being applied to sequence analysis studies where the limitation of enzyme action in this way is expected to permit the isolation of larger fragments from the enzyme degradation of nucleic acids.

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DIRECT NEF REACTION BY ACID-CATALYZED HYDROLYSIS OF 2-NITROÖCTANE TO 2-OCTANONE

Sir:

We wish to report the first example of a Nef reaction proceeding directly from a nitroalkane in acid solution. Ordinarily the nitronic acid intermediate required in this reaction is generated from a nitronate salt. Although the reaction of nitroalkanes with hot mineral acids has been examined,[1,2] no instance is known of the direct conversion of these substances in acidic medium to an aldehyde or ketone having the same carbon content.

2-Nitroöctane (I)[3] (1.0 g.) was refluxed with *N* hydrochloric acid (500 ml.) for 335 hr. (heterogeneous mixture). The product was isolated by extraction with methylene chloride to yield 0.9 g. of a mixture of 2-octanone (II) and I b.p. 160–210° (690 mm.) (infrared spectrum identical with a mixture of authentic I and II containing 65% I.) The extinction coefficient of the product mixture in "90%" ethanolic 0.05 *N* sodium hydroxide solution at 230 mμ (λ max.) indicated 62% I; ϵ_{max}^{230} 12,000 for authentic I in this medium. The 2-octanone was separated by distillation, b.p. 160–170° (690 mm.); semicarbazone m.p. 122–123°; *p*-nitrophenylhydrazone, m.p. 85–87° (no depression of melting point of these derivatives when mixed with authentic samples).

The hydrolysis reaction was conducted with *d*-2-nitroöctane[3] $[\alpha]^{25}D$ + 4.55 (c, 27 in chloroform) in refluxing *N* hydrochloric acid. After 87.5 hr. 13.6% II had formed and the recovered (distilled) I had retained its optical activity $[\alpha]_D^{25}$ + 4.53 (*c*, 27 in chloroform). A sample of *d,l*-2-nitroöctane refluxed with *N* deuteriosulfuric acid in deuterium oxide for 124 hr. produced 4.5% II[4]; the recovered I was found to contain no deuterium (absence of CD stretching absorption near 2100 cm.$^{-1}$ in 0.5 mm. thick sample; spectrum identical with I); comparison of the n.m.r. spectrum of this product with authentic I revealed no differences.

The rate of disappearance of 2-nitroöctane dissolved in "50%" ethanolic *N* hydrochloric acid at 100° was measured. Samples were placed in ethanolic sodium hydroxide and the extinction coefficient at 230 mμ determined at intervals. The rate was first order in 2-nitroöctane ($k = 1.2 \times 10^{-5}$ min.$^{-1}$); excellent first-order plots of log *c versus* time passing through the origin were obtained through two reaction half-lives. The rate of tautomerization of octane-2-nitronic acid (generated from the sodium salt by neutralization with hydrochloric acid) to I at 25° in "85%" ethanol was found to be much faster. Excellent first order plots of log *c versus* time through three reaction half-lives were obtained ($k = 3.1 \times 10^{-3}$ min.$^{-1}$).

The above observations are consistent with a slow rate-determining proton removal from a protonated intermediate (III) by a base such as water or chloride ion, leading to a nitronic acid (IV). Hydrolysis of IV to II (Step 3, Nef reaction)[5] evidently occurs more rapidly than tautomerization to I,[6] although the rate has not been measured.

$$C_6H_{13}(CH_3)CHNO_2 + H^+ \rightleftharpoons C_6H_{13}(CH_3)CHNO_2H^+ \quad (1)$$
I III

$$C_6H_{13}(CH_3)CHNO_2H^+ + B \overset{\text{slow}}{\rightleftharpoons} C_6H_{13}(CH_3)C{=}NO_2H + BH^+ \quad (2)$$
III IV

$$2\ C_6H_{13}(CH_3)C{=}NO_2H \longrightarrow 2\ C_6H_{13}(CH_3)C{=}O + N_2O + H_2O \quad (3)$$
IV II

The kinetic data on acid-catalyzed bromination of nitroalkanes[7] are also in agreement with a slow proton removal step (2), then halogenation of a nitronic acid intermediate (rate independent of halogen or halogen concentration).

(1) W. E. Noland, *Chem. Revs.*, **55**, 137 (1955).
(2) M. J. Kamlet, A. Kaplan, and J. C. Dacons, *J. Org. Chem.*, **26**, 4371 (1961).
(3) We wish to thank Prof. N. Kornblum for supplying generous samples of *d,l*- and *d*-2-nitroöctane.
(4) A parallel experiment with *N* sulfuric acid in water produced 5.5% II in 124 hr.
(5) M. F. Hawthorne, *J. Am. Chem. Soc.*, **79**, 2510 (1957).
(6) For nitronic acids derived from β-hydroxynitroalkanes, such as 2,5-dinitro-1,6-hexanediol, acid-catalyzed tautomerization proceeds more rapidly than the competing Nef reaction (H. Feuer and A. T. Nielsen, forthcoming publication).
(7) R. Junell, *Z. physik. Chem.*, **141A**, 71 (1929).

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NEW BORON HETEROCYCLES. 5-, 6- AND 7-MEMBERED SYSTEMS CONTAINING NITROGEN, OXYGEN AND SULFUR

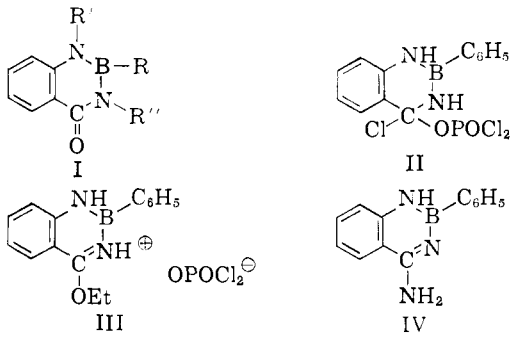
Sir:

We have for some time been interested in the synthesis of new boron heterocycles for the purpose of studying their chemical and pharmacological properties. Recent publications by Dewar and his collaborators[1] prompt us to communicate recent work, which has led to stable and biologically active boron–nitrogen heterocycles.

Condensation of a variety of N-substituted anthranilamides with aryleneboronic acids in boiling toluene using a Dean–Stark separator for the continuous removal of water furnished compounds of

(1) S. S. Chissick, M. J. S. Dewar and P. M. Maitlis, *J. Am. Chem. Soc.*, **83**, 2708 (1961), and earlier papers cited therein.

type I[2] in yields of 42 to 91%. Thus, anthranilamide and mesityleneboronic acid gave Ib (R = mesityl, R′ = R″ = H) m.p. 202–204°; λ_{max}^{EtOH} 311 mμ (ε = 5,200); λ_{max}^{Nujol} 2.96, 3.07, 6.00, 6.20, 6.27, 6.58, 6.73, 6.90 μ; calcd. for $C_{16}H_{17}BN_2O$ (264.14): B, 4.10; N, 10.60; found: B, 4.19; N, 10.56. The stability of compounds of type I was greatly influenced by substitution. Thus, ultraviolet spectroscopy showed complete alcoholysis of Ic (R = Ph, R′ = H, R″ = $(CH_3)_2N(CH_2)_3$, m.p. 170–172°) to occur at room temperature in less than one hour, and in less than two hours with Id (R = Ph, R′ = R″ = CH_3, m.p. 92–94°) and Ie (R = Ph, R′ = CH_3, R″ = H, m.p. 170–172°). In the same solvent If (R = 1-naphthyl, R′ = H, R″ = CH_3, m.p. 218–220°) and Ig (R = 1-naphthyl, R′ = H, R″ = $PhCH_2$, m.p. 250–252°) were completely stable for at least 120 hours and Ib for at least 144 hours. In contrast to the experience of Chissick, *et al.*[1] reac-

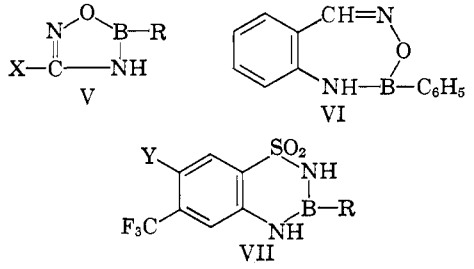


I II III IV

tion of Ia with $POCl_3$ at reflux temperature furnished in 85% yield, a deep yellow, crystalline adduct,[3] m.p. 181–182° (dec.); $\lambda_{max}^{Tetrahydrofuran}$ 323 mμ (ε = 4,805); λ_{max}^{Nujol} 3.24, 5.25, 6.15, 6.23, 6.33, 6.55, 6.68, 7.80, 9.03 μ[4]; calcd. for $C_{13}H_{11}BN_2O \cdot POCl_3$ (375.41): B, 2.88; Cl, 28.40; N, 7.47; P, 8.26; found: B, 2.61; Cl, 28.21; N, 7.53; P, 7.98, to which we assign the covalent structure II, because of its failure to titrate as a base with perchloric acid in acetic acid in the presence of mercuric acetate and of the reactions described below. Treatment of II with concentrated aqueous ammonia at room temperature yielded *o*-aminobenzonitrile and benzeneboronic acid.[5] When II was dissolved in boiling chloroform containing 0.75% alcohol, a new product was formed in 62% yield, formulated as III, m.p. 138–140° (dec.), $\lambda_{max}^{Tetrahydrofuran}$ 359 mμ (ε = 4,200); λ_{max}^{Nujol} 3.15, 6.12, 6.22, 6.30, 6.50, 6.72, 7.70, 9.02 μ; calcd. for $C_{15}H_{16}BCl_2N_2O_3P$ (385.00): Cl, 18.42; N, 7.28; B, 2.81; P, 8.04; OEt, 11.70; found: Cl, 18.64; N, 7.33; B, 2.53; P, 7.48; OEt, 11.93, neut. equiv., ($HClO_4$ in AcOH, $Hg(OAc)_2$), 388. III with aqueous sodium bicarbonate gave the hydrated base, m.p. 120–121°; λ_{max}^{EtOH} 233, 390 mμ (ε = 29,400, 4,790); λ_{max}^{Nujol} 2.84, 2.98, 6.10, 6.19, 6.40, 6.70, 7.00 μ; calcd. for $C_{15}H_{15}BN_2O \cdot H_2O$ (268.14): C, 67.19; H, 6.38; OEt, 16.80; found: C, 67.12; H, 6.43; OEt, 16.74, neut. equiv., ($HClO_4$ in AcOH), 267. Reaction of III with concentrated aqueous ammonia at room temperature gave a 50% yield of 4-amino-1,2-dihydro-2-phenyl-1,4,2-benzodiazaborine (IV),[6] which crystallized *from boiling water* as a trihydrate; drying *in vacuo* at 110° gave anhydrous IV, m.p. 260–263° (dec.); λ_{max}^{EtOH} 378 mμ (ε = 4,350); λ_{max}^{Nujol} 3.0, 6.1, 6.25, 6.55 μ; calcd. for $C_{13}H_{12}BN_3$ (221.07); C, 70.66; H, 5.48; N, 19.02; B, 4.89; found: C, 70.15; H, 5.84; N, 18.61; B, 4.73; neut. equiv., ($HClO_4$ in AcOH), 225.

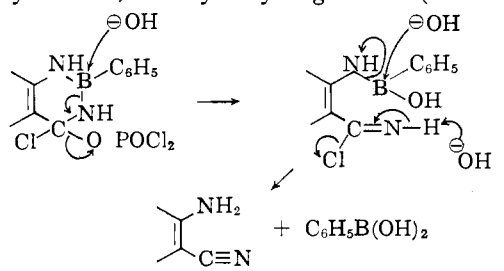
Slow distillation of a toluene solution of a substituted anthranilamide and trimethyl borate, then hydrolysis of the intermediate 2-methoxy derivative, gave compounds represented by I, where R is OH. Thus, *o*-amino-N-benzylbenzamide gave Ih (R = OH, R′ = H, R″ = $C_6H_5CH_2$), m.p. > 315°; λ_{max}^{EtOH} 218,311 mμ (ε = 20,150, 4,540); λ_{max}^{Nujol} 2.95, 3.05, 6.15, 6.30, 6.50, 6.57, 6.70 μ; calcd. for $C_{14}H_{13}BN_2O_2$ (252.08): B, 4.29; N, 11.12; found: B, 4.40; N, 11.29.

Compounds of type V were prepared by the reaction of a benzamidoxime or pyridocarboxamidoxime with an aryleneboronic acid or trimethyl borate in boiling toluene or xylene, separating the water (or methanol) as formed. Thus, isonicotinamidoxime [m.p. 172–174°; calcd. for $C_6H_6N_3O$, N, 30.88; found: N, 30.61] and mesityleneboronic acid gave Va (R = mesityl, X = 4-pyridyl), m.p. 159–160°; λ_{max}^{EtOH} 236, 260 mμ (ε = 14,540, 7,580); λ_{max}^{Nujol} 3.17, 6.18, 6.30, 6.50 μ; calcd. for $C_{15}H_{16}BN_3O$ (265.12): B, 4.08; N, 15.86; found: B, 4.06; N, 15.54, and



V VI VII

then reaction of *p*-chlorobenzamidoxime and trimethyl borate, and hydrolysis gave Vb (R = OH,



(2) Compound Ia (R = Ph, R′ = R″ = H, m.p. 212–214°) has been described by Chissick, *et al.* (ref. 1), who stated that an "alcoholic solution of Ia was not stable; after a few hours the ultraviolet spectrum became identical with that of a mixture of *o*-aminobenzamide and phenylboronic anhydride."

(3) 1:1 Addition products of carboxylic acid amides and $POCl_3$ were first reported by R. C. Shah, R. K. Deshpande and J. S. Chaubal, *J. Chem. Soc.*, 642 (1932). More recently, H. Bredereck and his coworkers [*Chem. Ber.*, **92**, 837, 1456 (1959); **94**, 1883, 2278 (1961)] have found that a large variety of amides and lactams form 1:1 addition compounds. 1:1-Addition products of 9-acridanones and $POCl_3$ have been described by K. Gleu, S. Nitzsche and A. Schubert, *Ber.*, **72**, 1093 (1939); K. Gleu and A. Schubert, *Ber.*, **73**, 805 (1940), and N. S. Drozdov, *Trudy Kafedry Biochim. Moskov Zootekh. Inst. Konevodsta* **1944**, 42 (1945) [*C.A.* **41**, 763b (1947)] *J. Gen. Chem.* (*U.S.S.R.*) **16**, 455 (1946) [*C.A.* **41**, 966d (1947)].

(4) We have prepared the $POCl_3$-addition compound of 9-acridanone and find it to have strong bands at 7.77 and 9.05 μ.

(5) Proposed mechanism:

(6) The unusual stability of IV to boilin g water again demonstrates the influence of substituents on the stability of this heterocyclic system. Moreover, IV remains unchanged in absolute alcohol at room temperature for at least 192 hours.