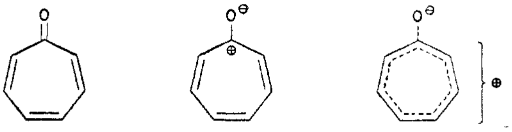
COMMUNICATIONS TO THE EDITOR

SYNTHESIS OF TROPONE

Sir:

Indications of aromaticity in the tropolones[1a] and in azulene[1b] direct attention to the need for determining the necessary minimum structural features for and the nature of this property in seven-membered ring systems. We wish to report the synthesis of 2,4,6-cycloheptatrien-1-one (tropone) (I)[2] and evidence bearing on its aromatic character.



(I) (II) (III)

2-Cyclohepten-1-one on treatment with four equivalents of bromine in acetic acid and heating for fifteen hours yields 38% 2,4,7-tribromotropone, cream needles (MeOH), m.p. 182–183° (calcd. for $C_7H_3OBr_3$: C, 24.51; H, 0.88; Br, 69.93. Found: C, 24.61; H, 1.11; Br, 70.80) (u.v. max. (EtOH): 275 $m\mu$ (22,100), 345 $m\mu$ (9400)), which absorbs (Pd–$BaSO_4$, EtOH) 6.0 moles of hydrogen to give cycloheptanone, is inert to ethanolic silver nitrate, and dissolves in ethanolic sodium hydroxide to furnish 88% dibromobenzoic acid(s), hydrogenolyzed to benzoic acid or fractionally crystallized to 2,5-dibromobenzoic acid.

Hydrogenolysis of tribromotropone in absolute ethanolic potassium acetate using poisoned palladium–barium sulfate catalyst interrupted at 2.9 moles yields 95% ionic bromine and 40% tropone (I), b.p. 104–105.5° (10 mm.), $n^{25}D$ 1.6070, viscous, almost colorless, hygroscopic (limited analyses to *ca.* C_7H_6O), (u.v. max. (HOH): 225 $m\mu$ (21,200); 228 $m\mu$ (22,100); 231.5 $m\mu$ (22,100); 239 $m\mu$ (12,700); 304 $m\mu$ inflection (8000); 312.5 $m\mu$ (8400)), (i.r. max.(liq.), 5–8 μ region; 5.86 μ (m); 6.09 μ (s); 6.35 μ (s); 6.60 μ (s); 6.75 μ (s); 7.98 μ (s); 8.22 μ (s). Reactions of tropone: (i) *salt formation:* hydrochloride, white hygroscopic needles by ether–hydrogen chloride and sublimation; picrylsulfonate, m.p. 266–267°, pale needles from aqueous picrylsulfonic acid (calcd. for $C_{13}H_9O_{10}N_3S$: C, 39.10; H, 2.27. Found: C, 38.93; H, 2.54); dipicrate, m.p. 100–101°, yellow needles from aqueous picric acid, (calcd. for $C_{19}H_6O_{15}N_6$: C, 40.43; H, 2.14. Found: C, 39.99; H, 2.44); (ii) *hydrogenation:* (Pd–$BaSO_4$, EtOH) 3.0 moles (only) in 17 min. to give 91% cycloheptanone; (PtO_2, HOAc) 4.0 moles in 28 min.; (iii) *carbonyl reactions:* no 2,4-dinitrophenylhydrazone in ethanol-sulfuric acid or acetic acid; hydroxylamine consumption (titration) only on heating (0.67 equiv., 2 hr.); (iv) *ring reactions:* aqueous permanganate, rapidly decolorized; benzenediazonium chloride in aqueous sodium acetate, immediate orange precipitate; bromination at 25°, moderately rapid in water, slower in aqueous acetic acid, very slow in carbon tetrachloride, to give addition products which eliminate hydrogen bromide partially during preparation but more readily on heating to furnish crystalline bromotropones.

These reactions and properties of tropone resemble strikingly those of its isostere, 4-pyrone, and this similarity suggests that aromatic character in tropone may originate from analogous carbonyl polarization (II) and resonance of six π-electrons among seven π-orbitals (III). This system would acquire a benzene-like $2p_\pi$ molecular orbital energy pattern which has been considered[3] as being largely responsible for aromatic behavior. Aromaticity in tropolone and azulene may arise from this type of resonance, stabilized by exocyclic structural features, or from other types.

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[1] Pertinent references in (a) M. J. S. Dewar, *Nature*, **166**, 790 (1950); (b) A. G. Anderson, Jr. and J. A. Nelson, THIS JOURNAL, **72**, 3824 (1950).

[2] *Cf.* 4,5-benztropone, J. Thiele and E. Weitz, *Ann.*, **377**, 1 (1910).

[3] *Cf.* F. O. Rice and E. Teller, "The Structure of Matter," John Wiley and Sons, New York, N. Y., 1949, p. 107.

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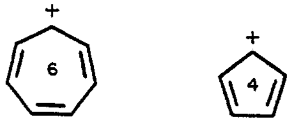
CYCLOHEPTATRIENYLIUM OXIDE

Sir:

The general molecular orbital theory ascribing peculiar stability to cyclic molecular orbitals containing 2 + 4*n* electrons[1] has, among others, the corollary that the cycloheptatrienylium ion (I) should be more stable than the cyclopentadienylium ion (II) whereas the stability of the anions, $C_7H_7^-$ and $C_5H_5^-$, should be reversed. We have now synthesized C_7H_6O (III) and found its properties to be represented by the structure cycloheptatrienylium oxide (IIIa) in accord with the theory.



I II

Hydroxycycloheptatrienylium bromide (IV) is obtained from methoxytropilidene, prepared by the photochemical decomposition of diazomethane in anisole, by treatment with one equivalent of bromine, either directly or after preliminary acid hydrolysis to cycloheptadienone. IV is a colorless, sublimable salt from which aqueous sodium bicarbonate liberates III: m.p. −8 to −5°; b.p. 113° at 15 mm.; $n^{22}D$ 1.6172; d^{22}_4 1.095; M_D 33.9 (calcd. for "cycloheptatrienone" (IIIb), 30.9); C, 79.07; H, 5.88; miscible with water; crystallizable from ether. III is reconverted to IV with hydrogen bromide and forms a picrate: m.p. 99–100°; C, 46.65; H, 2.84. The infrared spectrum (we thank Mr. Alfred P. Wolf, Columbia University)

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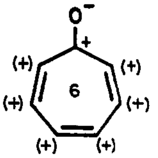
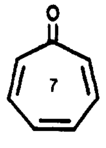
[1] E. Hückel, "Grundzüge der Theorie ungesättigter und aromatischer Verbindungen," Verlag Chemie, Berlin, 1938, pp. 71–85.

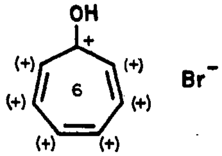
has prominent maxima at 3425, 2970, 1638, 1582, 1524, 1475, 1225, 1217, 1009, 936, 898, 834 and 785 cm.$^{-1}$. The ultraviolet spectrum in isoöctane shows maxima at 225 mu (log E 4.33), 297 (3.74) and 310 (3.67). Both III and IV react with three molecules of hydrogen with Adams platinum catalyst in ethanol to give *cycloheptanone*, identified as the semicarbazone, m.p. and m.p. mixed with authentic material 162.5–163°. The possible presence of an O–H bond inferred from the 3425 cm.$^{-1}$ band is excluded by the failure of III to exchange more than negligibly with deuterium oxide (analysis by Mr. Arthur K. Hoffmann, Columbia University). The arrangement of atoms in III is unquestionable (IIIa or IIIb).



IIIa



IIIb



IV

As an extreme electronic structure, IIIa and not IIIb satisfactorily expresses (a) the basicity which reflects a high electron density on oxygen and a stabilization of positive charge (IV), (b) the large dipole moment implied by the high boiling point (*cf.* benzaldehyde, b.p. 68° at 15 mm.), miscibility with water and the large exaltation, and (c) the shift of the carbonyl frequency. The stability of IIIa relative to IIIb and the very existence of III in contrast to the non-existence of cyclopentadienones (having fewer than two phenyl substituents),[2] find insufficient theoretical explanation in terms of resonance structures (IIIa) alone, but are explained by the molecular orbital theory which predicts peculiar stability from *six* electrons in a cyclic resonating system.

This investigation was supported in part by a research grant from the National Institutes of Health, Public Health Service.

[2] C. F. H. Allen and J. A. VanAllan, This Journal, 72, 5165 (1950).

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COUNTERCURRENT DISTRIBUTION OF INSULIN

Sir:

Our success in applying the technique of countercurrent distribution to the study of the purity of polypeptides in the molecular weight range of a few thousand has encouraged us to attempt a similar study with proteins. Insulin as a type substance has given promise from the first attempts and has now been studied in several systems.

Active material has been found to give an interchange between phases sufficiently rapid to permit a true partition ratio to hold. This in itself would appear to be a finding of considerable interest. Although runs involving approximately 100 transfers did not clearly reveal more than a single major component, higher numbers of transfers were more revealing. The major band did not continue to behave as a single component.

For example, an experiment made with 500 mg. of a sample of beef insulin (activity 27 μ/mg. Sample No. T 2344), supplied by the Eli Lilly Company, gave the result shown in Fig. 1 at 424 transfers (System 2-butanol/1% aqueous dichloroacetic acid; temp. 24°; pH of system 2.7; single withdrawal procedure[1] used). The distribution apparatus contained 220 equilibration cells in the train and was operated automatically.[2]

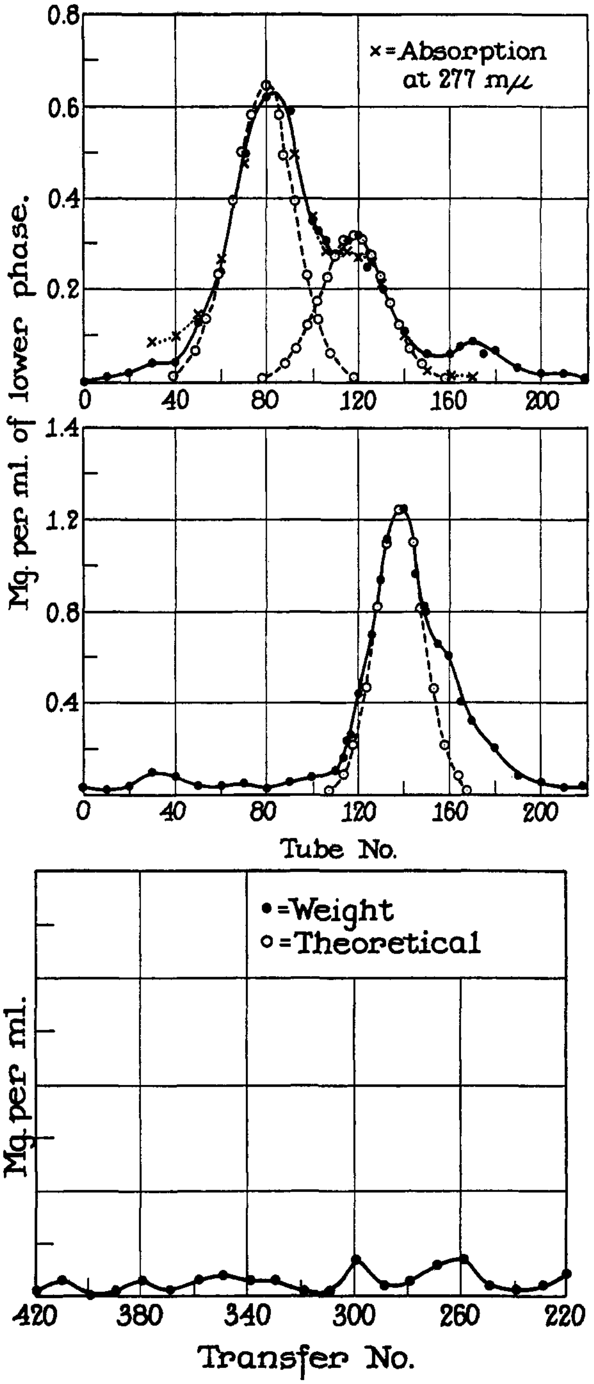

Fig. 1.—Distribution patterns of insulin: ●, weight; ○, theoretical: lower 424 transfers; upper 909 transfers.

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[1] L. C. Craig and O. Post, *Anal. Chem.*, 21, 500 (1949).

[2] L. C. Craig, *ibid.*, 22, 1345 (1950).