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A Novel 2,3-Pyrrolidinedione Ring Closure of 1,1,1,5,5,5-Hexachloro-4-dimethylamino-3,3-dimethyl-2-pentanone

Toshiaki Morimoto and Minoru Sekiya

Shizuoka College of Pharmacy[1)]

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A novel 2,3-pyrrolidinedione ring closure has been found to be induced on heating 1,1,1,5,5,5-hexachloro-4-dimethylamino-3,3-dimethyl-2-pentanone in ethanol in competition with the formation of α-chloro-γ-ketoacylamine.

Keywords——hydrolysis; 2,3-pyrrolidinedione; pyrrolidinone; ring closure; pyrrolidinium intermediate; dealkylation; reduction

In our previous paper[2)] it was reported that the hydrolysis of β-acyl-α-trichloromethylated *tert*-amines proceeds through aziridinium intermediates to give α-chloro-γ-ketoacylamines. Attention was also drawn to a second product formed in the hydrolysis of 1,1,1,5,5,5-hexachloro-4-dimethylamino-3,3-dimethyl-2-pentanone (**1**). We have now found another new course of hydrolysis of this substrate involving a 2,2-dichloro-3-pyrrolidinone intermediate.

The hydrolysis of **1** has been reported to give 2,5,5,5-tetrachloro-N,N,3,3-tetramethyl-4-oxovaleramide (**2**) on prolonged heating in 99% EtOH. A considerable amount of another less soluble material obtained from the reaction mixture in addition to the above product remained unidentified. The material was purified by recrystallization from EtOH to give prisms, mp 191.5—192.5°. Elemental analysis and the mass spectrum indicate a molecular formula of $C_8H_{10}Cl_3NO_2$. The infrared (IR) spectrum exhibits two carbonyl bands at 1770 cm^{-1} and 1720 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum shows three methyl singlets at δ 1.34, 1.58 and 3.46, and a methine singlet at δ 4.25. These data suggest the structure 1,4,4-trimethyl-5-trichloromethyl-2,3-pyrrolidinedione (**3**). Another possible structure, the aziridinone **3'**, could be excluded since the product is reasonably stable on refluxing in EtOH and its IR spectrum exhibits no α-lactam carbonyl band above 1800 cm^{-1}.[3)]

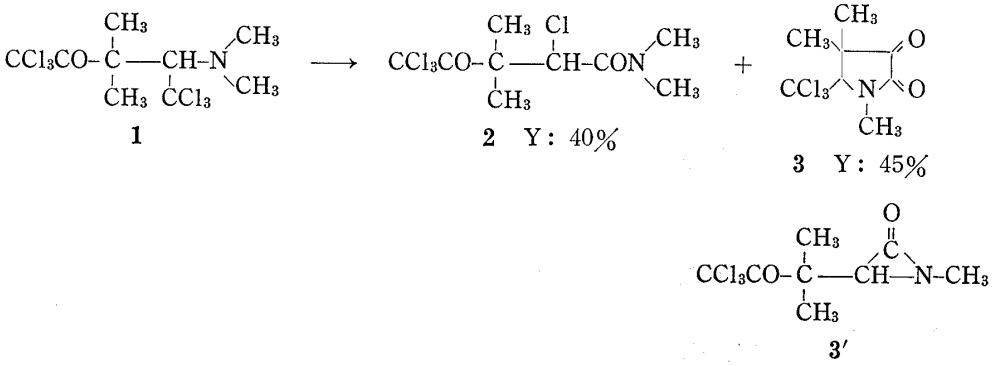
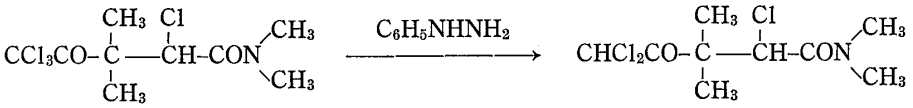


Chart 1

Compound **3** was allowed to react with several reagents, *i.e.* phenylhydrazine, sodium methoxide, sodium borohydride, and zinc-acetic acid, to obtain further evidence for the structure. Reaction of **3** with phenylhydrazine gave a phenylhydrazone **4**. Its IR spectrum exhibits a carbonyl band at 1690 cm^{-1}. The absence of phenylhydrazone formation from a

1) Location: *2-2-1, Oshika, Shizuoka, 422, Japan.*
2) T. Morimoto and M. Sekiya, *Chem. Pharm. Bull.* (Tokyo), **26**, 1586 (1978).
3) I. Lengyel and J.C. Sheehan, *Angew. Chem.*, **80**, 27 (1968).



2 5

trichloroacetyl structure was substantiated by the fact that reaction of **2** with phenylhydrazine gave a reduction product, 2,5,5-trichloro-N,N,3,3-tetramethyl-4-oxovaleramide (**5**). Reaction of **3** with sodium methoxide in MeOH gave a dehydrochlorinated product, 5-dichloromethylene-1,4,4-trimethyl-2,3-pyrrolidinedione (**6**), which was identified by elemental analysis and from the IR and NMR spectral measurements. When **3** was treated with sodium borohydride in EtOH, a reduction product, 3-hydroxyl-1,4,4-trimethyl-5-trichloromethyl-2-pyrrolidinone (**7**) was obtained. The structure was supported by the presence of an OH band at 3395 cm^{-1} in the IR spectrum and a doublet of the OH at δ 4.46 (J=4 Hz) and a doublet of methine proton at δ 3.91 (J=4 Hz) in the NMR spectrum. Compound **3** was also reduced by zinc dust in acetic acid to give an alcohol, 5-dichloromethyl-3-hydroxy-1,4,4-trimethyl-2-pyrrolidinone (**8**), which was identified by elemental analysis and IR and NMR spectral measurements.

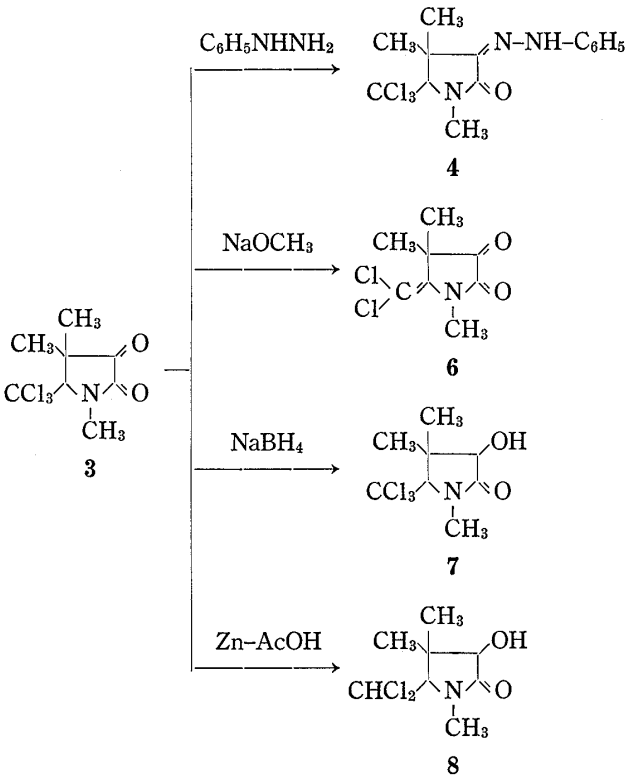


Chart 2

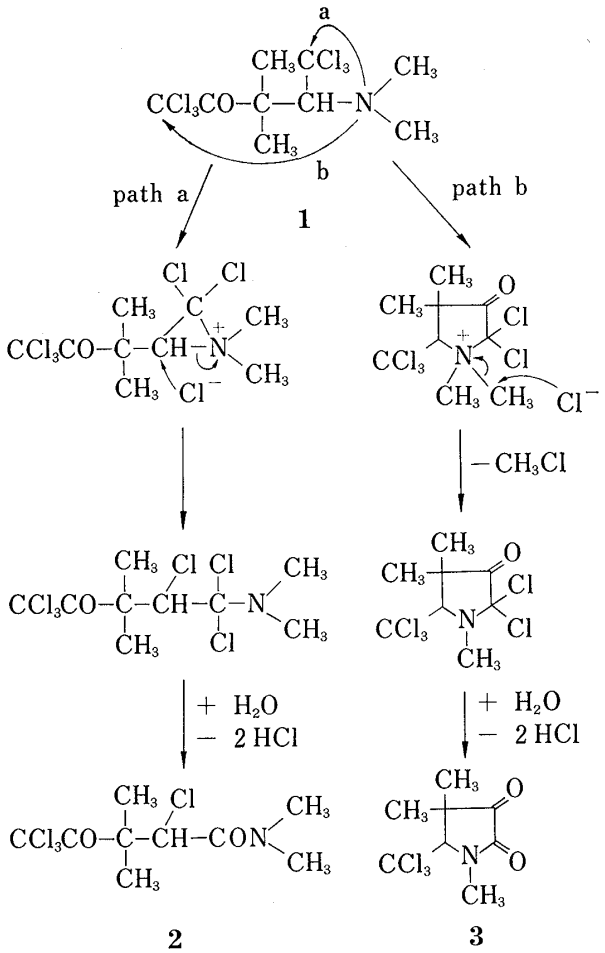


Chart 3

The hydrolysis course from **1** to **2** can be illustrated as path a in Chart 3 by analogy with the previously reported hydrolysis[4] of α-trichloromethylated *tert*-amines involving dichloroaziridinium intermediates. The course of the hydrolysis to **3** presented herein can be explain-

4) G.H. Alt and A.J. Speziale, *J. Org. Chem.*, **31**, 1340 (1966); A. Lukasiewicz, *Tetrahedron*, **24**, 7 (1968).

ed by path b. As distinct from the initial attack of tertiary amine nitrogen at the α-carbon trichloromethyl group in the former reaction, the present hydrolysis is initiated by an attack at the γ-carbon trichloromethyl group proceeding through a pyrrolidinium intermediate, followed by dealkylation. The step of dealkylation can be interpreted by analogy with the von Braun cyanogen bromide reaction[5] and the dealkylation reaction of dichloromethylenaminium salts.[6] The hydrolysis producing 2,3-pyrrolidinedione was only observed with the substrate **1**, and not with its analogs possessing morpholine and piperidine amine moieties. Presumably dealkylation may be suppressed in these cases.

Experimental[7]

Hydrolysis of 1,1,1,5,5,5-Hexachloro-4-dimethylamino-3,3-dimethyl-2-pentanone (1)——A solution of 2.0 g of **1** in 99% EtOH (20 ml) was heated under reflux for 8 hr. After the reaction solution had been cooled in an ice-bath, crystalline precipitates were collected by filtration. Recrystallization from EtOH gave 0.65 g (45%) of 1,4,4-trimethyl-5-trichloromethyl-2,3-pyrrolidinedione (**3**) as colorless needles, mp 191.5—192.5°. *Anal.* Calcd. for $C_8H_{10}Cl_3NO_2$: C, 37.16; H, 3.90; N, 5.42. Found: C, 37.19; H, 3.87; N, 5.37. MS *m/e*: 257 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1770 (C=O), 1720 (N–C=O). NMR ($CDCl_3$) δ: 1.34 (3H, s, CH_3), 1.58 (3H, s, CH_3), 3.46 (3H, s, NCH_3), 4.25 (1H, s, >CH). From the filtrate, 2,5,5,5-tetrachloro-N,N,3,3-tetramethyl-4-oxovaleramide (**2**) (0.7 g, 40%) was obtained as described in our previous paper.[2]

Hydrolysis of 1,1,1,5,5,5-Hexachloro-3,3-dimethyl-4-piperidino-2-pentanone——A solution of 4.0 g of 1,1,1,5,5,5-hexachloro-3,3-dimethyl-4-piperidino-2-pentanone in 99% EtOH (40 ml) was heated under reflux for 14 hr. The solvent was removed by evaporation and ether was added to the residue. A small amount of insoluble piperidine hydrochloride was filtered off. Removal of the solvent left an oily residue which was fractionally distilled under reduced pressure to give 2.4 g (69%) of 1-(2,5,5,5-tetrachloro-3,3-dimethyl-4-oxovaleryl)piperidine as a viscous liquid, bp 135—136° (0.02 mmHg). *Anal.* Calcd. for $C_{12}H_{17}Cl_4NO_2$: C, 41.29; H, 4.91; N, 4.01. Found: C, 41.62; H, 4.94; N, 3.83. IR ν_{max}^{neat} cm^{-1}: 1726 (C=O), 1656 (N–C=O). NMR ($CDCl_3$) δ: 1.2—2.0 (6H, m, $3\times CH_2$), 1.67 (3H, s, CH_3), 1.89 (3H, s, CH_3), 3.4—3.7 (4H, m, $N(CH_2)_2$), 5.00 (1H, s, >CH).

Reaction of 1,4,4-Trimethyl-5-trichloromethyl-2,3-pyrrolidinedione (3) with Phenylhydrazine——A solution of 0.26 g of **3** and 0.16 g of phenylhydrazine in EtOH (10 ml) was heated under reflux for 3.5 hr. After removal of the solvent by evaporation, the crystalline residue was triturated with isopropyl ether and filtered. Recrystallization from EtOH gave 0.25 g (72%) of phenylhydrazone **4** as colorless prisms, mp 140—141°. *Anal.* Calcd. for $C_{14}H_{15}Cl_3N_3O$: C, 48.37; H, 4.34; N, 12.09. Found: C, 48.30; H, 4.57; N, 12.11. IR ν_{max}^{KBr} cm^{-1}: 3280 (NH), 1690 (C=O), 1592 (C=C). NMR ($CDCl_3$) δ: 1.50 (3H, s, CH_3), 2.05 (3H, s, CH_3), 3.31 (3H, s, NCH_3), 3.82 (1H, s, >CH), 7.0—7.35 (5H, m, C_6H_5), 8.48 (1H, s, NH).

Reaction of 2,5,5,5-Tetrachloro-N,N,3,3-tetramethyl-4-oxovaleramide (2) with Phenylhydrazine——A solution of 0.31 g of **2** and 0.32 g of phenylhydrazine in EtOH (5 ml) was heated under reflux for 1 hr. After removal of the solvent by evaporation, the crystalline residue was triturated with water, filtered, and dried. Recrystallization from petr. ether gave 0.255 g (93%) of 2,5,5-trichloro-N,N,3,3-tetramethyl-4-oxovaleramide (**5**) as colorless needles, mp 116—117°. *Anal.* Calcd. for $C_9H_{14}Cl_3NO_2$: C, 39.37; H, 5.14; N, 5.10. Found: C, 39.23; H, 5.15; N, 5.11. IR ν_{max}^{KBr} cm^{-1}: 1728 (C=O), 1635 (N–C=O). NMR ($CDCl_3$) δ: 1.45 (3H, s, CH_3), 1.64 (3H, s, CH_3), 2.91, 3.12 (3H, 3H, s, s, $N(CH_3)_2$), 4.80 (1H, s, >CH), 6.64 (1H, s, $CHCl_2$).

Reaction of 3 with Sodium Methoxide——Compound **3** (0.26 g) was added to a methanolic solution of sodium methoxide (prepared from 0.046 g of sodium metal and 20 ml of anhydrous MeOH), and the mixture was stirred at room temperature for 2 hr. CO_2 gas was bubbled into the reaction mixture. After removal of the solvent by evaporation, the residue was extracted with ether. Removal of the solvent left a crystalline residue which on recrystallization from hexane gave 0.20 g (91%) of 5-dichloromethylene-1,4,4-trimethyl-2,3-pyrrolidinedione (**6**) as pale yellow plates, mp 93—94°. *Anal.* Calcd. for $C_8H_9Cl_2NO_2$: C, 43.27; H, 4.08; N, 6.31. Found: C, 43.06; H, 4.01; N, 6.23. IR ν_{max}^{KBr} cm^{-1}: 1768 (C=O), 1746, 1726 (N–C=O), 1626 (C=C). NMR ($CDCl_3$) δ: 1.47 (6H, s, $2\times CH_3$), 3.64 (3H, s, NCH_3).

Reaction of 3 with Sodium Borohydride——A solution of 0.13 g of **3** and 0.076 g of sodium borohydride in EtOH (20 ml) was stirred at room temperature for 1 hr. After acidification with dil. HCl, the solvent was

5) H.A. Hageman, "Organic Reactions," Vol. 7, ed. by R. Adams, John Wiley and Sons, Inc., New York, 1953, p. 198.
6) Z. Janousek and H.G. Viehe, "Advances in Organic Chemistry: Methods and Results," Vol. 9, ed. by H. Böhme and H.G. Viehe, John Wiley and Sons, Inc., New York, 1976, p. 343.
7) Boiling point and melting points are uncorrected. IR spectra were measured with a Hitachi EPI-G2 spectrophotometer, NMR spectra with a Hitachi R-24 spectrometer using tetramethylsilane as an internal standard, and mass spectra with a Hitachi PMS-4 mass spectrometer.

removed by evaporation. Water was added to the residue and the sparingly soluble crystals were filtered and dried. Recrystallization from isopropyl ether gave 0.064 g (36%) of 3-hydroxy-1,4,4-trimethyl-5-trichloromethyl-2-pyrrolidinone (**7**) as colorless plates, mp 148—149°. *Anal.* Calcd. for $C_8H_{12}Cl_3NO_2$: C, 36.88; H, 4.64; N, 5.38. Found: C, 37.04; H, 4.57; N, 5.30. IR ν_{max}^{KBr} cm^{-1}: 3395 (OH), 1686 (C=O). NMR ($CDCl_3$) δ: 1.22 (3H, s, CH_3), 1.49 (3H, s, CH_3), 3.17 (3H, s, NCH_3), 3.91 (1H, d, J=4 Hz, >CHO–), 4.11 (1H, s, >CH), 4.46 (1H, d, J=4 Hz, OH).

Reaction of 3 with Zinc in AcOH——A mixture of 0.26 g of **3** and 0.65 g of zinc dust in AcOH (4 ml) was heated at 70° for 1 hr with stirring. The precipitates were filtered off, and the filtrate was evaporated to dryness under reduced pressure. Water was added to the residue and insoluble material was extracted with ether. The ethereal extract was dried over anhydrous $MgSO_4$. Removal of the solvent left a crystalline residue which on recrystallization from isopropyl ether gave 0.114 g (50%) of 5-dichloromethyl-1,4,4-trimethyl-2-pyrrolidinone (**8**) as colorless needles, mp 141—142°. *Anal.* Calcd. for $C_8H_{13}Cl_2NO_2$: C, 42.50; H, 5.79; N, 6.15. Found: C, 43.04; H, 5.76; N, 6.15. IR ν_{max}^{KBr} cm^{-1}: 3266 (OH), 1686 (C=O). NMR ($CDCl_3$) δ: 1.19 (3H, s, CH_3), 1.26 (3H, s, CH_3), 3.17 (3H, s, NCH_3), 3.65 (1H, d, J=3 Hz, >CHN<), 3.79 (1H, br. >CHO–), 4.67 (1H, br. OH), 6.06 (1H, d, J=3 Hz, $CHCl_2$).

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Phosphorylation of Alcohols *via* Anodic P-Halogenation of Dialkyl Hydrogen Phosphites[1]

Hidenobu Ohmori, Shiro Nakai, Masahiro Sekiguchi, and Masaichiro Masui

Faculty of Pharmaceutical Sciences, Osaka University[2]

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Trialkylphosphates, $(RO)_2P(O)OR'$, were prepared from dialkyl hydrogen phosphites, $(RO)_2PHO$, and lithium chloride in R'OH by constant current electrolysis at a glassy carbon anode. Electrolysis at an anode having a larger area and at a lower current density gives better yields of the products. The electrolytic phosphorylation was also performed in acetone and in acetonitrile.

Keywords——electrochemical oxidation; constant current electrolysis; anodic phosphorylation; anodic P-halogenation; dialkyl hydrogen phosphites; trialkyl phosphates

Various methods have been reported for the phosphorylation of alcohols.[3] One of the methods used to prepare mixed trialkyl phosphates involves the reaction of alcohols with dialkyl halophosphonates,[4] which can be conveniently prepared from dialkyl hydrogen phosphites and halogens.[5] As a continuation of our studies on anodic substitution reactions involving organophosphorus compounds,[6] an electrochemical modification of the methods

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2) Location: *133-1 Yamadakami, Suita, Osaka, Japan.*
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4) F.R. Atherton, H.T. Openshaw, and A.R. Todd, *J. Chem. Soc.*, **1945**, 382; H.D. Orloff, C.J. Worrel, and F.X. Markley, *J. Am. Chem. Soc.*, **80**, 727 and 734 (1958); T. Mukaiyama, H. Kuoda, and K. Kodera, *Bull. Chem. Soc. Jpn.*, **39**, 2721 (1966).
5) W. Gerrard and H.R. Hudson, reference 3), Vol. 5, Chapter 13.
6) H. Ohmori, S. Nakai, and M. Masui, *J. Chem. Soc. Perkin I*, **1978**, 1333; *idem, ibid.*, in press; *idem, Chem. Pharm. Bull.* (Tokyo), **27**, 1271 (1979).