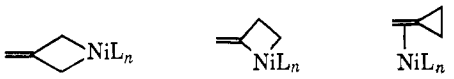
(C=O) and 883 cm^{-1} (=CH_2); nmr (CCl_4) δ 1.00 and 1.10 (s, 3 H each, $C(CH_3)_2$), 1.6–2.9 (m, 5 H, >CH and $>CH_2$), 3.58 (s, 3 H, $COOCH_3$), and 4.74 (m, 2 H, $=CH_2$). Ozonolysis gave the previously reported methyl 3,3-dimethyl-4-oxocyclopentanecarboxylate.[13] Similar cycloaddition using isopropylidenecyclopropane (**1c**)[14] furnished the isomeric adduct **6** (61%), which upon ozonolysis gave **3**: mass *m/e* 168 (M^+); ir (neat) 1735 cm^{-1} (C=O); nmr (CCl_4) δ 1.60 (s, 6 H, $=C(CH_3)_2$), 1.7–3.0 (m, 7 H, >CH and $>CH_2$), and 3.60 (s, 3 H, $COOCH_3$). If a trimethylenemethane complex such as **4** were involved as the intermediate, these two reactions should give the same adduct or an identical mixture of isomers. The lack of crossover of the products suggests that methylenecyclopropanes enter into the cycloaddition with olefins at C-2 and C-3 or C-1 and C-3.[15]

Thus the present reaction, which would formally be analyzed as a [$_\sigma 2 + {}_\pi 2$] process, serves as a single-step synthesis of methylenecyclopentane derivatives starting with readily available materials.[16] Further studies on the scope and the detailed mechanism including the stereochemistry of the addition will be published at a later time.

(13) J. C. Bardhan, S. K. Banerji, and M. K. Bose, *J. Chem. Soc.*, 1127 (1935).

(14) (a) K. Sisido and K. Utimoto, *Tetrahedron Lett.*, 3267 (1966); (b) E. E. Schweizer and J. G. Thompson, *Chem. Commun.*, 666 (1966).

(15) σ complexes i or ii or simple π complex ii (L = CH_2=CHZ) could be the possible intermediate.



i ii iii

(16) Difficulty in Wittig condensation between cyclopentanone and phosphoranes is well known. See A. Maercker, *Org. React.*, 14, 270 (1965).

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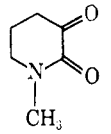
Rearrangement of Pyruvates to Malonates[1]

Sir:

Although α-ketocarboxylic acids are known to react with periodate to give carbon dioxide and the carboxylic acid with one less carbon,[2] the reaction of α-keto acyl derivatives with periodate has not been reported. We have synthesized the pyruvyl derivatives **1** and **2a–c**[3–5] and now report their reaction with periodate which leads to skeletal rearrangement.



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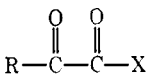


2a, R = CH_3CH_2; X = OC_2H_5
b, R = CH_3CH_2; X = $N(CH_3)_2$
c, R = $CH_3(CH_2)_4$; X = NH_2

(1) This work was supported in part by Grant No. MH12797 from the National Institute of Mental Health, U. S. Public Health Service.

(2) D. B. Sprinson and E. Chargraff, *J. Biol. Chem.*, 164, 433 (1964).

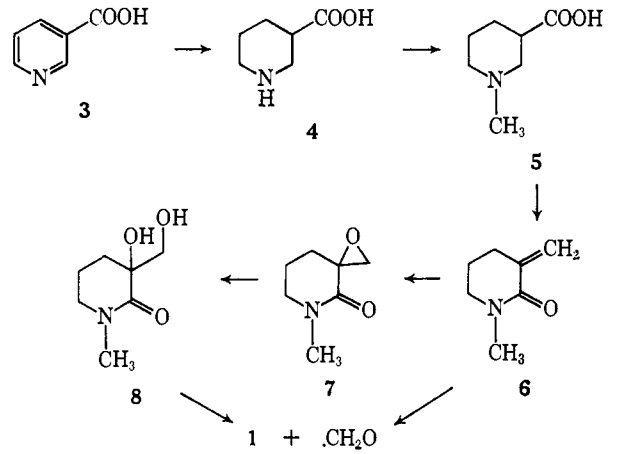
(3) All compounds reported in this communication have been characterized spectrally (uv, ir, nmr) and analytically (elemental, mass spectrum).

(4) E. Vogel and H. Schinz, *Helv. Chim. Acta*, 33, 116 (1950).

(5) M. Igarashi and H. Midorikawa, *J. Org. Chem.*, 28, 3088 (1963).

1-Methyl-2,3-piperidinedione (**1**) was synthesized as shown in Scheme I. Nicotinic acid (**3**) was catalyt-

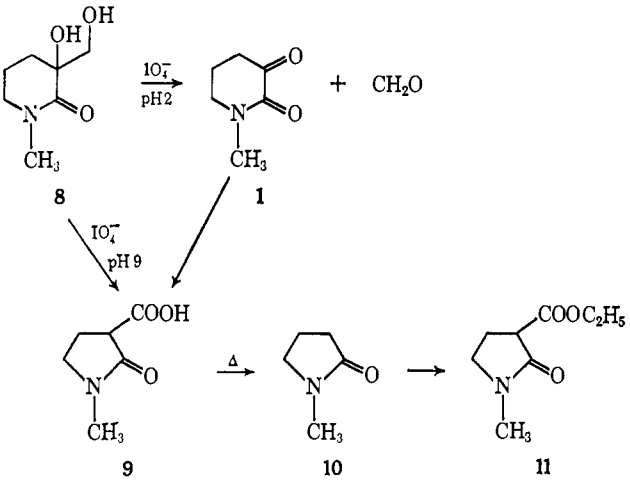
Scheme I



ically (PtO_2) hydrogenated to nipecotic acid (**4**) which was reductively methylated to give *N*-methyl derivative **5** (100%).[6] Reaction of **5** in refluxing acetic anhydride for 3 hr gave 1-methyl-3-methylene-2-piperidone (**6**) in 93% yield.[7] Ozonolysis of **6** at −78° followed by addition of trimethoxyphosphine[8] or dimethyl sulfide[9] and chromatography gave the piperidinedione **1** in 65% yield. Alternately, **6** was epoxidized (*m*-chloroperbenzoic acid) to **7** (88%), epoxide **7** was hydrolyzed with 6% $HClO_4$ to **8**,[10] and glycol **8** was oxidized with $NaIO_4$ in dilute HCl, giving **1** (83%).[11]

Although reaction of glycol **8** with excess periodate at pH 2 gave piperidinedione **1** and formaldehyde, the reaction (Scheme II) of either **8** or **1** with 6 equiv of

Scheme II



$NaIO_4$ at pH 7 or 9 for 10 hr gave 3-carboxy-1-methyl-2-pyrrolidinone (**9**) in 80% yield. Heating **9** at 150°

(6) N. A. Preobrazhenskii and L. B. Fisher, *J. Gen. Chem. USSR*, 11, 140 (1941).

(7) M. Ferles, *Collect. Czech. Chem. Commun.*, 29, 2323 (1964).

(8) W. S. Knowles and Q. E. Thompson, *J. Org. Chem.*, 25, 1031 (1960).

(9) J. J. Pappas, W. P. Keaveney, E. Gancher, and M. Berger, *Tetrahedron Lett.*, 4273 (1966).

(10) E. E. Van Tamelen, A. Storni, E. J. Hessler, and M. Schwarz, *J. Amer. Chem. Soc.*, 85, 3295 (1963).

(11) Due to the high water solubility of most of the compounds reported here, continuous extraction with methylene chloride has been used for isolation from aqueous solution.

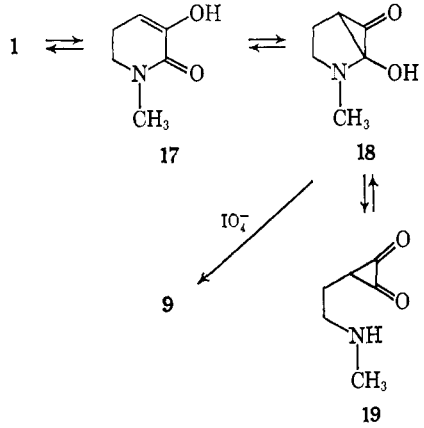
(evolution of CO_2) gave 1-methyl-2-pyrrolidinone (**10**). Also, **9** was identical with authentic 3-carboxy-1-methyl-2-pyrrolidinone obtained by hydrolysis of 3-ethoxycarbonyl-1-methyl-2-pyrrolidinone (**11**), prepared by condensation of diethyl carbonate with **10** (benzene, sodium hydride).

In order to examine the scope of the periodate reaction, α-ketoacyl derivatives **2a–c** were prepared by the addition of ethanol, dimethylamine, and ammonia, respectively, to the corresponding acid chloride. The acid chlorides were synthesized from the appropriate acid using $SOCl_2$ and a catalytic amount of dimethylformamide[12] at room temperature for 2 hr. Reaction of ethyl 2-oxobutanoate (**2a**) with $NaIO_4$ at pH 7 in the dark for 22 hr followed by esterification with diazomethane and preparative glpc indicated the presence of two compounds in addition to methyl propionate formed by hydrolysis of **2a** and periodate oxidation[2] of the resulting keto acid. The first compound (20%) was identical with an authentic sample of methyl ethyl 2-methylmalonate (**12**), the expected esterified rearrangement product. The second compound (17%) was characterized as methyl ethyl 2-hydroxy-2-methylmalonate (**13**), most probably formed from malonate **12** by further reaction with periodate.[13]

In an analogous manner, oxidation of α-ketodimethylamide **2b** with 1.5 equiv of $NaIO_4$ at pH 9 for 72 hr gave in 69% yield the rearrangement product, *N,N*-dimethyl 2-methylmalonamic acid (**14**), identical with an authentic sample prepared by hydrolysis of ethyl *N,N*-dimethyl 2-methylmalonamate (**15**).[14] Finally, periodate oxidation of 2-oxoheptanamide (**2c**) at pH 9 gave 2-butylmalonamic acid (**16**) in 19% yield. No attempts have been made to optimize the yields of the oxidation products of **1** and **2a–c**. Based on these models, any cyclic or acyclic α-keto ester or amide is potentially convertible to an α-dicarboxylic acid derivative by this rearrangement unless unfavorable steric or electronic influences are present.

The postulated mechanism for the oxidative rearrangement of pyruvyl derivatives is shown in Scheme III, using **1** as the example. α-Ketoamide **1** would be

Scheme III



expected to be in equilibrium with its enol **17** which in turn would reversibly form cyclol **18**. Cyclol **18** should have two alternate reaction modes: (a) oxidation by periodate[15] to give the observed product **9**, or (b) reversal of cyclol **18** formation by C–N bond cleavage, giving the symmetrical intermediate cyclopropanedione **19**.

Support for this mechanism has been obtained in several ways. First, the fact that **1** is stable to periodate at pH 2 is consistent with the proposed requirement for enolization to **17**. Secondly, the enol form of a cyclopropanedione has been synthesized[16] giving credence to the postulation of **19** as an intermediate. Finally, several isotopic labeling experiments have been carried out, and the results are consistent with the proposed mechanism.

Starting with nicotinic acid-*7*-^{14}C, glycol **8** labeled in the carbonyl carbon was obtained. Periodate oxidation of glycol **8**-*2*-^{14}C (14.1×10^4 dpm/m*M*; 100.0%) at pH 9 gave the rearrangement product pyrrolidinone **9** (14.0×10^4 dpm/m*M*; 99.3%) and formaldehyde (24 dpm/m*M*; 0.0%). Decarboxylation of **9** gave 1-methyl-2-pyrrolidinone (14.0×10^4 dpm/m*M*; 99.3%) and carbon dioxide (853 dpm/m*M*; 0.6%). Resubmission of the labeled sample of **9** to oxidation, isolation, and decarboxylation did not alter the specific activity of **10** and the carbon dioxide obtained. As a result, the observed scrambling of label is a consequence of the reaction and is consistent with the postulated equilibrium between cyclol **18** and cyclopropanedione **19**.

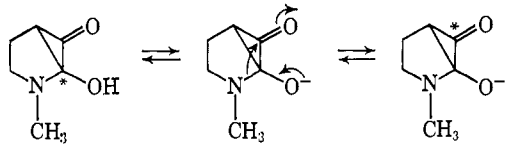
Systematic degradation of the 1-methyl-2-pyrrolidinone (**10**) formed by decarboxylation of **9** has established that all the activity is located in the carbonyl carbon, as the mechanism predicts. Degradation proceeded *via* alkaline hydrolysis to 4-methylaminobutanoic acid,[17] reductive methylation[18] to 4-dimethylaminobutanoic acid,[19] acid chloride formation, reaction with benzene to ω-dimethylaminobutyrophenone,[20,21] and oxidation[21] with CrO_3 to benzoic acid and *N,N*-dimethyl-β-alanine. All the activity was in the benzoic acid, corresponding to the carbonyl carbon; the β-alanine was inactive.

The postulated mechanism for the oxidation rearrangement involves the symmetrical intermediate, cyclopropanedione **19**, and leads to the prediction that the amount of label scrambling could be increased if 1-methyl-2,3-piperidinedione-*2*-^{14}C (**1**) were allowed to stand at pH 9 before oxidation. Accordingly, **1** (13.9×10^4 dpm/m*M*; 100%) was allowed to stand at pH 9 for 27 hr and 3-carboxy-1-methyl-2-pyrrolidinone (**9**) was isolated after adding periodate. Decarboxylation of **9** gave CO_2 (2.0×10^4 dpm/m*M*; 14.4%) and **10** (11.9×10^4 dpm/m*M*; 85.6%). The increased scrambling of label observed is consistent with the postulated symmetrical intermediate **19**.[22]

(12) H. H. Brosshard, R. Mory, M. Schmid, and Hch. Zollinger, *Helv. Chim. Acta*, 42, 1653 (1959).
(13) C. F. Huebner, S. R. Ames, and E. C. Bubl, *J. Amer. Chem. Soc.*, 68, 1621 (1946).
(14) W. Sucrow, *Chem. Ber.*, 101, 4230 (1968).
(15) P. W. Clutterbuck and F. Reuter, *J. Chem. Soc.*, 1467 (1935); B. Sklarz, *Quart. Rev., Chem. Soc.*, 21, 3 (1967).
(16) D. G. Farnum and P. E. Thurston, *J. Amer. Chem. Soc.*, 86, 4206 (1964); D. G. Farnum, J. Chickos, and P. E. Thurston, *ibid.*, 88, 3075 (1966).
(17) F. Korte, K. H. Buchel, H. Mader, G. Romer, and H. H. Schulze, *Chem. Ber.*, 95, 2424 (1962).
(18) R. E. Bowman and H. H. Stroud, *J. Chem. Soc.*, 1342 (1950).
(19) V. Prelog, *Collect. Czech. Chem. Commun.*, 2, 712 (1930).
(20) J. Sadet and P. Rumpf, *C. R. Acad. Sci.*, 254, 3105 (1962).
(21) A. A. Liebman, B. P. Mundy, and H. Rapoport, *J. Amer. Chem. Soc.*, 89, 664 (1967).

Work is continuing on the application of this rearrangement to other systems.

(22) Another mechanism consistent with the observed scrambling of label is equilibration in **18** *via* **18′** and **18″**. Further data that reflect



18 **18′** **18″**

on these mechanisms and further applications of this reaction will be presented in our full paper.

(23) National Science Foundation Predoctoral Fellow, 1967–1970.

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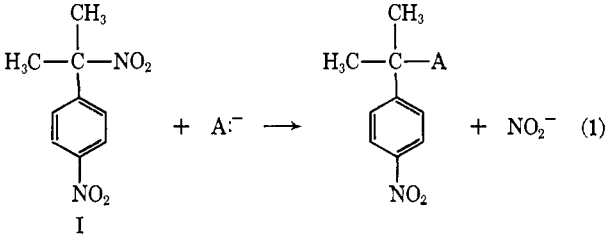
Received June 22, 1970

A New Reaction of α-Nitro Esters, Ketones, and Nitriles and α,α-Dinitro Compounds

Sir:

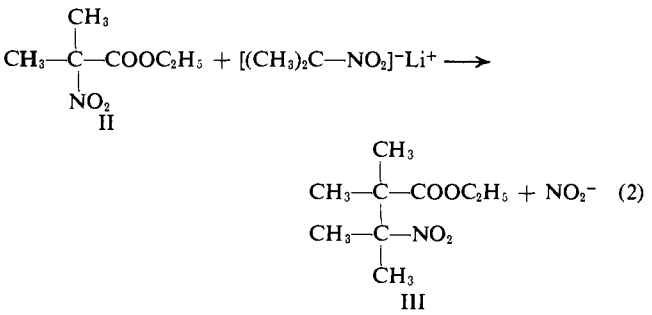
The aliphatic nitro group of α,*p*-dinitrocumene (I) is readily replaced by a variety of anions (eq 1).[1] We



I (1)

now report a new set of reactions in which displacement of a nitro group is observed in purely aliphatic systems. These reactions take place readily at room temperature and give excellent yields of pure products. They are noteworthy for providing very highly branched compounds which, at best, would be exceedingly difficult to prepare by any other means.

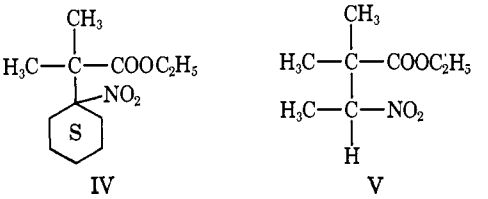
For example, the reaction of eq 2 takes place at



III (2)

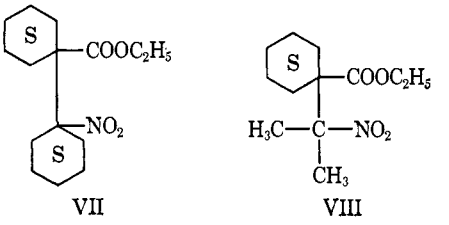
room temperature and gives a 95% yield of pure product. Significantly, ethyl α-chloroisobutyrate, $(CH_3)_2C(Cl)COOC_2H_5$, reacts far less rapidly than the α-nitro ester and, what little reaction does occur, does not follow the pattern of eq 2. With ethyl α-bromoisobutyrate, $(CH_3)_2CBrCOOC_2H_5$, the reaction with the lithium salt of 2-nitropropane is again slower than with the α-nitro ester and, again, the reaction pattern of eq 2 is not followed; instead, a complex set of products is formed. Clearly, the displacement of the nitro group of ethyl α-nitroisobutyrate (II) by the 2-nitropropane anion is not an SN2 process.[2]

The reaction of α-nitro esters with nitroparaffin salts appears to have wide applicability; when II is treated with the salt of nitrocyclohexane the corresponding alkylate IV is obtained in 82% yield. The salts of primary nitroparaffins may also be employed and, indeed, it is easy to isolate the monoalkylate; thus, with the lithium salt of nitroethane, V is obtained in 88% yield. In the same way, the reaction of the



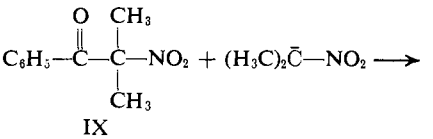
IV V

ethyl ester of α-nitrocyclohexanecarboxylic acid (VI) with the salt of nitrocyclohexane gives VII in 96% yield, while the salt of 2-nitropropane produces the pure β-nitro ester VIII in 94% yield.

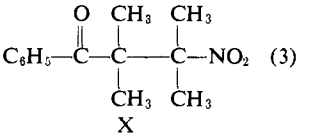


VII VIII

The nitro group of α-nitro ketones is also readily replaced. The reaction of eq 3 takes place in 30 hr in



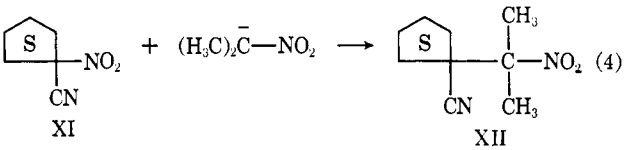
IX



X (3)

DMSO but requires only 3 hr in hexamethylphosphoramide; the yield of β-nitro ketone X is 80–85%. Here again it is significant that α-bromoisobutyrophenone gives a complex mixture of products and that α-chloroisobutyrophenone reacts less rapidly than α-nitroisobutyrophenone (IX).[2]

α-Nitro nitriles also react cleanly. For example, the reaction of nitro nitrile XI is complete after 4 hr and gives an 84% yield of the pure product (eq 4). Treat-



XI XII (4)

ment of α-nitroisobutyronitrile with the salt of 2-nitropropane gives XIII (90% yield in 1 hr); with the salt

(1) N. Kornblum, T. M. Davies, G. W. Earl, G. S. Greene, N. L. Holy, R. C. Kerber, J. W. Manthey, M. T. Musser, and D. H. Snow, *J. Amer. Chem. Soc.*, **89**, 5714 (1967).

(2) The matter of mechanism is discussed in the accompanying communication: N. Kornblum and S. D. Boyd, *ibid.*, **92**, 5784 (1970).