than chlorides II and V. There is every reason to believe that similar difficulties were encountered for the corresponding *endo*-bromo derivatives.

As a further check on the reactivity of the nortricyclyl halides, the pure chloride I has been prepared and it was found that this material was about one-seventh as reactive as chloride V. Bromide I is about one-tenth as reactive as bromide V.[3] Chloride I solvolyses at very nearly the same rate as cyclopentyl chloride and about 1/50 to 1/100 as fast as cyclopropylcarbinyl chloride. The reactivity sequence is now: cyclopropylcarbinyl chloride > V > III > I ~ cyclopentyl chloride > IV > II.

The earlier conclusion[3] regarding the driving force contributed by the double bond in the solvolyses of III can now be disputed on the basis that III is actually much more reactive than II irrespective of its reactivity relationship to V. The low reactivity of I relative to what might have been expected from the extraordinary reactivity of cyclopropylcarbinyl chloride[5] may be interpreted as resulting from (1) steric inhibition of conjugation,[3] (2) the unusual character of the carbonium ion intermediate formed in the solvolysis of cyclopropylcarbinyl derivatives,[6] or (3) differences in the degree of relief of strain in the formation of the solvolysis transition states from the respective chlorides.

Experimental

Dehydronorbornyl Chloride.—A total of 120 g. of cyclopentadiene and 120 ml. of liquid vinyl chloride was heated for 14 hours in glass tubes at 170°. The reaction products were fractionated through a 1-m. glass-helix packed column and had b.p. 66–70° (40 mm.), $n^{25}D$ 1.4914–1.4932. A heart-cut of 31 g., b.p. 69–70° (40 mm.), $n^{25}D$ 1.4927, was used for the rate runs and preparation of *endo*-norbornyl chloride.

***endo*-Norbornyl Chloride.**—Hydrogenation of 20 g. of *endo*-dehydronorbornyl chloride was complete in an hour over platinum oxide in ethyl acetate at room temperature and atmospheric pressure. The product was distilled through a glass-helix packed column and had b.p. 75° (41 mm.). All of the fractions solidified and the material used for the rate runs had m.p. 34–36° (previously reported[3] 28°).

Nortricyclyl chloride was prepared by isomerization of *endo*-dehydronorbornyl chloride. The adduct (50 g.) of cyclopentadiene and vinyl chloride was refluxed with 1 g. of anhydrous zinc chloride for five minutes. The mixture was cooled, shaken with water, dried over potassium carbonate, and distilled. The crude product amounted to 34 g. and had b.p. 160–170°. Quantitative hydrogenation indicated that about 60% of the crude product was nortricyclyl chloride. The remaining unsaturated material was removed by shaking the crude products with sodium permanganate solution until no further reaction occurred. The residual saturated chloride had b.p. 60.4–61.0° (32 mm.), $n^{25}D$ 1.4947–1.4948. The infrared spectrum of the material used in the rate runs is given in Fig. 1. The strong infrared absorption in the neighborhood of 12.5 μ is typical of nortricyclene derivatives.[7]

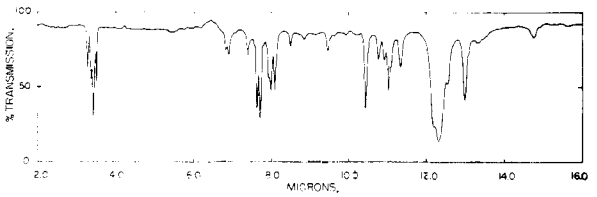

Fig. 1.—Infrared spectrum of nortricyclyl chloride, 50 mg. in 0.50 ml. of CS_2 except in the region 4.2–5.0 and 6.2–7.4 μ where CCl_4 was the solvent.

Anal. Calcd. for C_7H_9Cl: C, 65.38; H, 7.05. Found: C, 65.71; H, 7.02.

Solvolysis rate measurements were made as previously described.[3] Attempts to obtain more accurate rate constants for the less-reactive chlorides by extrapolation from higher temperatures were unsuccessful since at 105° the reaction of hydrochloric acid with 80% ethanol was comparable to the rate of solvolysis. The rate constants for the runs at 85.0 ± 0.1° are summarized in Table I.

(5) J. D. Roberts and R. H. Mazur, THIS JOURNAL, **73**, 2509 (1951).
(6) J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 3542 (1951).
(7) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett and R. Armstrong, *ibid.*, **72**, 3116 (1950).

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Arsenic-containing Salts of Some 9-Aminoacridines

BY EDGAR A. STECK AND WILLIAM F. WETTERAU

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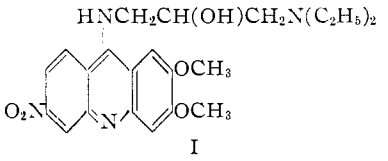
During the 1939–1945 war it was learned that German investigators had found high anti-typhus activity in work on a substance called Rutenol. The earlier reports[1,2] indicated that the drug was a salt comprised of two moles of 9-(3-diethylamino-2-hydroxypropylamino)-2,3-dimethoxy-6-nitroacridine (I) and three moles of arsenious oxide. Our work was nearly completed when the correct nature of Rutenol was disclosed[3] as the salt of one mole of (I) with two moles of 4-glycolylaminophenylarsonic acid. The study was not pursued further, for this salt (Rutenol) has been investigated thoroughly;[4] this program involved the salts of 9-aminoacridines, in particular, with arsenious oxide.



I

The reaction of 9-(3-diethylamino-2-hydroxypropylamino)-2,3-dimethoxy-6-nitroacridine dihydrochloride with sodium arsenite produced a substance in which the ratio of base to acid was 3:1. A series of variations gave only the so-called Rutenol or recovered base. The material isolated was a reddish-orange solid, m.p. 197–199° dec. (cor.), soluble in water to 1% w./v.; the aqueous solution (*p*H 6.25) contained no ionic arsenic. In hope of obtaining information concerning this complex from I, trials were made to obtain related substances from other 9-aminoacridines, including: quinacrine, 6-chloro-9-(3-diethylamino-2-hydroxypropylamino)-2-methoxyacridine ("Acranil"), 6-chloro-9-(4-diethylaminobutylamino)-2-methoxyacridine, 6-chloro-9-(4-dimethylaminoanilino)-2-methoxyacridine and 6-chloro-9-(4-diethylamino-1-methylbutylamino)-

(1) G. Holler, *Med. Klinik*, **40**, 374 (1944).
(2) Office of the Publication Board, Dept. of Commerce, Washington, D. C., 1945: (a) V. Conquest, E. C. Kleiderer, J. B. Rice and J. H. Williams, Report 4, p. 15; (b) H. M. Leaper, J. E. Smadel, L. M. White and E. H. Volwiler, Report 241, p. 5; (c) E. C. Kleiderer, J. B. Rice, V. Conquest and J. H. Williams, Report 981, p. 19.
(3) J. E. Smadel, J. C. Snyder, E. B. Jackson, J. P. Fox and H. L. Hamilton, *J. Immunol.*, **57**, 155 (1947).
(4) M. Bockmühl and A. Fehrle, U. S. Patent 2,040,070.

2,3-dimethoxyacridine. The bulk of the trials gave products which contained minor amounts of arsenic, and repetition failed to yield substances having constant ratios of nitrogen to arsenic content. 6-Chloro-9-(4-diethylaminobutylamino)-2-methoxyacridine (II) yielded a yellow substance which had the approximate formula (II)·2HCl·H_3AsO_3; it contained no ionic arsenic. No structure has been formulated for either of the products containing non-ionic arsenic.

A number of unsuccessful attempts were made to prepare arsenic(III) complexes of several amines (4-diethylamino-1-methylbutylamine, 4-diethylaminobutylamine, 3-diethylamino-2-hydroxypropylamine and N-(2-hydroxyethyl)-ethylenediamine) and also certain 4-aminoquinolines (chloroquine and its 3-methyl analog, and also 7-chloro-4-[2-(2′-hydroxyethylamino)-ethylamino]-quinoline).

Experimental

Arsenic(III) Complex of 9-(3-Diethylamino-2-hydroxypropylamino)-2,3-dimethoxy-6-nitroacridine.—A solution of 1.1 g. of 9-(3-diethylamino-2-hydroxypropylamino)-2,3-dimethoxy-6-nitroacridine dihydrochloride[5] in 5 cc. of water was treated with a solution prepared by dissolving 0.2 g. of arsenic(III) oxide in aqueous sodium hydroxide (0.16 g. in 3 cc. of water). At first, a precipitate formed, then dissolved to produce a clear garnet solution. No solid separated on chilling, however the addition of *ca.* 50 cc. of dioxane caused a reddish solid to precipitate. The crude substance was crystallized twice from methanol to yield 0.7 g. of reddish-orange microcrystals, m.p. 197–199° dec. (cor.). It dissolved in water to 1% w./v.; the solution had a *p*H 6.25 and gave a precipitate at *p*H 6.30 when 0.1 *N* NaOH was added. No ionic arsenic was present in a solution of the substance.[6]

Anal. Calcd. for $3C_{22}H_{27}N_4O_5 \cdot As_2O_3 \cdot H_2O$: N, 11.22; As, 10.01; H_2O, 1.20. Found[7]: N, 11.16; As, 9.92, 9.99; H_2O, 1.28.

Alteration of the ratio of the acridine to arsenic over a reasonable range produced the same substance. When the original reaction mixture was diluted with water, or concentrated *in vacuo*, the base I, was obtained in most cases. It was undesirable to reflux the reaction mixtures, for otherwise the base was the only product. This latter fact does not lend much support to the possibility that ring arsenation occurs in the reaction.

Arsenic(III) Complex of 6-Chloro-9-(4-diethylaminobutylamino)-2-methoxyacridine Dihydrochloride.—Arsenic(III) oxide (0.7 g.) was dissolved in aqueous sodium hydroxide (0.61 g. in 3 cc. of water); this solution of sodium arsenite was added to 5.13 g. of 6-chloro-9-(4-diethylaminobutylamino)-2-methoxyacridine dihydrochloride trihydrate[8] in 6 cc. of water at 60°. A reddish oil separated, then a carmine solution resulted when some dioxane was added; however, dilution with dioxane to a total volume of 250 cc. gave an orange precipitate (3.9 g.). The product was crystallized twice from methanol–dioxane, from which it separated as yellow microcrystals (after drying at 100° (1 mm.) it weighed 3.2 g.), m.p. 222–223° dec. (cor., immersed at 210°). An aqueous solution failed to give a test for ionic arsenic.[6]

Anal. Calcd. for $C_{22}H_{28}ClN_3O \cdot 2HCl \cdot H_3AsO_3$: N, 7.18; Cl (ionic), 12.12; As, 12.81. Found[7]: N, 7.29; Cl (ionic), 11.70; As, 11.30.

Repetition of the experiment gave a product which melted at 226–227° dec., but contained only 9.33% arsenic.

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(5) Prepared by a method essentially as reported by C. S. Miller and C. A. Wagner, *J. Org. Chem.*, **13**, 891 (1948).

(6) As indicated by lack of uptake of iodine in usual conditions with sodium hydrogen carbonate present. The original solution of sodium arsenite responded to this test as expected.

(7) Analyses by Mr. M. E. Auerbach and staff of the Analytical Division of this Institute.

(8) W. Huber, R. K. Bair and S. C. Laskowski, THIS JOURNAL, **67**, 1619 (1945).

Regarding the Inherent Order of Electron Release by Alkyl Groups Attached to Electron Demanding Unsaturated Systems

BY W. A. SWEENEY AND W. M. SCHUBERT

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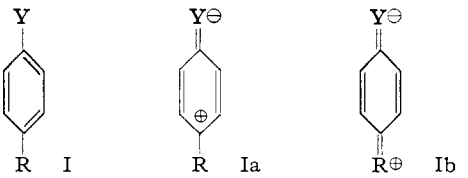
We have evidence that the inherent *order* of electron release by alkyl attached to electron demanding unsaturated systems may not be the same as that postulated for predominant C–H hyperconjugation.[1] In Table I are values for the E-band of compounds of type I. This band results from excitation to a state in which there is a greater contribution of dipolar structures (Ia, Ib).[2] Y is electron attracting to enhance differences in electron release of *p*-alkyls.



I Ia Ib

TABLE I

Compound[a]	λ_{max}	mμ (ε)
Acetophenone	242.0	13,100
p-Methylacetophenone	253.0	14,100
p-Isopropylacetophenone	253.5	15,600
p-*t*-Butylacetophenone	253.0	16,600
Nitrobenzene	260.0	8,160
p-Methylnitrobenzene	275.0	9,400
6-Acetylindane	258.0	13,200
7-Acetyltetralin	258.5	13,400
2-Acetyltetrahydrocycloheptabenzene	258.5	14,400
2-Acetylhexahydrocyclooctabenzene	258.5	13,400
Conjugate acid of:		
Acetophenone[c]	295.5	21,500
p-*t*-Butylnitrobenzene	275.0	9,950
Benzoic acid[b]	228.0	11,830
p-Methylbenzoic acid[b]	236.5	14,620
p-*t*-Butylbenzoic acid[b]	237.5	16,290
p-Methylacetophenone[c]	312.5	24,500
p-Isopropylacetophenone[c]	315.0	24,500
p-*t*-Butylacetophenone[c]	315.5	27,100
p-Methylnitrobenzene[d]	375.5	
p-*t*-Butylnitrobenzene[d]	380.5	

[a] All spectra in 95% ethanol except as noted. Beckman DU used. [b] Solution about 0.01 *N* in HCl. [c] Spectrum in concentrated H_2SO_4. [d] Measured in 101% H_2SO_4 in which nitro compounds are known to fully ionize to conjugate acid. Extrapolated to zero time (slow sulfonation was occurring) without an exact measure of the extinction coefficient being obtained.

The trend, both in λ_{max} and ϵ, may be opposite in *order* to the number of α-hydrogens, and the spread in λ_{max} is greatest when Y is most strongly electron demanding. Furthermore, no ring size effect in the order of steric inhibition of C–H hyperconjugation is observed.[9,10] The ionization potentials of alkylbenzenes[3] also are opposite in *order* to that expected for predominant C–H hyperconjugation, despite a large demand for electron

(1) *Cf.* J. W. Baker, "Hyperconjugation," Oxford University Press, London, 1952.

(2) See, *e.g.*, K. Bowden and E. A. Braude, *J. Chem. Soc.*, 1068 (1952).

(3) W. C. Price, *Chem. Reviews*, **41**, 262 (1947).