It seems likely that the bond formation observed in this system could be avoided if the isopropylidene group were replaced by a cyclohexane or smaller ring system. Attempts to synthesize such compounds are in progress.

Acknowledgments.—We wish to acknowledge fruitful discussions with Professor S. I. Weissman. Some of the e.p.r. and n.m.r. studies were performed by R. M. R. Cramer and E. W. Anderson, respectively (at BTL), and we thank them for their assistance.

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RECEIVED JULY 11, 1963

The Synthesis and Properties of Homotropone

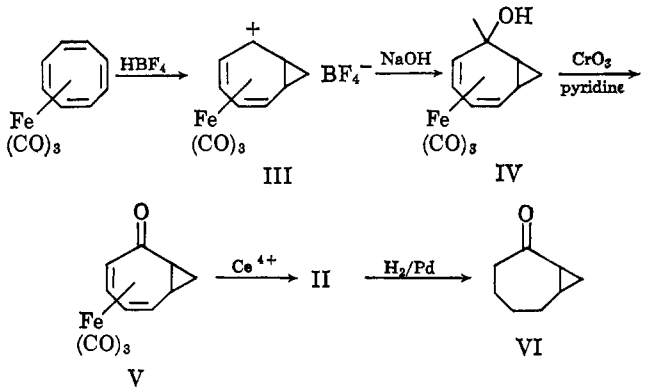
Sir:

Following the recent synthesis of the homotropylium cation (I),[1] it became of interest to study the related ketone (II) for which the trivial name homotropone is applicable.[2]

I II

One probable factor which contributes to the stability of the cation I is the presence of a "pseudoaromatic" sextet of electrons, two of which in a classical structure are part of a cyclopropane ring. Since many of the unusual properties of tropone (cycloheptatrienone), in particular its high basic strength,[3a,b] can be attributed to the stability of the aromatic tropylium cation it was considered desirable to determine whether homotropone would exhibit abnormal properties for analogous reasons.

We have synthesized homotropone by means of the reaction sequence



Cyclooctatetraeneiron tricarbonyl[4] was converted to the salt (III) following published procedures.[5a,b] Treatment of the salt with sodium hydroxide in aqueous acetone at low temperatures afforded the alcohol complex IV. (Yellow needles from petroleum ether, m.p. 90–91.5°; *Anal.* Calcd. for $C_{11}H_{10}O_4Fe$: C, 50.41; H, 3.81. Found: C, 50.36; H, 3.85.) Oxidation of IV with chromic oxide in pyridine gave the complex ketone V. (Yellow needles from benzene–petroleum ether, m.p. 131–132.5°; *Anal.* Calcd. for $C_{11}H_8O_4Fe$: C, 50.80; H, 3.08. Found: C, 50.85; H, 3.19.) Oxidative degradation of the ketone complex with ceric ammonium nitrate removed the iron tricarbonyl residue and liberated homotropone. The ketone was obtained as a pale yellow oil. *Anal.* Calcd. for C_8H_8O: C, 79.97; H, 6.71; O, 13.32. Found: C, 80.05; H, 6.88; O, 13.5. The semicarbazone of II crystallized as yellow plates from aqueous alcohol; m.p. 146–147°. *Anal.* Calcd. for $C_9H_{11}ON_4$: C, 61.00; H, 6.26; N, 23.71. Found: C, 60.98; H, 6.28; N, 23.80.

Proof of structure of the ketone was provided by reduction with H_2/Pd (hydrogen uptake, 1.84 moles) to give bicyclo-(5,1,0)-octan-2-one (VI). The dinitrophenylhydrazone derivative of this ketone had identical properties (ultraviolet and infrared spectra, m.p., and mixture m.p.) with an authentic specimen.[6]

The most revealing property of ketone II concerns its basic strength. The basicity of II was measured using spectrophotometric methods in aqueous sulfuric acid solutions and Hammett's H_0 acidity values.[7] The pK_{BH^+} of II is found to be −2.8, which is significantly higher (2.1 pK units) than that found for eucarvone (2,6,6-trimethylcyclohepta-2,4-dienone, pK_{BH^+} = −4.9). For purposes of comparison the introduction of two methoxyl groups in the p,p'-positions of benzophenone has the effect of raising the pK_{BH^+} value by 1.8 pK units, from −6.16 to −4.39.[8]

It would be desirable to compare the basicity of II with a planar heptatrienone molecule but unfortunately no such system appears readily available. However, the value of −2.8 for the pK_{BH^+} value for II lies significantly higher than that which would be predicted on the basis of molecular orbital theory for such a planar heptatrienone molecule, the predicted value being −4.7.[9,10]

Homotropone, when treated with $HSbCl_6$ in a benzene–methylene chloride mixture, forms a pale yellow, crystalline hexachloroantimonate salt; m.p. 89–90° dec. *Anal.* Calcd. for $C_8H_9OSbCl_6$: C, 21.09; H, 1.99, Cl, 46.69. Found: C, 20.76; H, 2.41; Cl, 46.5. The salt is stable when stored under nitrogen but rapidly decomposes in moist air. We have not been able to isolate crystalline hydrogen halide salts of II; tropone, on the other hand, forms such salts readily.[3]

The most ready explanation for the high basicity of homotropone would appear to involve enhanced conjugation of the cyclopropane ring in the protonated form of II.

The n.m.r. spectrum of homotropone is also interesting. Taken neat the spectrum of II consists of unresolved multiplets centered at 3.5, 4.2, 7.6, 8.0, and 8.5 τ with areas of 2:2:1:2:1, respectively. In concentrated sulfuric acid the bands are centered at 2.2, 3.0, 6.2, and 9.3 τ with areas of 2:2:3:1, respectively. The appearance, in the protonated form, of three of the cyclopropyl hydrogens at low field and one at high field is analogous to that seen in the n.m.r. spectrum of the cation I[1] and is compatible with the existence of a ring current present in the system.

(1) J. L. von Rosenberg, Jr., J. E. Mahler, and R. Pettit, *J. Am. Chem. Soc.*, **84**, 2842 (1962).

(2) S. Winstein and J. Sonnenberg, *ibid.*, **83**, 3244 (1961).

(3) (a) H. J. Dauben, Jr., and H. J. Ringold, *ibid.*, **73**, 876 (1951); (b) W. von E. Doering and F. L. Detert, *ibid.*, **73**, 876 (1951).

(4) T. A. Manuel and F. G. A. Stone, *ibid.*, **82**, 366 (1960).

(5) (a) G. N. Schrauzer, *ibid.*, **83**, 2966 (1961); (b) A. Davison, W. McFarlane, L. Pratt, and G. Wilkinson, *J. Chem. Soc.*, 4821 (1962).

(6) We are very grateful to Professor A. C. Cope for providing us with an authentic specimen of the dinitrophenylhydrazone derivative of the ketone (VI).

(7) L. A. Flexser, L. P. Hammett, and A. Dingwall, *J. Am. Chem. Soc.*, **57**, 2103 (1935).

(8) R. Stewart, M. R. Granger, R. B. Moodie, and L. J. Muenster, *Can. J. Chem.*, **41**, 1065 (1963).

(9) The value of a_{or}^2 for heptatrienone is 0.25; this predicts a pK_{BH^+} value of −4.7 for this ketone according to the linear relationship between pK_{BH^+} and a_{or}^2.[10] Justification for the use of this relationship in the present series of compounds is seen in the reasonable agreement of the observed basicity of eucarvone (pK_{BH^+} = −4.9) and that predicted for heptadienone [pK_{BH^+} = −5.3; a_{or}^2 = 0.33).

(10) G. Culbertson and R. Pettit, *J. Am. Chem. Soc.*, **85**, 741 (1963).

Other properties of homotropone also indicate a trend toward those of tropone. Thus the carbonyl stretching frequency of II in the infrared occurs at 1650 cm.$^{-1}$ compared with 1660 cm.$^{-1}$ for both eucarvone and cyclooctatrienone. Homotropone also has a higher boiling point than cyclooctatrienone and is twice as soluble in water as is the trienone (4.3 g./100 ml. as compared to 2.4 g./100 ml.).

In conclusion we believe that the above data indicate that in this particular system the effects of homoconjugation of the cyclopropyl ring are not insignificant. However when the systems I and II are compared with the tropylium cation and tropone, respectively, it is of course clear that this type of conjugation compares unfavorably with that possible with an ethylenic type double bond.

Acknowledgment.—We thank the Alfred P. Sloan Foundation and the Robert A. Welch Foundation for financial assistance.

(11) Celanese Corporation Fellow, University of Texas, 1962–1963.

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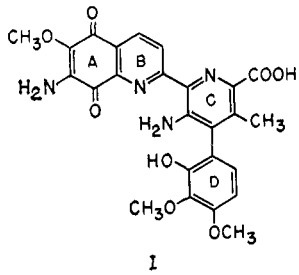
RECEIVED JULY 11, 1963

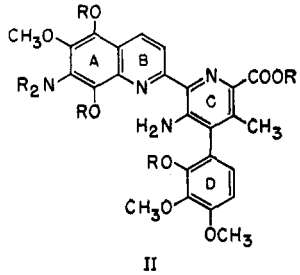
The Structure of Streptonigrin

Sir:

Streptonigrin, a metabolite of *Streptomyces flocculus*,[1] is an antibiotic which exhibits striking activity against a variety of animal tumors.[2,3] We wish to record our conclusion that streptonigrin possesses the unique structure I.



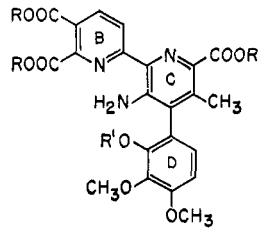
I



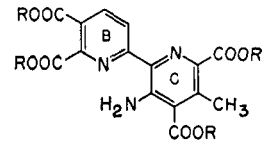
II

Streptonigrin is a monobasic acid and is readily susceptible to reversible two-electron reduction. Its composition, $C_{25}H_{22}O_8N_4$, only approximately determinable by elementary analyses,[1] was deduced exactly by mass spectrometric comparison of hexamethyldihydrostreptonigrin (II, R = CH_3), $C_{31}H_{36}O_8N_4$ (mol. wt.[4] 592), m.p. 185–186°, and hexadeuteriomethyldihydrostreptonigrin (II, R = CD_3), $C_{31}H_{18}D_{18}O_8N_4$ (mol. wt. 610), m.p. 185–186°, prepared by catalytic hydrogenation of streptonigrin followed by alkylation with, respectively, light and heavy dimethyl sulfate, in acetone in the presence of potassium carbonate. That the acidity of streptonigrin is associated with a carboxyl group was demonstrated by the observation that pentamethyldihydrostreptonigrin (II, COOH in place of COOR), $C_{30}H_{34}O_8N_4$ (mol. wt. 578), m.p. 215–216°, obtained by alkaline hydrolysis of the hexamethyldihydro derivative (II, R = CH_3), when volatilized directly into the ion source of the mass spectrometer, showed pyrolytic evolution of carbon dioxide (*m/e* 44), a small peak at *m/e* 578, and an intense peak at *m/e* 534–the molecular weight of the decarboxylation product (II, H in place of COOR).

Streptonigrin was oxidized by alkaline hydrogen peroxide to the *tribasic* streptonigric acid (III, R = R′ = H), $C_{22}H_{19}O_9N_3$, m.p. 210–215° dec. [tetramethyl derivative (III, R = R′ = CH_3), $C_{26}H_{27}O_9N_3$ (mol. wt. 525), m.p. 166–167°]. Oxidation of streptonigric acid with alkaline permanganate gave the *tetrabasic* streptonigrinic acid (IV, R = H), $C_{15}H_{11}O_8N_3$, m.p. >300°



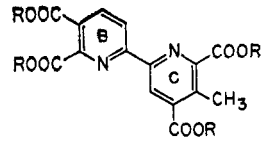
III



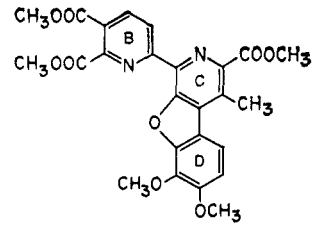
IV

[tetramethyl derivative (IV, R = CH_3), $C_{19}H_{19}O_8N_3$ (mol. wt. 417), m.p. 145–146°]. The empirical relationships among the members of this degradative series bespeak the presence in streptonigrin of methoxyaminoquinone, or methoxyhydroxyquinonimine, and hydroxydimethoxyphenyl systems as substituents in place of three of the hydrogen atoms of a $C_{12}H_{11}O_2N_3$ moiety. The latter is known to include a carboxyl group (*vide supra*), and further, nuclear magnetic resonance studies[5] demonstrated the presence in all of these compounds of a primary amino group and a methyl group attached to an aromatic ring [*e.g.*, in IV, R = CH_3: 7.42 τ (CH_3) and 2.16 τ (NH_2, lost on deuteration)]. The residual grouping of atoms, $C_{10}H_8N_2$, clearly suggests that streptonigrin is a *diazabiphenyl*, bearing amino, carboxyl, methyl, hydroxydimethoxyphenyl, and methoxyaminoquinone or methoxyhydroxyquinonimine substituents; it remains to verify that deduction, and choose among the 1,944,576 formulas (!), exclusive of tautomeric modifications, which can be constructed from the general hypothesis.

Tetramethyl streptonigrinate (IV, R = CH_3) was converted by nitric acid–ether to tetramethyldesaminostreptonigrinate (V, R = CH_3), $C_{19}H_{18}O_8N_2$ (mol. wt. 402), m.p. 143–144°.[6] The corresponding acid (V, R = H), m.p. 165° dec., obtained by alkaline hydrolysis, was decarboxylated over soda lime at 350° to 5-methyl-2,2′-bipyridyl, m.p. ~5°, identified by direct comparison (identical infrared, ultraviolet, and nuclear magnetic resonance spectra) with a synthetic sample, obtained by decarboxylation of the dicarboxylic acid from alkaline permanganate oxidation of 3-methyl-1,10-phenanthroline.[7] Streptonigrinic acid (IV, R = H) was oxidized by sodium hypochlorite to pyridine-2,3,6-tricarboxylic acid, m.p. 255–256°,[8] which was de-



V



VI

(1) K. V. Rao and W. P. Cullen, *Antibiot. Ann.*, 950 (1959–1960).

(2) J. J. Oleson, L. A. Calderella, K. J. Mjos, A. R. Reith, R. S. Thie, and I. Toplin, *Antibiot. Chemotherapy*, **11**, 158 (1961).

(3) W. L. Wilson, C. Labra, and E. Barrist, *ibid.*, **11**, 147 (1961).

(4) All molecular weights reported in this communication are experimental values determined by single-focus mass spectrometry. Because of the crucial importance of the composition of II (R = CH_3), its molecular weight was also determined using a double-focusing spectrometer: found, 592.2553; calcd., 592.2531.

(5) All nuclear magnetic resonance measurements were made on $CDCl_3$ solutions.

(6) *Cf.* K. N. Menon, W. H. Perkin, and R. Robinson, *J. Chem. Soc.*, 830 (1930), and O. Fischer and W. Boesler, *Ber.*, **45**, 1930 (1912), for other deaminations by nitric acid.

(7) F. H. Case, *J. Am. Chem. Soc.*, **70**, 3994 (1948).

(8) A. Eckert and S. Loria, *Monatsh. Chem.*, **38**, 241 (1917).