stituted or unsubstituted nitrobenzenes[2,5] or the isomeric dinitrobenzenes,[3,4] the anion radical derived from *t*-nitrobutane is unstable.

We have found that *t*-nitroalkanes form transient anion radicals which undergo relatively complex reactions.[6] As a result of detailed e.s.r. studies on anion radicals of *t*-nitroalkanes formed either by alkali metal or electrochemical reduction, some gross aspects of these reactions have become clear.

Polarographic reduction of *t*-nitrobutane in acetonitrile using tetra-*n*-propylammonium perchlorate as the supporting electrolyte proceeds cleanly by a one electron transfer. Identification of the product formed by one electron reduction of *t*-nitrobutane was accomplished by controlled potential electroreduction in acetonitrile within the microwave cavity of an e.s.r. spectrometer using the technique of Geske and Maki.[2] Electrolyses also were performed in the cavity using glyme and tetra-*n*-butylammonium perchlorate as supporting electrolyte. Electrolysis of *t*-nitrobutane in glyme led to an unstable paramagnetic species, most probably the anion radical of *t*-nitrobutane.

The spectrum in glyme consists of three equally spaced narrow lines of equal intensity. This spectrum is attributed to the isotropic hyperfine coupling of the unpaired electron with an N^{14} nucleus. The hyperfine coupling constant has the value 26.30 gauss. Any hyperfine interaction with the protons in the radical must have a hyperfine coupling constant less than the observed line width of 900 milligauss. On discontinuing the electrolysis, this spectrum fades to be completely replaced within seconds by a new spectrum consisting of a triplet of equal intensity distribution, but a hyperfine coupling constant of 15.45 gauss which is not subject to further change and which is identical with the spectrum of di-*t*-butylnitroxide[6] dissolved in glyme. Upon prolonged electrolysis the observed spectrum becomes a combination of the two, the triplet with hyperfine coupling constant of 15.45 gauss growing at the expense of the triplet with hyperfine coupling constant of 26.30 gauss. During the reaction of *t*-nitrobutane with sodium, however, only the triplet with hyperfine coupling constant of 15.45 gauss could be observed.

In contrast to glyme, electroreduction of *t*-nitrobutane in acetonitrile immediately produced two triplets with hyperfine coupling constants of 26.45 and 15.75 gauss. On discontinuing electrolysis, the 26.45 gauss triplet disappeared within seconds leaving only the 15.75 gauss triplet. A hyperfine coupling constant of 15.75 gauss corresponds to the hyperfine coupling constant for di-*t*-butylnitroxide in acetonitrile. This small change of coupling constant from that observed in glyme arises from the differences in solvent. Small changes of coupling constant with solvent have been observed previously.[1,2]

These observations strongly suggest that the anion radical of *t*-nitrobutane decomposes to di-*t*-butylnitroxide. The reaction of *t*-nitrobutane with sodium, therefore, like the reductive cleavage of triphenylphosphine oxide by sodium to diphenyl phosphinite anion and phenyl free radical,[7] is consistent with a similar interpretation, *i.e.*, as involving the collapse of a *t*-nitrobutyl anion radical to nitrite anion and a *t*-butyl free radical. Oxygen abstraction from *t*-nitrobutyl anion radical by *t*-butyl free radical can lead to the formation of *t*-nitrosobutane which by further reaction with *t*-butyl free radicals is converted to the nitroxide and trisubstituted hydroxylamine[8]

R = *t*-butyl,

(1) $RNO_2 + e^- \longrightarrow RNO_2^{-\cdot}$

(2) $RNO_2^{-\cdot} \longrightarrow NO_2^- + R\cdot$

(3) $R\cdot + RNO_2^{-\cdot} \longrightarrow \left[R{-}N(O{-}R)(O^{\ominus})\right] \longrightarrow R{-}N{=}O + RO^-$

(4) $R\cdot + R{-}N{=}O \longrightarrow R_2N{-}O\cdot$

(5) $R_2N{-}O\cdot + R\cdot \longrightarrow R_2NOR$

This interpretation is supported by the observation that the reaction products comprise, in addition to nitroxide and trisubstituted hydroxylamine, sodium *t*-butoxide, sodium nitrite and small amounts of *t*-nitrosobutane. The demonstrated ability of the nitroso group to add free radicals to form trisubstituted hydroxylamines[10,11] supports equations 4 and 5 as reasonably depicting the source of both di-*t*-butylnitroxide and tri-*t*-butylhydroxylamine. Similar transformations to a stable nitroxide also have been observed for 2-nitro-2,4,4-trimethylpentane.

(5) A. H. Maki and D. H. Geske, *J. Am. Chem. Soc.*, **83**, 1853 (1961).

(6) A. K. Hoffmann and A. T. Henderson, *ibid.*, **83**, 4671 (1961).

(7) A. K. Hoffmann and A. G. Tesch, *ibid.*, **81**, 5519 (1959).

(8) Although *t*-nitrosobutane also might arise *via* attack of *t*-nitrobutane by *t*-butyl anion, Step 3 is preferred because no products corresponding to the attack of solvent by the strongly nucleophilic[9] *t*-butyl anion have been observed.

(9) P. D. Bartlett, S. Friedman and M. Stiles, *ibid.*, **75**, 1771 (1953).

(10) L. Phillips, *Proc. Chem. Soc.*, 204 (1961).

(11) B. A. Gingras and W. A. Waters, *J. Chem. Soc.*, 1920 (1954).

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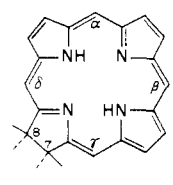
RECEIVED SEPTEMBER 15, 1961

A NEW ASPECT OF THE CHEMISTRY OF CHLORINS

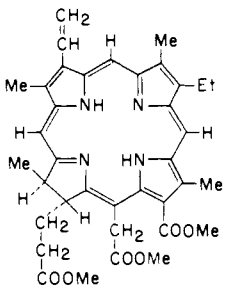
Sir:

We wish to record the remarkable and hitherto entirely unrecognized fact that the chlorins (I) are extraordinarily susceptible to selective electro-

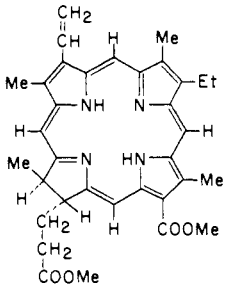


I

philic attack at the γ and δ bridge positions. The phenomenon is most simply and forcefully demonstrated through proton magnetic resonance studies. The spectrum of chlorin e_6 trimethyl ester (II) contains three sharp low-field bands [at τ = 0.45, 0.64



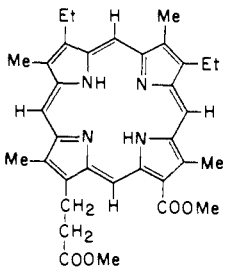
II



III

and 1.37 (measured in $CDCl_3$)] corresponding to the three bridge hydrogen atoms. After the chlorin has been heated for two hours at 80° in deuterioacetic acid [CH_3COOD], its spectrum is unchanged, *except that one of the bands* [that at τ = 1.37] *associated with the bridge hydrogen atoms has disappeared.* The locus of attack is established through the fact that treatment of rhodochlorin dimethyl ester (III) [bands at τ = 0.28, 0.57, 0.70 and 1.45 (measured in $CDCl_3$)] under the same conditions for four hours leads to the clean disappearance of *two* bridge hydrogen bands [those at τ = 0.28 and 1.45]. That no attack takes place upon the α and β positions is clearly shown by the fact that no diminution of the remaining bands associated with bridge hydrogen atoms occurs on further long-continued treatment with deuterioacetic acid. When the deuterated chlorins are heated in normal acetic acid, the missing bridge hydrogen bands reappear completely.

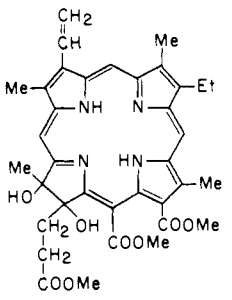
We were led to explore the possibility that the γ and δ bridge positions of the chlorins might be readily susceptible to electrophilic attack, and the α and β positions resistant to that process, by a simple qualitative hypothesis that in electronic networks such as those present in the porphyrins and chlorins, the π electrons tend to congregate in sextets within the small rings embedded in the larger system. The same hypothesis suggests that *all* of the bridge positions of the porphyrins will resist attack by electron-deficient reagents and, in fact, no change whatsoever is observed in the proton magnetic resonance spectrum of rhodoporphyrin dimethyl ester (IV)



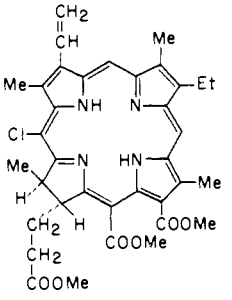
IV

[bridge hydrogen bands at τ = −1.48, −0.60, −0.40 and −0.40 (measured in $CDCl_3$ containing a small amount of CF_3COOH)] when it is treated with deuterioacetic acid at 90° for five hours.

The far-reaching synthetic and other chemical implications of our new observations may be exemplified by our elucidation of the nature of the so-called *dioxychlorins*. Numerous compounds of this class have been prepared from corresponding natural chlorins through the use of various oxidizing agents[1]—a preferred method involves treatment of the chlorin in dioxane/pyridine solution with silver oxide and oxygen. Fischer formulated the substances [with some subsequent reservations[1e,f]] as 7,8-dihydroxy compounds [*cf.* I], but this view is hardly compatible with the observed distinct changes in spectroscopic properties *vis-a-vis* the parent substances,[2] nor does it account for the unusually *low* adsorbability of the compounds in chromatographic experiments. Further, the claim that the added oxygen atoms at C.7 and C.8 can be removed under various very mild reducing conditions can only be regarded as extraordinary. Finally, it is difficult to formulate a mechanism for the substitution of hydrogen atoms at C.7 and C.8 without introducing intermediates which should suffer too ready degradation to porphyrins. We have now found that dioxychlorin p_6 dimethyl ester,[1a] hitherto formulated as (V), *contains one atom of chlorine* [Calcd. for $C_{36}H_{39}N_4O_6Cl$: Cl, 5.38. Found: Cl, 4.99, 4.96, 5.04]. Its proton magnetic resonance spectrum [*two* low field bands only, at τ = 0.60 and 0.77 (measured in $CDCl_3$, containing a small amount of CF_3COOH)], demonstrates that the chlorine atom is situated at a bridge position, and the relationships established earlier in this communication leave no doubt that the substance is in fact δ-chlorochlorin p_6 dimethyl ester (VI).



V



VI

It is now clear that the "dioxychlorins" are produced by a very facile chlorination reaction, which occurs at that stage in their preparation when, ostensibly for purposes of purification, fractionation between ether and hydrochloric acid is carried out in the presence of agents capable of oxidizing the halogen acid to chlorine [*e.g.*, peroxides from dioxane, in the procedure cited above]. Indeed, we find that a new, simple and effective method of preparing the substances consists in distributing a chlorin between ether containing a small amount of hydrogen peroxide, and aqueous hydrochloric acid of sufficient strength [initially 12% in the case of chlorin p_6] to extract the starting material, but not the less basic δ-chloro compound.

(1) (a) H. Fischer and W. Lautsch, *Ann.*, **528**, 247 (1937); (b) H. Fischer and K. Kahr, *ibid.*, **531**, 209 (1937); (c) H. Fischer and M. Strell, *ibid.*, **540**, 232 (1939); (d) H. Fischer and F. Gerner, *ibid.*, **553**, 67 (1942); (e) H. Fischer and F. Baláž, *ibid.*, **555**, 81 (1943); (f) H. Fischer and H. Pfeiffer, *ibid.*, **556**, 131 (1944).

(2) A. Stern and M. Deželić, *Z. physik. Chem.*, **179**, 275 (1937); F. Pruckner, *ibid.*, **188**, 41 (1941).

In a number of instances,[3] ready halogenation of chlorins has been observed, but it has been assumed that the reactions involve substitution at the 7 or 8 positions. Although these cases deserve reinvestigation in detail, there can now be little doubt that the views previously advanced are erroneous, and that the products of these reactions are γ or δ halogenated derivatives.

This work was generously supported by the National Institutes of Health.

(3) (a) H. Fischer and K. Herrle, *Ann.*, **530**, 236 (1937); (b) H. Fischer and E. A. Dietl, *ibid.*, **547**, 234 (1941); (c) H. Fischer, H. Kellermann and F. Baláž, *Ber.*, **75**, 1778 (1942); (d) H. Fischer and F. Baláž, *Ann.*, **555**, 81 (1943); (e) H. Fischer and F. Gerner, *ibid.*, **559**, 77 (1948).

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INTRAMOLECULAR CYCLIZATION OF UNSATURATED DIAZOKETONES

Sir:

The intermolecular reaction of diazoketones with olefins has been described by Sorm and his collaborators.[1]

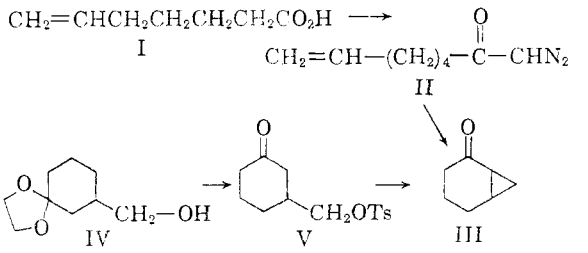
So far as we are aware the *intramolecular* counterpart of this reaction has not yet been reported. We were interested in exploring the feasibility of such a reaction for the synthesis of [0,1,4]bicycloheptane derivatives and have succeeded in synthesizing [0,1,4]bicycloheptanone-2 (III), one of the simplest substances that might be prepared by the "Δ^5 diazoketone" route.

Pure 5-hexenoic acid (I) was prepared from 4-penten-1-ol[2] *via* the corresponding bromide and nitrile.[3] The unsaturated acid was transformed into its acid chloride by reaction with oxalyl chloride in benzene at room temperature, and the acid chloride was converted, without distillation, into its diazoketone (II).

The diazoketone (5 g.) was refluxed for eleven hours in 250 ml. of cyclohexane in the presence of 0.5 g. of copper bronze. Shorter time led to incomplete reaction as evidenced by the presence of diazoketone in the mixture (infrared). Distillation gave 2.5 g. of a fraction boiling at 74–76° (8 mm.). This consisted mainly (see below) of the desired [0,1,4]bicycloheptanone-2 but was not completely homogeneous, as shown by the presence of two absorption bands in the carbonyl region of the infrared and by gas chromatography. The latter (5 ft. silicone column, 150°) showed the product to be contaminated with about 20% of a substance with absorption at 5.85 μ in the infrared. The pure III from the chromatogram had its carbonyl absorption at 5.96 μ, λ_{max}^{EtOH} 220 mμ and 275 mμ (ϵ 34),[4] and gave its 2,4-dinitrophenylhydrazone, m.p. 158° (calcd. for $C_{13}H_{14}N_4O_4$: C, 53.79; H, 4.86; N, 19.30. Found: C, 53.96; H, 4.90; N, 19.47). The same 2,4-dinitrophenylhydrazone was obtained before gas chromatography in 75% yield. The ultraviolet absorption spectrum of this derivative had $\lambda_{max}^{CHCl_3}$ 370 mμ as anticipated (*cf.* 2,4-dinitrophenylhydrazone of acetylcyclopropane: $\lambda_{max}^{CHCl_3}$ 371 mμ[5]). The n.m.r. spectrum of III showed absorption due to two non-equivalent hydrogens of the cyclopropane methylene at τ *ca.* 8.9 (lowered by conjugation with the carbonyl).

Unambiguous confirmation of the structure of our [0,1,4]bicycloheptanone-2 was obtained by an independent synthesis. Catalytic hydrogenation (rhodium-charcoal) of *m*-hydroxybenzoic acid, then esterification and oxidation with chromic acid–acetone–sulfuric acid, gave the known[6] ethyl-3-oxocyclohexanecarboxylate. Ketalization with ethylene glycol and reduction with lithium aluminum hydride gave the ketal of 3-oxo-cyclohexanemethanol (IV) b.p. 116–124° (0.2 mm.) (found: C, 62.32; H, 9.43). Reaction of IV with *p*-toluenesulfonyl chloride in pyridine and deketalization with aqueous methanolic hydrochloric acid produced the tosylate of 3-oxocyclohexanemethanol (V); 2,4-dinitrophenylhydrazone, m.p. 118° (found: C, 52.21; H, 4.99).

Cyclization of the keto tosylate V with sodium hydride[7] in tetrahydrofuran gave, in low yield, the bicyclic ketone III; 2,4-dinitrophenylhydrazone, m.p. 162–163°, undepressed by the sample from the diazoketone decomposition. The infrared spectra of the ketones made by the two routes were essentially identical, and so were the characteristic n.m.r spectra.



(5) D. H. R. Barton, T. Braun and A. S. Lindsey, *J. Chem. Soc.*, 2210 (1952).

(6) G. K. Komppa, T. Hirn, W. Rohrmann and S. Beckmann, *Ann.*, **521**, 242 (1936).

(7) *Cf.* N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957).

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RECEIVED OCTOBER 20, 1961

THE STRUCTURE OF INDOLMYCIN

Sir:

We wish to propose structure **1** for indolmycin, previously designated PA-155A.[1,2] This antibiotic is the first example of a new structural type.

Indolmycin was isolated from a culture of *Streptomyces albus*[1] and some of its properties have been described.[2,3] The compound has the molecular formula $C_{14}H_{15}N_3O_2$ and an ultraviolet absorption spectrum closely resembling that of tryptophan.

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(2) R. Paul and H. Normant, *Bull. soc. chim.*, 484 (1943).

(3) F. B. LaForge, N. Green and W. Gersdorff, *J. Am. Chem. Soc.*, **70**, 3709 (1948).

(4) *Cf.* A. Sandoval, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 2383 (1951).

(1) W. S. Marsh, A. L. Garretson and E. M. Wesel, *Antibiotics and Chemotherapy*, **10**, 316 (1960).

(2) K. V. Rao, *ibid.*, **10**, 312 (1960).

(3) A. R. English, T. J. McBride, *ibid.*, in press.