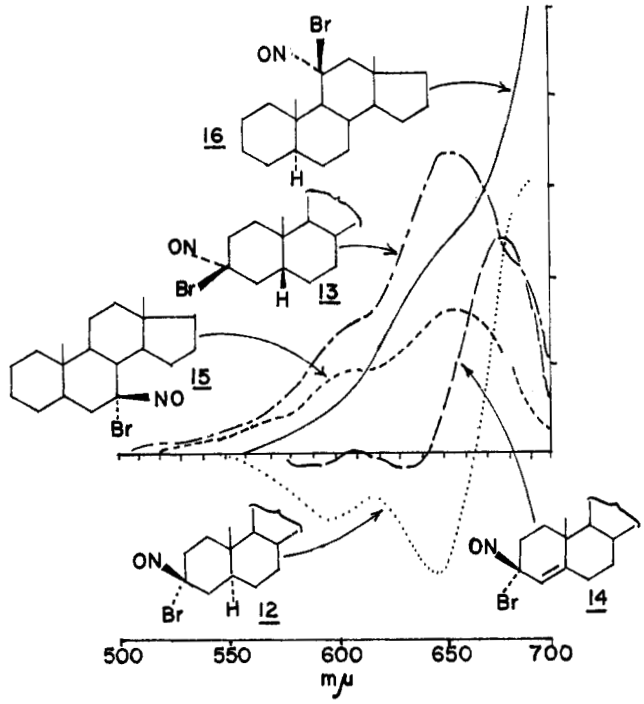


Figure 3.—Circular dichroism of geminal nitrosobromide derivatives in ethanol solution (amplitude differences between curves do not reflect molecular ellipticity differences).

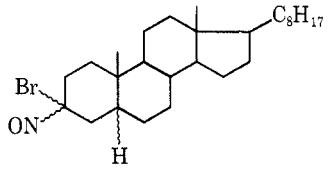
TABLE II
CIRCULAR DICHROISM OF *gem*-NITROSO HALOGEN COMPOUNDS

Compd	Sign of CD absorption	Position mμ
3α-Bromo-3β-nitroso-5α-cholestane (**12**)	+	694
	−	645
	Inflection	615
	Inflection	594
3β-Bromo-3α-nitroso-5β-cholestane (**13**)	Inflection	690
	+	655
	Inflection	620
	Inflection	570
17β-Hydoxy-3α-bromo-3β-nitroso-Δ⁴-androstene (**14**)	+	680
	−	635
	+	610
	−	590
7α-Bromo-7β-nitroso-5α-cholestane (**15**)	+	660
	Inflection	625
	+	610
	Inflection	570
11β-Bromo-11α-nitroso-5α-androstane (**16**)	+	700[a]
	Inflection	660
	+	640
	Inflection	610
12α-Bromo-12β-nitrosotigogenin acetate (**17**)	−	700[a]
	Inflection	690
	+	610
17α-Bromo-17β-nitroso-5α-androstane (**18**)	−	660[b]
3β-Hydroxy-20-bromo-20-nitroso-Δ⁵-pregnene (**19**)	+	685[b]
2-Bromo-2-nitrosocarvo-6,8-diene (**20**)	−	678
	+	632
	−	604

[a] Maximum absorption beyond the limits of our instrument. [b] Spectrum showed no fine structure.

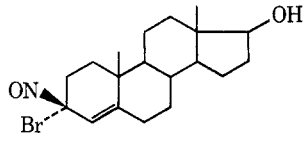
nitroso absorption shows shape and sign individuality characteristic of the position of the chromophore on the steroid nucleus, and the production of nitroso absorption promises to be useful in the examination of the asymmetric environment around a ketone group. Such analyses including synthesis and measurement can be carried out in less than 1 hr.

As with the nitroso derivatives obtained by oxidation of amines, no statement can be made about the intensities of the CD absorptions for the various compounds, as in most cases the monomeric materials are too transitory for isolation. This will probably continue to be the major drawback to this method of investigating asymmetry.



12, 5α H, 3α Br, 3β NO

13, 5β H, 3β Br, 3α NO



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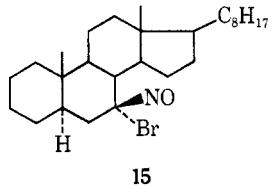

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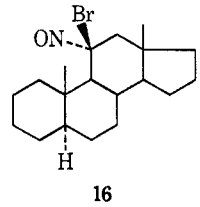

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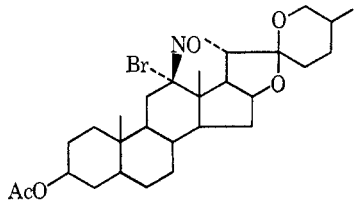

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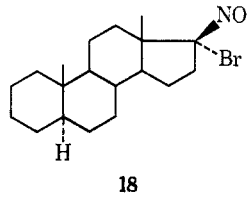

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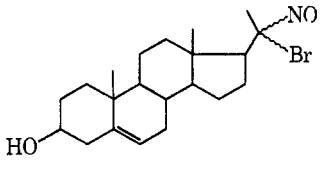

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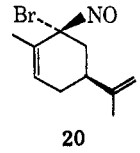

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Part B

Experimental Section

A Japan Spectroscopic Co. spectropolarimeter (Durrum-JASCO Model ORD-UV-5) was used for the CD measurements, which were measured by Mrs. Ruth R. Records.

Oxidation of *tert*-Butylamine.—When using 96% *m*-chlorobenzoic acid[15] as an oxidant for *tert*-butylamine, satisfactory blue color was obtained using the following solvents: $CHCl_3$, CH_2Cl_2, CCl_4, dioxane, tetrahydrofuran, pyridine, dimethylformamide, acetone, 2,2-dimethoxypropane, nitromethane, 1-propanol, 2-propanol, 1-butanol. All of these solvents, however, gave cloudy precipitates of *m*-chlorobenzoic acid which made the solutions unsatisfactory for direct spectral measurement. Although solutions of nitroso compounds such as this *tert*-butyl example can be filtered without loss of color, the same is not true for compounds such as nitrosocyclohexane in which the nitroso function is attached to a secondary carbon.

The use of 40% peracetic acid as oxidant yielded more satisfactory product solutions as no precipitate was formed and strong colors were formed when *tert*-butylamine was treated as above with this reagent, particularly in alcohol solution. Water and the liberated acetic acid could be removed using solid anhydrous sodium carbonate in the reaction mixture.

The following example is typical of these experiments. To a 50-ml erlenmeyer flask was added 1 g (13.7 mmol) of *tert*-butylamine and 20 ml of *n*-propyl alcohol. The solution was stirred vigorously and chilled to −10° in an ice–methanol bath. To this cold solution was added 3.6 ml (28 mmol) of a similarly chilled solution of 40% peracetic acid and 5 ml of *n*-propyl alcohol. The reaction mixture turned deep blue and the color remained during several days of standing at room temperature.

Oxidation of Cyclohexylamine.—The oxidation of cyclohexylamine was carried out in the manner of the above sequence. Colors were found for all of the solvents used for the oxidation of *tert*-butylamine. In addition acetonitrile, ether, ethyl acetate, *tert*-butyl alcohol, and a mixed solvent with pyridine, the peracid, and methylene chloride could all be used as for the reaction solvent. The reaction was best carried out at between −10 and 0° and color was retained longest in *n*-propyl alcohol or acetonitrile. Oxidant could be added in solution or neat without significant difference in the depth of color produced.

Preparation of Oximes.—All oximes were prepared by refluxing (15 min) the corresponding ketone with 1.5 equiv of hydroxylamine hydrochloride in an alcohol solution containing about 1% pyridine. Steroidal oximes were concentrated to dryness and recrystallized. The solutions of oximes of lower molecular weight were concentrated, diluted with chloroform, washed with water and saturated sodium chloride solution, dried ($MgSO_4$), and evaporated.

Reduction of Oximes with Sodium in Alcohol.—A standard procedure following Haworth[16] was used in all cases. The oxime in refluxing *n*-propyl alcohol was treated during 2 hr with a large excess (up to tenfold) of sodium spheres.[16] The cooled reaction mixture was then diluted with ether or chloroform, washed thoroughly with water, and, in the case of steroidal materials, evaporated, and recrystallized. Nonsteroidal amines were extracted from the organic layer using 10% hydrochloric acid solution and after washing with ether the acidic solution was treated with concentrated ammonia solution until basic and extracted with ether. The ether solution was dried ($MgSO_4$) and evaporated to yield the free amine. Amine hydrochlorides were prepared by precipitation from an ether solution of the amine using dry hydrogen chloride gas.

3α-Amino-5α-cholestane and **3β-amino-5α-cholestane** were synthesized according to the literature directions.[10,11]

17β-Amino-5α-androstane.—Dihydrotestosterone was reduced to 5α-androstan-17β-ol by the method of Nagata and Itazaki.[17] Oxidation of this product by the method of Jones[18] yielded androstan-17-one, the oxime of which was reduced by sodium in alcohol to 17β-amino-5α-androstane.[19]

Neomenthylamine[20] was synthesized by treating menthyl tosylate with lithium azide[21] by the method of Smith[22] and reducing the azide produced with lithium aluminum hydride.

Menthylamine (3-amino-*p*-menthane)[20] **and carvylamine (3-amino-*p*-mentha-1,8-diene)**[23] were synthesized by the reduction of menthane and carvone oximes with sodium in alcohol.

α-Pinene nitrosocholoride[24] was synthesized from α-pinene [$[\alpha]_D$ +39.6° (neat)] by treatment with nitrosyl chloride.[5,24]

Bromination of Oximes for CD Measurement.—The following example is typical. To a 50-ml erlenmeyer flask was added 100 mg of carvone oxime (0.6 mmol), 150 μl. of pyridine (1.86 mmol), and 20 ml of ethanol. The solution was chilled to 0° and 220 mg (1.23 mmol) of *N*-bromosuccinimide added. The deep green solution was kept in an ice bath until ready for measurement (less than 1 hr). The solution was filtered through a small pad of cotton using a pipet immediately prior to adding to the spectrometer cell.

(15) Pilot Chemical Company, London Road, Ware, Herts., England.

(16) D. P. Dodgson and R. D. Haworth, *J. Chem. Soc.*, 67 (1952).

(17) W. Nagata and H. Itazaki, *Chem. Ind. (London)*, 1194 (1964).

(18) A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 2555 (1953).

(19) C. W. Shoppee and J. C. P. Sly, *ibid.*, 345 (1959).

(20) J. Read and R. A. Storey, *ibid.*, 2761 (1930).

(21) R. L. Huisgen and I. Ugi, *Chem. Ber.*, **90**, 2914 (1957).

(22) (a) E. H. Massey, H. E. Smith, and A. W. Gordon, *J. Org. Chem.*, **31**, 684 (1966); (b) A. K. Bose, S. Harrison, and L. Farber, *ibid.*, **28**, 1223 (1963).

(23) A. Mailhe, *Bull. Soc. Chim. Fr.*, **33**, 83 (1923).

(24) E. V. Lynn, *J. Amer. Chem. Soc.*, **41**, 361 (1919).

Bromination of 5α-Cholestanone Oxime.—A sample of cholestanone oxime (1 g, 2.58 mmol) was synthesized in 1:1 ethanol–hexane solution containing a small amount of water by the addition of hydroxylamine hydrochloride, 180 mg (2.58 mmol), and 1.095 μl (7.74 mmol) of pyridine. The two-phase system was treated with 920 mg (5.06 mmol) of solid *N*-bromosuccinimide and stirred 15 min. The reaction product was diluted with pentane and the upper layer separated and concentrated on a steam bath. During the concentration acetone was added; cooling of the product solution in a refrigerator gave blue crystalline needles of 3α-bromo-3β-nitroso-5α-cholestane (**12**), mp 135–138° (three recrystallizations from methanol): nmr (δ ppm from TMS) 0.64 (methyl), 0.82 (methyl), 0.87 (methyl), 0.91 (methyl). Further purification of this product by preparative thin layer chromatography failed to yield an analytical sample because of its facile decomposition.

Results and Discussion

Nonhalogenated Nitroso Compounds.—In our initial experiments, we employed 96% *m*-chloroperbenzoic acid at −10° in methylene chloride solution, with solid calcium carbonate in order to neutralize the *m*-chlorobenzoic acid formed in the reaction. This standard[7b] reagent mixture was drastically changed during the course of our work because of the necessity of recording the spectra and circular dichroism of the nitroso compounds directly on the crude reaction solution. The chlorobenzoic acids both have low solubility in methylene chloride below 0° and cause fogging of the solution in the spectrometer. This could be overcome, however, by using peracetic acid as oxidant or by changing the solvent to an alcohol. Contrary to literature suggestions[4,25] that the tautomerism from nitroso to oxime is facilitated by polar solvents, it was found on test samples of nitrosocyclohexane that this chromophore could be prepared and maintained at −30° (ice–methanol bath) in chlorocarbon solvents, alcohols, ethers, benzene, pyridine, and dimethylformamide for 30 min without fading.

During attempts at measuring the CD absorption of the reaction solution containing nitrosomenthane at low temperature it was noticed that the brass cell imparted a deep blue color to the solution. This color could also be produced by the addition of cupric sulfate to the reaction mixture. The cause of the color (soluble in water and organic solvents) is possibly a chelate of the nitroso dimer. This product was stable (detection by color only) during 1 year in a refrigerator. This blue solution showed a broad diffuse CD absorption in the visible region and a sharp band at 370 mμ. The nitroso grouping has the ability to rotate freely and will do so in these saturated compounds, but the occurrence of the chelating phenomenon made low temperature analysis for rotation of the nitroso products impossible.

The configuration of the nitroso group is probably that of the parent amine, as the nitro groups produced by overoxidation in the same synthesis as used here have been shown to retain configurational identity.[13]

Strong bands occur at 300 mμ in the spectra of the reaction mixtures, but at this time it is not known if these are due to $\pi-\pi^*$ absorption in the monomer or in the dimer which is undoubtedly present also. The CD spectrum of the dimer from nitrosomenthane is shown in Figure 4 for reference purposes to illustrate the spectral characteristics of the pure dimer.

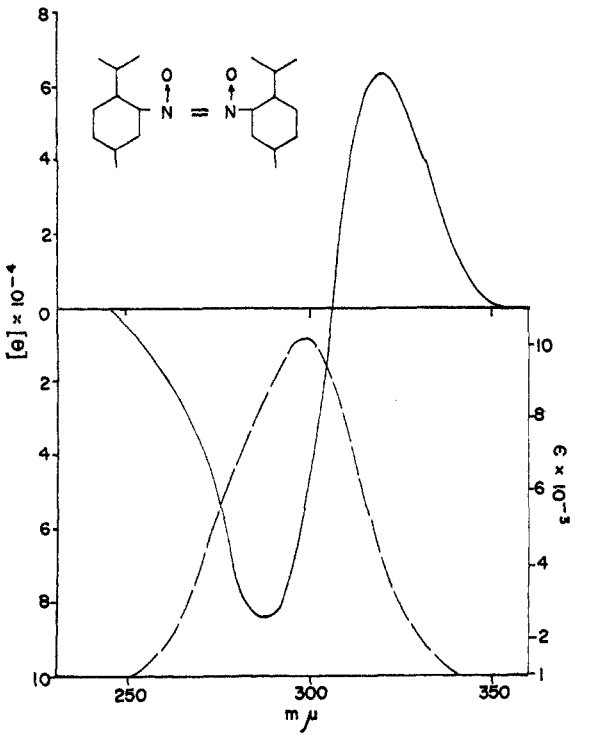
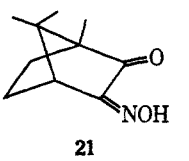


Figure 4.—Circular dichroism and ultraviolet spectrum of nitrosomenthane dimer in hexane solution.

Geminal Nitroso–Halogen Compounds.—Measurement of the geminal nitroso–halogen chromophores was first reported by Mitchell in 1940[26] with the curve of a menthol ester which showed very similar characteristics to those reported here.

We found that the synthesis of such derivatives can be conducted conveniently with *N*-bromosuccinimide, *N*-chlorosuccinimide, *N*-bromoacetamide, as well as fuming nitric acid and dinitrogen tetroxide (both of which give α-nitronitroso compounds). The reaction failed to yield visible blue color with iodine, *N*-iodosuccinimide, and cyanogen bromide. Isolation of the oxime is generally not necessary as the conversion of ketone to oxime can be carried out in virtually quantitative fashion. Syntheses of nitroso derivatives from acetone oxime (as a test material) could be carried out in alcohols, pyridine, ethers, and chlorocarbon solvents and were best carried out below 0°.

Cyclohexenone, carvone, benzophenone, salicylaldehyde, nitrosocamphor (**21**) propionaldehyde, and pentane-2,4-dione gave no blue coloration when they were reacted under the conditions used for the cyclohexanones. However, at temperatures below 0° carvone



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(25) N. V. Sidgwick, "The Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 3rd ed, 1966, p 339.

(26) S. Mitchell and G. K. Simpson, *J. Chem. Soc.*, 784 (1940).

gave color distinguishable in the CD spectrometer, but warming to room temperature yielded only a yellow solution with no detectable CD absorption. On reducing the temperature of a solution containing **12** to −187°, the spectrum amplitude increased but no position changes were noticed.

Registry No.—**1**, 25630-12-0; **2**, 25630-11-9; **3**, 25558-52-5; **4**, 25630-13-1; **5**, 25558-53-6; **6**, 25554-40-9; **7**, 25554-41-0; **8**, 25554-42-1; **9**, 25554-43-2; **10**, 25554-44-3; **12**, 1912-59-0; **13**, 25554-46-5; **14**, 25554-47-6; **15**, 25554-48-7; **16**, 25554-49-8; **17**, 25554-50-1; **18**, 25554-51-2; **19**, 25554-52-3; **20**, 25554-53-4.

Azacoumarins[1]

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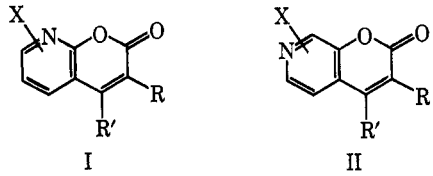
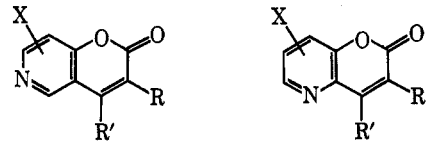
Eighteen azacoumarins were prepared by condensation of appropriate esters, acids, or anhydrides with *o*-hydroxypyridine aldehydes or ketones. This constitutes examples of all four possible types (I, II, III, and IV) of azacoumarins with N replacing CH of the benzene ring. Two 8-azaflavones and a number of intermediates and by-products are also reported.

Part A

Coumarins in which a CH group is replaced by a nitrogen can be called "azacoumarins." In a broad sense this could include the 2*H*-1,4-benzoxazin-2-ones[2] and 2*H*-1,3-benzoxazin-2-ones.[3] However, this paper comprises only those azacoumarins in which the nitrogen replaces a CH of the benzene ring (I, II, III, and IV). The literature contains only two references



I II



III IV

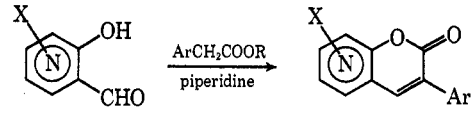
to 2*H*-pyranopyridin-2-ones,[4,5] both of which are of the [2,3-*b*] type, I. One of these[5] gives no information on the synthesis. Robinson and Watt[4] report the synthesis of 7-hydroxy-5-methyl-2*H*-pyrano[2,3-*b*]-pyridin-2-one (I, R and R′ = H; X = 7-OH, 5-CH_3) by the Pechmann synthesis from 2,6-dihydroxy-4-methylpyridine[6] and malic acid. This procedure was confirmed by our synthesis of the corresponding desmethyl analog **7**. However, in general, the Pechmann synthesis does not seem to work on monohydroxypyridines, doubtless because of the protonation of the pyridine ring by the strong acid used. The Kostanecki–Robinson modification of the Perkin reaction or the Knoevenagel reaction were found to be more generally applicable methods and examples of all four types of these azacoumarins were prepared. Types II, III, and IV appear to constitute new classes of compounds.

(1) Presented in part at the Great Lakes Regional Meeting of the American Chemical Society, Fargo, N. D., June 18–19, 1970.
(2) R. B. Moffett, *J. Med. Chem.*, **9**, 475 (1966).
(3) R. L. McKee, *Chem. Heterocycl. Compounds*, **17**, 351 (1962).
(4) R. Robinson and J. S. Watt, *J. Chem. Soc.*, 1536 (1934).
(5) K. v. Auwers, *J. Prakt. Chem.*, **150**, 166 (1938).
(6) Many 2- and 4-hydroxypyridines are known to exist in the pyridone form. However, in this article the pyridol nomenclature will be used since it is the hydroxy form that reacts in our syntheses.

Of the requisite pyridinol aldehydes or ketones only pyridoxal was available. 3-Hydroxy-2- (and -4-) pyridinecarboxaldehydes were prepared by the method of Heinert and Martell[7] and 3-acetyl-4-hydroxy-2,6-dimethylpyridine was made as described by Ziegler, Herbst, and Kappe.[8] 3-Acetyl-2-hydroxy-6- (and -4,6-di-) methylpyridines were prepared from the corresponding 3-nitriles by treatment with methyllithium in yields of 47–61%, respectively. Since this work was done the 4,6-dimethyl compound (**20**) has been reported by Bonsall and Hill[9] who prepared it by condensation of acetylacetone with acetoacetamide.

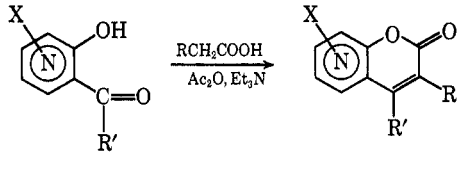
In general the Knoevenagel reaction (Scheme I) was

SCHEME I



used with the pyridol aldehydes employing an arylacetic ester and piperidine. Scheme I was not applicable with the pyridol ketones and so the Perkin reaction (Scheme II) was used.

SCHEME II



In the one case where a direct comparison was made, 3-phenyl-2*H*-pyrano[3,2-*b*]pyridin-2-one (**17**), about the same yield was obtained by both methods. Table I lists the azacoumarins prepared and their melting points.

An attempt was made to prepare the 4-hydroxy-8-azacoumarin **22** by condensation of the acetylpyridol **20** with diethyl carbonate in the presence of NaH.[10]

(7) D. Heinert and A. E. Martell, *J. Amer. Chem. Soc.*, **81**, 3933 (1959).
(8) E. Ziegler, I. Herbst, and Th. Kappe, *Monatsh. Chem.*, **100**, 132 (1969).
(9) C. Bonsall and J. Hill, *J. Chem. Soc. C*, 1836 (1967).
(10) Method described for 4-hydroxycoumarin: British Patent 705,316 (1954).