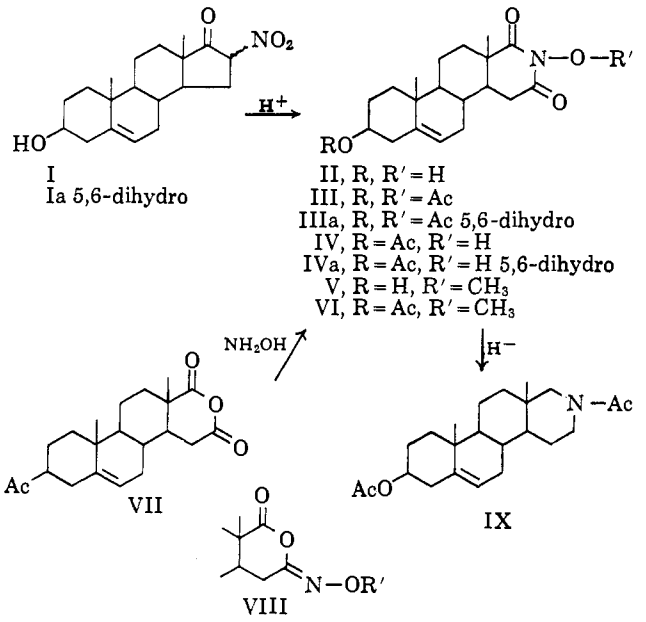
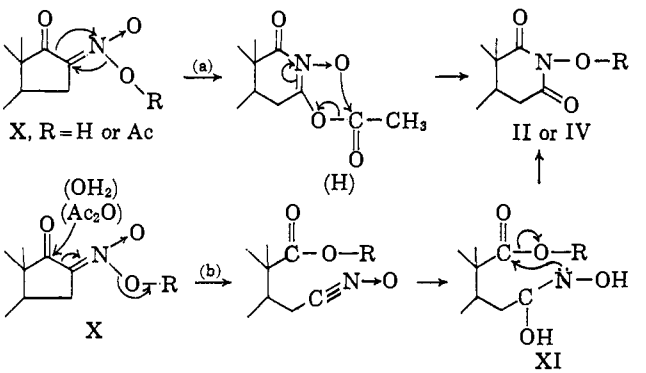


acid imide, m.p. 205–207° dec., from 2-nitrocholestanone, m.p. 135–136°, or from its potassium salt upon treatment with acetic anhydride or upon treatment first with hydrochloric acid followed by acetylation of the intermediate N-hydroxyimide, m.p. 184–188°. We also confirm the results of Lowry[3] and of Larson and Wat[1] for the isolation of N-hydroxycamphorimide from the rearrangement of α-nitrocamphor or from the reaction of camphoric anhydride with hydroxylamine.

The structure assignment of an N-hydroxyimide (*cf.* II–IV) rather than an isomeric anhydride oxime (*cf.* VIII) to the products described above is based on infrared spectra and chemical transformations. The infrared spectra (in KBr) of our steroidal N-hydroxyimides as well as of N-hydroxycamphorimide show strong absorption at 3250–3300 cm.$^{-1}$ (OH), 1720–1730 cm.$^{-1}$ and 1675–1690 cm.$^{-1}$ (imide carbonyls); anhydride oximes of type VIII have been shown[4] to absorb strongly above 1800 cm.$^{-1}$. The N-acetoxyimides (*i.e.*, III and IV) show strong absorption at 1800 cm.$^{-1}$ (acetate carbonyl attached to strong electron withdrawing groups),[5] 1720 and 1700 cm.$^{-1}$ (imide carbonyl).

3β,N-Dihydroxy-16,17-seco-5-androstene-16,17-dioic imide (II) is stable to acid hydrolysis even in the presence of levulinic acid. This and the other chemical properties of these compounds indicate a structure such as II rather than one of type VIII. Further evidence of the piperidine skeleton is supplied by lithium aluminum hydride–aluminum chloride reduction of III followed by acetylation to the known[6] 3β-acetoxy-N-acetyl-D-homo-17-aza-5-androstene (IX), m.p. 210–212°.

Two major paths may be considered to explain the rearrangement of these α-nitroketones to N-hydroxy- or N-acetoxyimides.[7] The mechanism proposed by Larson and Wat[1] involving protonation of the carbonyl and multiply-charged intermediates is unlikely and not applicable to the rearrangement proceeding in acetic anhydride. That the aci form of the nitro compound (*cf.* X) may be involved is suggested by the fact that even the salt of the nitroketone reacts with acetic anhydride and from the fact that 2-nitroindanone, which is known[8] to enolize to 1-hydroxy-2-nitroindene rather than to an aci form such as X, does not undergo rearrangement under acid conditions. Path (a) represents a Beckmann rearrangement of an aci form of a nitro compound analogous to that of a conventional oxime. Path (b) represents a cleavage reaction and is analogous to the cleavage of cyclic α-oximino ketones or



of their acetates to nitrile acids followed by ring closure to an imide[5,9]; it is also analogous to an acid-catalyzed rearrangement of a nitro compound reported by Noland and co-workers.[10] Path (b) involves a hydroxamic acid intermediate (*cf.* XI) and might be applicable even if the reaction proceeded first to VIII and thence to II. Hydroxamic acid XI is also the most likely intermediate in the formation of these N-hydroxyimides from cyclic anhydrides and hydroxylamine. Experiments to elucidate the mechanism are in progress.

Acknowledgment.—This investigation was supported in part by Public Health Service Grant CY-4474 from the National Cancer Institute.

(3) T. M. Lowry, *J. Chem. Soc.*, **73**, 986 (1898); *ibid.*, **83**, 953 (1903).

(4) L. A. Carpino, *J. Am. Chem. Soc.*, **79**, 98 (1957); D. E. Ames and T. F. Grey, *J. Chem. Soc.*, 631, 3518 (1955); *ibid.*, 2310 (1959).

(5) A. Hassner and I. H. Pomerantz, *J. Org. Chem.*, **27**, 1760 (1962).

(6) B. M. Regan and F. N. Hayes, *J. Am. Chem. Soc.*, **78**, 639 (1956).

(7) A third path, analogous to the acid-promoted rearrangement of primary nitroalkanes to hydroxamic acids [H. L. Yale, *Chem. Rev.*, **33**, 209 (1943)] except involving a cleavage reaction, may also be considered.

(8) R. D. Campbell and C. L. Pitzer, *J. Org. Chem.*, **24**, 1531 (1959).

(9) A. Hassner, W. A. Wentworth and I. H. Pomerantz, *ibid.*, **28**, 304 (1963).

(10) W. E. Noland, J. H. Cooley and P. A. McVeigh, *J. Am. Chem. Soc.*, **81**, 1209 (1959).

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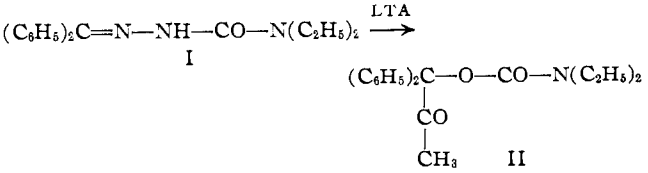
Conversion of a Semicarbazone to a Carbamate. A Novel Rearrangement

Sir:

We wish to report a new reaction of a semicarbazone. When benzophenone 4,4-diethylsemicarbazone, I, is treated with lead tetraacetate there is obtained a 63% yield of 2-oxo-1,1-diphenylpropyl diethylcarbamate, II.



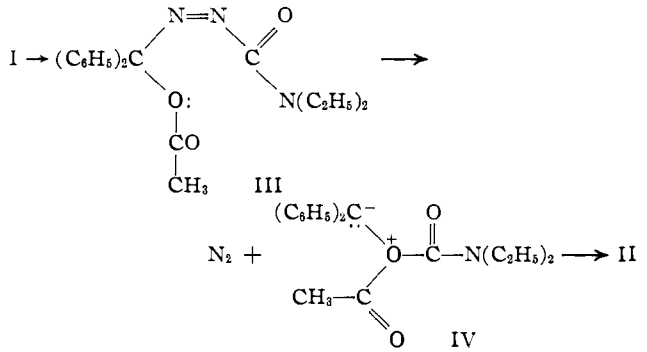
This reaction is in contrast to the behavior of ketohydrazones, which with lead tetraacetate form azoacetates in 55 to 90% yields.[1] The addition of 0.03 mole of I, m.p. 100–101° (*Anal.*[2] Calcd. for $C_{18}H_{21}N_3O$: N, 14.23. Found: N, 14.32) to lead tetraacetate (0.032 mole) at 0–5° in methylene chloride solution according

(1) D. C. Iffland, L. Salisbury and W. R. Schafer, *J. Am. Chem. Soc.*, **83**, 747 (1961).

(2) All elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

to the procedure employed with ketohydrazones[1] gave a mixture which slowly evolved nitrogen at 0—5°. After 20 hr. at this temperature, II was isolated, m.p. 70–71° (*Anal.* Calcd. for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.15. Found: C, 74.00; H, 7.22; N, 4.15). This compound was characterized as follows: hydrolysis in boiling 20% phosphoric acid gave carbon dioxide and 1-hydroxy-1,1-diphenylpropanone, m.p. 70–71° (*Anal.* Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.23. Found: C, 79.43; H, 6.05). Reported value[3]: m.p. 66–67°. A positive iodoform reaction and the isolation of benzilic acid (m.p. 150°) were achieved with the carbamate and the hydroxy ketone. Strong infrared bands for carbamate and saturated ketone carbonyl groups[4] were found at 1708 and 1720 cm.$^{-1}$, respectively.

The following mechanism is proposed to account for the over-all result

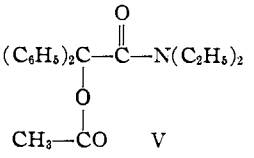


III

IV

The formation of azoacetate III parallels the reaction of hydrazones with lead tetraacetate[1] and is followed by an intramolecular nucleophilic displacement at the amide carbonyl group.[5] The formation of nitrogen by decomposition of the quasi-five-member ring undoubtedly provides significant driving force for this reaction. By a 1,2-shift analogous to the Stevens rearrangement,[6] IV is converted into II. This appears to be the first proposal of a Stevens-type rearrangement involving an oxonium ion intermediate.

The above formulation leads one to expect an alternate path for the rearrangement of the zwitterion IV, *viz.*, carbanion attack on the amide carbonyl carbon. While the ester V anticipated from this migration has



V

not been isolated, its presence has been indicated. Concentration of the mother liquor from which II was isolated (0.019 mole) provided an oil which exhibited an acetate infrared band at 1750 cm.$^{-1}$ in addition to bands at 1708 cm.$^{-1}$ and 1720 cm.$^{-1}$. Acid hydrolysis of this oil produced benzilic acid (0.0013 mole) as required for the second rearrangement product as well as the 1-hydroxy-1,1-diphenylpropanone (0.0093 mole) from II. Thus the ratio of the two rearrangement products (II to V) in the original reaction mixture may be approximately 20 to 1.

The following morpholine derivative of benzophenone semicarbazone also reacts with lead tetraacetate at 0 to 5° and produces a carbamate, $(C_6H_5)_2C{=}N{-}NH{-}CO{-}N(CH_2CH_2)_2O$, m.p. 104–105° (*Anal.* Calcd. for $C_{18}H_{19}N_3O_2$: N, 13.58. Found: N, 13.65). After reaction as above, 2-oxo-1,1-diphenylpropyl 4′-morpholine carboxylate was isolated in 52% yield, m.p. 160–161° (*Anal.* Calcd. for $C_{20}H_{21}NO_3$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.92; H, 6.20; N, 3.96).

A study of the generality of this new rearrangement reaction is in progress as is also the question of whether thiosemicarbazones undergo a similar reaction.

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(3) C. L. Stevens and A. E. Sherr, *J. Org. Chem.*, **17**, 1228 (1952).

(4) G. H. Beaven, E. A. Johnson, H. A. Willis and R. G. J. Miller, "Molecular Spectroscopy," Macmillan Co., New York, N. Y., 1961, pp. 239, 249.

(5) The possibility that acetic acid also formed in the reaction with lead tetraacetate may catalyze the transformation of III to IV by protonation of the amide carbonyl group is under study.

(6) J. H. Brewster and M. W. Kline, *J. Am. Chem. Soc.*, **74**, 5179 (1952).

On the Mechanism of the Reactions of α-Bromoketones with Triphenylphosphine[1]

Sir:

α-Bromoketones react with tricovalent organophosphorus compounds to give α-keto phosphonium salts[2] or derived α-keto phosphonates[3] or, alternatively, enol phosphonium salts[4] or the derived enol phosphates.

The mechanisms proposed for these reactions include initial attack of phosphorus on oxygen to give enol phosphonium salts directly[4c] or displacement on bromine to give an enolate bromophosphonium ion pair which is then converted to enol phosphonium salts. The formation of α-keto phosphonium salts has been envisaged to occur either by straightforward displacement[5] or by rearrangement of enol phosphonium salts.[6]

We now have found that the formation of α-keto phosphonium salts does not occur by straightforward displacement of bromide ion by tricovalent phosphorus and that enol phosphonium salts are formed irreversibly.

On the basis of our evidence we postulate that tricovalent organophosphorus compounds displace on bromine of α-bromoketones to give enolate bromophosphonium ion pairs which go either to enol phosphonium salts and enol phosphates or α-keto phosphonium salts and α-keto phosphonates.[7]

Reaction of phenacyl bromide with triphenylphosphine, in the presence of methanol, acetic acid, dimedone or diethyl malonate, leads to acetophenone (I) and a decreased yield of phenacyltriphenylphosphonium bromide (II) which is the product formed under anhydrous conditions.[2] The phosphonium bromide (II) has been shown to be stable to refluxing methanol.[4a] The data are summarized in Table I.

Debromination by methanol, acetic acid or dimedone can occur by three pathways: protonation of an enolate ion, or solvolysis of an enol phosphonium salt or a bromophosphonium salt. Diethyl malonate can be effective only as a proton donor and its utilization as a debrominating agent provides evidence for the presence of the enolate bromophosphonium ion pair at some

(1) This research was supported in part by a grant from the Society of the Sigma Xi.

(2) F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 41 (1957).

(3) F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961).

(4) (a) I. J. Borowitz and L. I. Grossman, *Tetrahedron Letters*, **No. 11**, 471 (1962); (b) H. Hoffman and H. J. Diehr, *ibid.*, **No. 13**, 583 (1962); (c) S. Trippett, *J. Chem. Soc.*, 2337 (1962).

(5) F. Cramer, *Angew Chem.*, **72**, 239 (1960).

(6) This possibility was suggested by Lord Todd in a discussion session: *Proc. Chem. Soc.*, 106 (1962).

(7) Similar conclusions concerning the Perkow reaction have been reached by: (a) A. J. Speziale and L. R. Smith, *J. Am. Chem. Soc.*, **84**, 1868 (1962); (b) B. Miller, *J. Org. Chem.*, **28**, 345 (1963).