Cleavage, Reduction, and Decarboxylation of 1-Carboxybicyclo[4.3.1]decan-10-one

RICHARD D. SANDS

Department of Chemistry, Alfred University, Alfred, New York 14802

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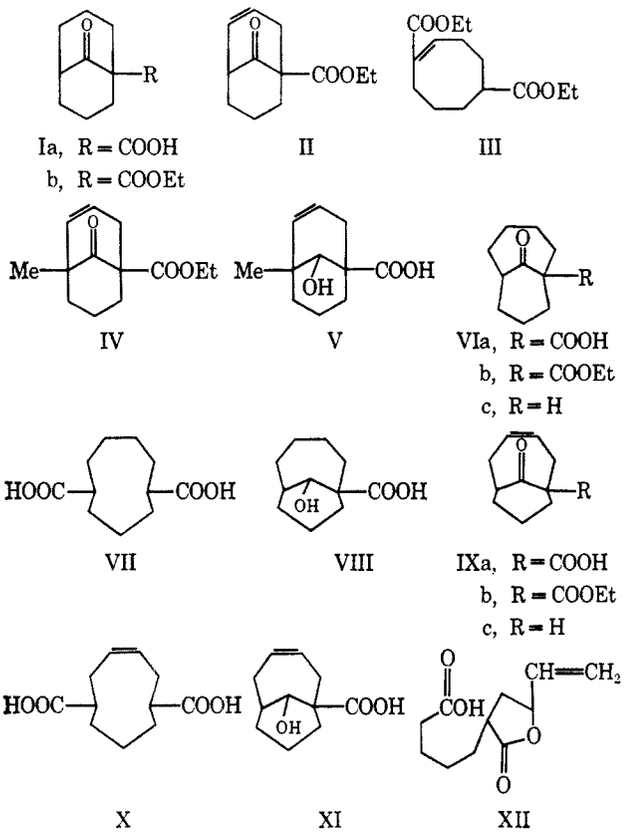
While 1-carboxybicyclo[3.3.1]nonan-9-one (Ia) has resisted decarboxylation,[1] and its ester, Ib, does not seem to have been cleaved, 1-carbethoxybicyclo[3.3.1]-non-3-en-9-one (II), which differs from Ib only by the double bond at C-3, has been smoothly converted into III with ethoxide.[2]

Suggestion has been made that the cleavage of II depends on the migration of the olefinic bond. That mechanism was supported when attempts to cleave IV under the same conditions resulted in formation of the alcohol V, because cleavage was blocked when the methyl group prevented the migration of the double bond.[3]



Ia, R = COOH
b, R = COOEt

II

III

IV

V

VIa, R = COOH
b, R = COOEt
c, R = H

VII

VIII

IXa, R = COOH
b, R = COOEt
c, R = H

X

XI

XII

In the present investigation, 1-carboxybicyclo[4.3.1]-decan-10-one (VIa), containing a six- and a seven-membered ring instead of the two six-membered rings of Ia, has been decarboxylated to VIc and has been cleaved upon heating with sodamide. The cleavage not only provides a convenient route to cyclononane-1,5-dicarboxylic acid (VII) but also demonstrates that the size of the ring as well as the double bond can help determine the course of the reaction. The reduction of the keto group of the ester, VIb, to the hydroxy acid, VIII, however, shows that the cleavage reaction still is not particularly easy.

Results similar to those obtained with VIa and VIb were obtained with IXa. The acid was cleaved to X with sodamide, it was decarboxylated to IXc by heat alone,[4] and the keto group of its ester, IXb, was reduced to an alcohol, XI, when the ester was heated with sodium hydroxide in methyl alcohol.

In addition to these reactions in common with VIa and VIb, however, IXb gave an unexpected cleavage of both rings. Upon standing in dilute ethoxide, IXb was partially converted to α-(δ-valeric acid)-γ-vinyl-γ-butyrolactone[5] (XII).

In an earlier investigation, 2-carbethoxycycloalkanones with five- and six-membered rings were cleaved during attempted alkylation while the seven-membered homolog was not.[5] It would now appear that a β-keto ester in a seven-membered ring is relatively easier to cleave when it is part of a bicyclic, instead of a monocyclic, molecule. The opposite apparently is true of a β-keto ester in a six-membered ring. It is concluded that the size of the rings involved is important in determining the occurrence of some of these cleavage, reduction, and decarboxylation reactions.

Experimental Section

Bicyclo[4.3.1]decan-10-one (VIc).—1-Carboxybicyclo[4.3.1]-decan-10-one[4] (8.75 g) was kept at its boiling point for 15 min and then distilled at 240° to give 5.0 g (72.7%) of solid with a camphor odor. Sublimation gave a pure white solid, mp 92–94°, whose infrared spectrum showed no carboxyl group and whose 2,4-dinitrophenylhydrazone derivative melted at 190°; ir ($CHCl_3$) 1690 cm^{-1} (C=O).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.95; H, 10.53. Found: C, 78.80; H, 10.45. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.83; H, 6.01. Found: C, 57.69; H, 5.95.

1-Carbethoxybicyclo[4.3.1]decan-10-one (VIb).—IXb (30 g) and 3.0 g of 5% Pd–$BaSO_4$ were placed in 300 ml of 95% alcohol and agitated overnight in a Parr low-pressure hydrogenator at 3 atm. Removal of the catalyst and the solvent was followed by distillation to give 19.3 g (63.6%) of light yellow liquid, bp 110–130° (2 mm). Redistillation gave a sample of pure material: bp 114° (1 mm), $n^{25}D$ 1.4752, ir (neat) 1712 cm^{-1} (C=O).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.64; H, 8.91. Found: C, 69.65; H, 8.99.

1-Carboxybicyclo[4.3.1]dec-3-en-10-ol (XI).[6]—IXb (20 g, 0.06 mol) was added dropwise with stirring to a solution of 15.2 g of sodium hydroxide in 45.6 ml of anhydrous methyl alcohol maintained at 100–120° in an oil bath. The resulting mixture was stirred overnight at 120°, cooled, and diluted with 200 ml of water, and then the alcohol was distilled off. The residue was acidified, heated with decolorizing carbon, and filtered. The filtrate was extracted with ether, and the ether was in turn washed with $NaHCO_3$ solution.

Acidification of the $NaHCO_3$ solution produced an oil which was taken up in ether and dried (Na_2SO_4). Evaporation of the ether produced 3.5 g of an impure solid which was heated with 60–110° ligroin, treated with decolorizing carbon, filtered, and allowed to evaporate partially. Filtration gave 1.0 g of hard white crystals, mp 108–110°, ir ($CHCl_3$) 1695 cm^{-1} (C=O).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.35; H, 8.16. Found: C, 66.98; H, 8.44.

1-Carboxybicyclo[4.3.1]decan-10-ol (VIII).[6]—1-Carbethoxybicyclo[4.3.1]decan-10-one (VIb) (15 g) was added over 30 min to a solution of 11.4 g of NaOH in 34.1 ml of methanol maintained at 125° in an oil bath. The resulting mixture was kept at 125° overnight, cooled, treated with 150 ml of water, and then distilled until the temperature of the residue reached 98°. Ex-

(1) A. C. Cope and M. E. Synerholm, *J. Amer. Chem. Soc.*, **72**, 5228 (1950).

(2) A. C. Cope, E. S. Graham, and D. J. Marshall, *ibid.*, **76**, 6159 (1954).

(3) G. L. Buchanan, A. McKillop, and R. A. Raphael, *J. Chem. Soc.*, 833 (1965).

(4) R. D. Sands, *J. Org. Chem.*, **29**, 2488 (1964).

(5) R. D. Sands, *ibid.*, **32**, 3681 (1967).

(6) The epimeric structure shown was assigned to V.[3] Similar considerations would lead to similar assignments for VIII and XI.

actly 74 ml of concentrated HCl was added over 1.5 hr, producing an orange–brown precipitate. The solid was taken up in ether, which was washed with $NaHCO_3$ solution. Acidification of the $NaHCO_3$ solution produced 11.4 g of crude solid, which yielded 8 g (60.3%) of white solid upon recrystallization from methylcyclohexane: mp 130–132°, neut equiv 198, ir ($CHCl_3$) 1700 cm^{-1} (C=O).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.67; H, 9.08. Found: C, 66.60; H, 9.09.

Ethyl ester had bp 115° (2 mm); $n^{22}D$ 1.4982; nmr ($CDCl_3$) 1.1–2.2 (m, 18 H), 3.8 (1 H), 3.9–4.3 (m, 3 H); ir (neat) 1700 (C=O), 3530 cm^{-1} (O–H); mass spectrum, *m/e* (rel intensity) 226 (5), 208 (25), 135 (100), 134 (44), 123 (31), 93 (43), 91 (25), 81 (51), 73 (28), (72).

Cyclononane-1,5-dicarboxylic Acid (VII).—1-Carboxybicyclo[4.3.1]decan-10-one (VIa) (1.0 g) was refluxed with 2 g of sodium amide in 50 ml of xylene for 1 week. The xylene was distilled off, the residue was treated with water, and the mixture was then extracted with ether. Next the water suspension was acidified and again extracted with ether. The ether extract was washed with water and dried (Na_2SO_4). Evaporation gave a small amount of white solid and 0.4 g of crude, sticky solid. Recrystallization from ethyl acetate gave 0.3 g of a clear white solid: mp 138–140°.

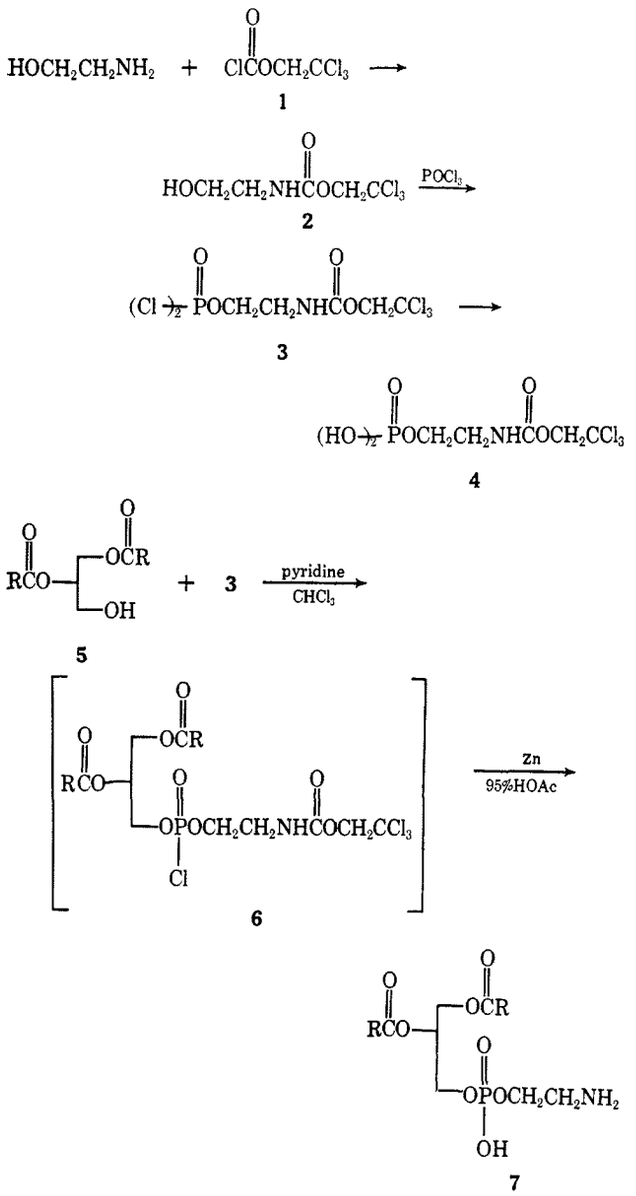
Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.68; H, 8.41. Found: C, 61.36; H, 8.39.

1-Cyclononene-4,8-dicarboxylic Acid (X).—1-Carboxybicyclo[4.3.1]dec-3-en-10-one[4] (IXa) (6.0 g) was refluxed for 1 week with 5 g of sodium amide in 200 ml of xylene. The above work-up, followed by recrystallization from ethyl acetate, produced 0.70 g of a white solid: mp 183–185°.

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.26; H, 7.56. Found: C, 61.89; H, 7.56.

α-(δ-Valeric acid)-γ-vinyl-γ-butyrolactone (XII).—1-Carbethoxybicyclo[4.3.1]dec-3-en-10-one (IXb) (20 g) in a solution of 0.92 g of sodium in 58.3 ml of absolute ethyl alcohol was left at room temperature for 3 days. Treatment with $NaHCO_3$ solution was followed by extraction with ether. From the ether extract, 9.5 g of starting material was recovered. Acidification of the bicarbonate layer, followed by extraction with ether, drying, and evaporation of the ether produced a crude solid. Upon recrystallization from toluene, only about 1 g of pure white solid was recovered. Its infrared spectrum identified it as XII.[5]

Registry No.—VIa, 13348-05-5; VIb, 13348-03-3; VIc, 20440-21-5; VIc (2,4-dinitrophenylhydrazone), 20440-22-6; VII, 20440-24-8; VIII, 20440-23-7; VIII (ethyl ester), 20440-25-9; X, 20440-26-0; XI, 20440-27-1.



Glycerolipids. II.[1] Use of the β,β,β-Trichloroethoxycarbonyl Protecting Group in Phosphatidylethanolamine Synthesis

F. R. PFEIFFER, S. R. COHEN, AND J. A. WEISBACH

Research and Development Division, Smith Kline and French Laboratories, Philadelphia, Pennsylvania 19101

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Phosphorylation of 1,2-diacylglycerols with phosphorus oxychloride or with a phosphorylated, protected amine is an approach to phosphatidylethanolamines. This method was limited by (1) the availability of appropriate optically active 1,2-diglycerides and (2) the current use of the carbobenzoxy[2,3] and phthaloyl[2–6] protecting groups, which suffer from complications, including the difficulty of purifying the final products. Our recent facile and direct synthesis of either optical modification of 1,2-diacylglycerols[1] and the use of a new amine protecting group described below, which is removed under reductive, nonhydrolytic conditions, provides renewed impetus for use of this general sequence to phosphatidylethanolamines.

The new protecting group, β,β,β-trichloroethoxycarbonyl, was originally introduced in the total synthesis of cephalosporin C;[7] recently, further demonstrations of its utility,[8] as well as that of the closely related β,β,β-tribromoethoxycarbonyl group,[9] have been reported. Removal of the β,β,β-trichloroethoxycarbonyl group is accomplished with zinc in 90% acetic acid[7] or in refluxing methanol.[8] Under these conditions, phosphatidylethanolamine variants containing mono- or poly-

(1) Part I: F. R. Pfeiffer, S. R. Cohen, K. R. Williams, and J. A. Weisbach, *Tetrahedron Lett.*, 3549 (1968).
(2) W. G. Rose, *J. Amer. Chem. Soc.*, **69**, 1384 (1947).
(3) E. Baer, *J. Amer. Oil Chemists Soc.*, **42**, 257 (1965).
(4) R. Hirt and R. Berchtold, *Helv. Chim. Acta*, **40**, 1928 (1957).
(5) I. R. Hunter, R. L. Roberts, and E. B. Kester, *J. Amer. Chem. Soc.*, **70**, 3244 (1948).
(6) E. Baer and D. Buchnea, *Can. J. Biochem.*, **39**, 1471 (1961).
(7) R. B. Woodward, J. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan, and H. Vorbruggen, *J. Amer. Chem. Soc.*, **88**, 852 (1966).
(8) T. B. Windholz and D. B. R. Johnston, *Tetrahedron Lett.*, 2555 (1967).
(9) A. F. Cook, *J. Org. Chem.*, **33**, 3589 (1968).