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; $\epsilon^{230}_{\max}$ 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] $[\alpha]^{25}\mathrm{D}$ + 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 $[\alpha]^{25}_{\mathrm{D}}$ + 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.

$$\underset{\mathrm{I}}{C_6H_{13}(CH_3)CHNO_2} + H^+ \rightleftarrows \underset{\mathrm{III}}{C_6H_{13}(CH_3)CHNO_2H^+} \qquad (1)$$

$$\underset{\mathrm{III}}{C_6H_{13}(CH_3)CHNO_2H^+} + B \overset{\text{slow}}{\rightleftarrows} \underset{\mathrm{IV}}{C_6H_{13}(CH_3)C{=}NO_2H} + BH^+ \qquad (2)$$

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

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).

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(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

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