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Lactone Carboxylic Acids. VI.[1] A Synthesis of α,β-Epoxybutyrolactone *via* α-Diazolactones

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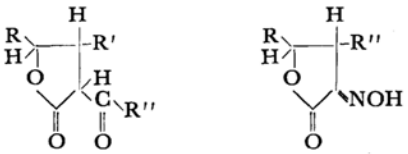
Reaction of α-carboxy-β-carbethoxy-γ,γ-dimethylbutyrolactone (**3**) with equimolar amount of nitrous acid gave ethyl α-hydroxyaminoaconate (**7**). However, the nitrosation of **3** using excess nitrous acid afforded a variety of compounds such as α-diazo (**4** and **5**), α-nitro (**8**), and α-azoxybutyrolactone (**9**) derivatives. Each of the products (**4**, **5**, **8**, and **9**) could be synthesized from **7**, independently. By the action of phosphoric acid, α-diazolactones (**4** and **5**) were converted into ethyl α,β-epoxyparaconate (**6**). The nature of the product **7** was demonstrated through its conversion into ethyl α-hydroxyaconate and through its thermal decomposition to ethyl α-aminoaconate and α-isopropylidenecyanoacetic acid derivatives. A possible mechanism for the formation of **6** through **4** and **5** is described.

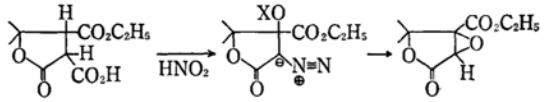
All of the previous reports concerning the nitrosation of α-substituted butyrolactones (**1**)[2] have only described the formation of α-hydroximinobutyrolactones (**2**) as a main product. However, we found that nitrosation of α-carboxy-β-carbethoxybutyrolactones,[3] readily prepared from α,β-dicarbethoxybutyrolacetones,[4] afforded a mixture of complex substances, some of which can be used as a potential intermediate in the synthesis of α,β-epoxyparaconic acid.



1 **2**

R=R'=H, Alkyl;
R''=CH_3, OC_2H_5, OH

In this paper, nitrosation of a model compound, α-carboxy-β-carbethoxy-γ,γ-dimethylbutyrolactone (**3**)[3] with sodium nitrite in an aqueous acetic acid, which leads ultimately to the formation of the corresponding ethyl α,β-epoxyparaconate (**6**) *via* α-diazolactones (**4** and **5**), is described.



3 **4** X=Ac, **5** X=H **6**

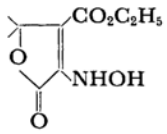
The nitrosation of **3** with an approximately equimolar amount of sodium nitrite in an aqueous acetic acid at 0—5°C, or with a large excess of sodium nitrite at about −5°C for a short reaction period, gave mainly ethyl α-hydroxyamino-γ,γ-dimethylaconate (**7**), white crystals, mp 73°C, which showed an intense band in the 3500—3100 region, consistent with NH and OH functions, 1775, 1695 (lactone, conjugated ester C=O), and 1655 cm^{-1} due to double bond.[5] The ultraviolet spectrum of **7** had λ_{max} 224 mμ (ε 11000) and 258 mμ (ε 760) in ethanol. The NMR spectrum of **7** showed one hydroxy proton at τ 6.10, six gamma dimethyl protons at 8.44 and 8.50, three methyl protons centered at 8.73, two methylene protons centered at 5.78, and one imino proton, as a multiplet form centered at −0.90.

1) For the preceding article in this series, see A. Takeda and S. Torii, This Bulletin, **41**, 1468 (1968).

2) M. Fedorchuk and F. T. Semeniuk *J. Pharm. Sci.*, **52**, 733 (1963); *Chem. Abstr.*, **63**, 11350a (1965); A. E. Lansilotti and M. J. Weiss, *J. Org. Chem.*, **24**, 1003 (1959); W. Reppe and co-workers, *Ann.*, **596**, 164 (1955); R. Sudo, Y. Akiyama, T. Kato and M. Ohta, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **74**, 1009 (1953); H. R. Snyder, J. H. Andreen, G. W. Cannon and C. F. Peters, *J. Am. Chem. Soc.*, **64**, 2082 (1942); V. Feofilaktov and A. Onishchenko, *J. Gen. Chem. USSR*, **9**, 304 (1939); *Chem. Abstr.*, **34**, 378 (1940); V. Feofilaktov and A. Onishchenko, *Compt. rend. acad. sci., URSS*, **20**, 133 (1938); *Chem. Abstr.*, **33**, 1725 (1939).

3) Half-hydrolysis of the lactone diesters was carried out by treating with an equimolar amount of 1 N alcoholic sodium hydroxide solution at room temperature: A. Takeda and S. Torii, *Memoirs of School of Engineering, Okayama Univ.*, **1**, 44 (1966).

4) K. Sisido, S. Torii and M. Kawanisi, *J. Org. Chem.*, **29**, 904, 2290 (1964); E. E. Von Tamelen and S. R. Bach, *J. Am. Chem. Soc.*, **80**, 3079 (1958); G. V. Chelintsev and E. D. Osetrova, *J. Gen. Chem. USSR*, **7**, 2373 (1937); *Chem. Abstr.*, **32**, 2099 (1938); A. Haller and G. Blanc, *Compt. Rend.*, **142**, 1471 (1906).

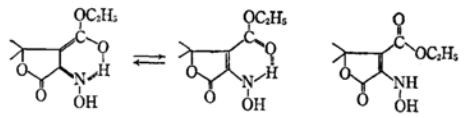


7

On the other hand, when the lactone acid **3** was allowed to react with a large excess of sodium nitrite in an aqueous acetic acid at 5—10°C for 4—5 hr, a mixture having a sharp band in the infrared at 2100 cm^{-1} was obtained together with **7**. Thin-layer chromatography (tlc) on silica gel G (E. Merck), developed by acetone - benzene mixture (1 : 8), revealed that this mixture consisted of more than four components which corresponded to R_f values: 0.70, 0.35, 0.26, and 0.16. Separation of each constituents was carried out by the extraction of the crude product with the alternate use of saturated aqueous sodium bicarbonate and saturated aqueous sodium carbonate, or by collecting each spots on silica gel plates individually. The compound corresponding to the third spot (R_f 0.26) was found to be identical with **7** by the comparison of their infrared and NMR spectral data. The top and the second constituents (R_f 0.70 and 0.35) gave total yield of 65—70% and have a sharp absorption at 2100 cm^{-1}. The elongated oval shape of the fourth spot (R_f 0.16) suggested the presence of two components.

The structure of the compound, pale yellow oil, of the top spot (R_f 0.70) is considered to be **4**, since the infrared spectrum of **4** had a sharp band at 2100 cm^{-1} due to diazo group[6] and a broad band at 1760—1750 cm^{-1}, corresponding to lactone and ester carbonyls. The NMR spectrum of **4** showed three acetoxy protons at τ 7.80 as a singlet.

5) Dr. H. Wamhoff of Bonn University suggested that from the NMR data of the compound (**7**) provided by us, there is a H-bridge from the NH-proton to the neighboring C=O group and this causes a shift of NH-proton signal to lower field down to τ −0.64 in deuterochloroform. Furthermore, he mentioned that the infrared spectrum of **7** in chloroform showed three peaks between 1600—1800 cm^{-1}: 1780 (lactone C=O), 1740 (ester C=O), and 1660 cm^{-1} (C=C), and these values are similar to those of the saturated lactones. These facts reveal that concerning the α,β-unsaturated ester group, **7** may have structures such as A or B in chloroform in contrast to the solid state in Nujol mull, which may not undergo a solvation and have a structure of C.

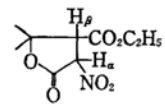


B A C

6) Diazo carbonyl compounds have a sharp infrared absorption in the 2100—2150 cm^{-1} region: G. R. Harvey, *J. Org. Chem.*, **31**, 1587 (1966); D. Hauser and H. P. Sigg, *Helv. Acta Chim.*, **50**, 1327 (1967); S. Julia, G. Cannic and G. Linstrumelle, *Compt. Rend.*, **264**, 1890 (1967).

The structure of the second component (R_f 0.35), pale yellow oil, was assigned to **5**, whose infrared spectrum showed a sharp band at 2100 cm^{-1} and a characteristic broad band at 3500—3000 cm^{-1} due to diazo and hydroxy group, respectively. It was observed that the NMR spectrum of **5** has a band at τ 5.60 due to hydroxy proton in place of a band at 7.80 due to acetoxy group of **4**. Nitrosation of **7** by treating with an excess sodium nitrite in an aqueous acetic acid at 3—7°C for 3 hr gave a major product (**5**) and a minor product (**4**) (*ca.* 5 : 1).

From the head part of the fourth constituents (R_f 0.16) was obtained the white crystals, mp 65.5—66.5°C, which exhibited sharp absorptions at 1565 and 1378 cm^{-1} due to nitro group[7] and was assigned to **8**. Its infrared spectrum exhibited two absorption bands at 1785 and 1728 cm^{-1} due to lactone and ester carbonyls. The NMR spectrum of **8** showed an AB pattern of two bands (doublet, $J_{\alpha,\beta}$ 9—10 cps) centered at τ 4.10 ($\underline{H}_\alpha$) and 5.96 ($\underline{H}_\beta$), indicating that the dihedral angle between two protons is close to 180° from the Karplus curve.[8] Confirmation of the structure of **8** was provided by an independent synthesis involving oxidation of **7** with excess sodium nitrite or nitric acid in an aqueous acetic acid at 0—2°C for about 30 min.



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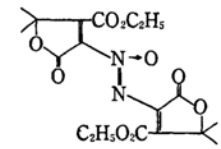

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The last component, amorphous pale yellow solid, mp 120—123°C, was obtained from the tail part of the oval spot (R_f 0.16)on the tlc plate and purified by repeating tlc on the silica gel G plates. The infrared spectrum indicated the absence of nitro group. Its structure was assigned to **9**, which have absorptions at 1780, 1750 (lactone, ester C=O), 1635 (C=C), and strong bands at 1260 and 1300 cm^{-1}, one of which may be due to azoxy group.[9] The NMR spectrum of **9** showed no absorption except for bands in the regions of 8.9—9.3(*gem*-$C\underline{H}_3$, $C\underline{H}_3$-C-O) and 6.0—5.3 (C-$C\underline{H}_2$-O). The ultraviolet spectrum of **9** had λ_{max} 226 mμ (ε 12000) in ethanol. Considering the preparative methods of the azoxy compound such as the oxidation of hydroxyamine derivatives in neutral media[10]

7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., John Wiley and Sons, Inc., New York, N. Y. (1958), p. 299; K. Nakanishi, "Infrared Absorption Spectroscopy," Nankodo, Co. Ltd., Tokyo (1960), p. 54.

8) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

9) J. Jander and R. N. Haszeldine, *J. Chem. Soc.*, **1954**, 919; B. W. Langley, B. Lythgoe and L. S. Rayner, *ibid.*, **1952**, 4191.

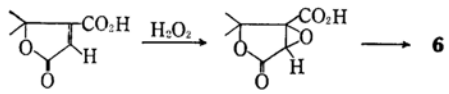
10) E. Bamberger, *Ber.*, **33**, 113 (1900).

TABLE 1. ETHYL α-SUBSTITUTED γ,γ-DIMETHYLACONATES

Compd.	Yield %	Bp °C/mmHg	Formula	Calcd, %		Found, %		Spectrum: Infrared, cm^{-1}			NMR, τ α-Subst.
				C	H	C	H	$\nu_{C=O}$		$\nu_{C=C}$	
13	95	123/2.5	$C_{10}H_{14}O_5$	56.07	6.59	56.30	6.85	1765	1705	1645	5.75
14	85	110—112/1.5	$C_{11}H_{16}O_5$	57.89	7.07	57.99	7.37	1765	1705	1645	—
15	95	100/2.5	$C_{11}H_{14}O_6$	54.54	5.83	54.46	5.92	1780	1725	1670	7.63

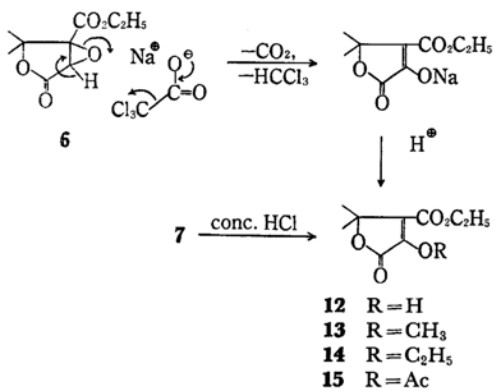
and the reaction of nitroso group with hydroxyamine,[11] we attempted the oxidation of **7** with manganese dioxide in acetone for 2 days and obtained **9** in quantitative yield.

Treatment of α-diazolactone (**4** and **5**) with phosphoric acid gave the α,β-epoxybutyrolactone (**6**), bp 100°C/2 mmHg, in excellent yield (*ca.* 90%). A proof of the structure of **6** was obtained by epoxidation[12] of aconic acid (**10**),[13] followed by esterification of α,β-epoxyparaconic acid (**11**) with ethyl orthoformate.[14]



10 **11**

Several aspects of the chemical property of the *intermediates (**6** and **7**) are of particular interest.* Namely, ethyl α-hydroxyaconate (**12**)[15] was obtained readily in good yield by the treatment of **7** with concentrated hydrochloric acid at room temperature. Treatment of **6** with sodium trichloroacetate at 90—130°C also gave **12** in excellent yield along with the evolution of carbon dioxide and chloroform.[16] The structure of **12** was inferred from its spectral data[15] and microanalysis. A mechanism of the formation of **12** is given in Scheme I. The physical constants of a series of the derivatives (**12**, **13**, **14** and **15**) are shown in experimental part and Table 1.



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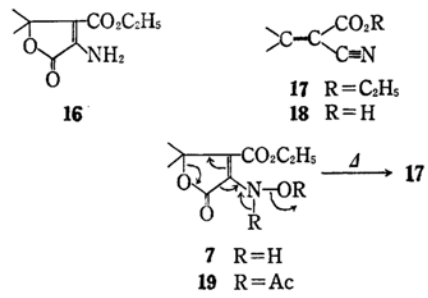
Scheme I

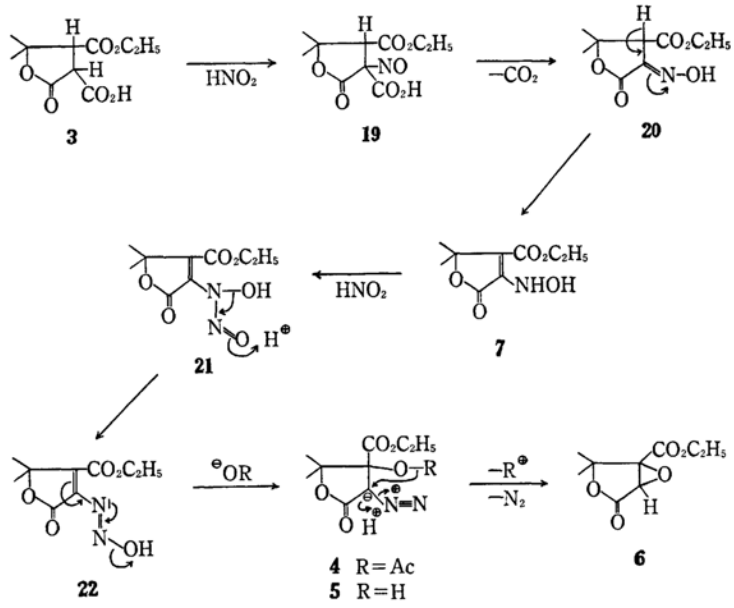
On the other hand, ethyl α-aminoaconate (**16**) was obtained in 15—20% yield together with isopropylidenecyanoacetic acid derivatives (**17**[17] and **18**[18]), when **7** was subjected to thermal decomposition at 140—160°C under reduced pressure. Pyrolysis of diacetate (**19**), prepared by boiling **7** with acetic anhydride, gave only **17**, indicating that normal thermal decomposition may proceed *as below, and formation of **16** may be due to a* disproportionation.



The structure of **16** was proven by its spectral data and microanalysis. Thus, mass spectrum of **16** exhibited a peak at *m/e* 199, corresponding to molecular ion. The infrared spectrum showed two bands at 3350—3450 (NH_2), two bands at 1760 and 1686 (lactone, ester C=O) and a band at 1640 cm^{-1} (C=O). The NMR spectrum showed the following absorptions: τ 4.40 (broadened, $N\underline{H}_2$), 8.76 and 5.65 (triplet and quartet, $C\underline{H}_3C\underline{H}_2O$-), and 8.30 (singlet, 2 $C\underline{H}_3$).

The possible mechanism of the formation of the

11) J. G. Aston and D. E. Ailman, *J. Am. Chem. Soc.*, **60**, 1930 (1938).
12) T. Oyamada and H. Baba, This Bulletin, **39**, 507 (1966).
13) R. Fittig and B. Frost, *Ann.*, **226**, 370 (1884).
14) H. Cohen and J. D. Mier, *Chem. & Ind.*, **1965**, 349.
15) G. W. Stacy, J. Wm. Cleary and M. J. Gortatowski, *J. Am. Chem. Soc.*, **79**, 1451 (1957). Recently, oxobutyrolactones, derivatives of **12**, having antiviral activity and low toxicity, have been reported: H. G. Monsimer, U. S. Pat. 3185711 (1965); *Chem. Abstr.*, **63**, 9879 (1966).
16) R. E. Buckles and C. J. Thelen, *Anal. Chem.*, **22**, 676 (1950).
17) T. Hayashi, M. Igarashi, S. Hayashi and H. Midorikawa, This Bulletin, **38**, 2063 (1965).
18) R. Carrie, R. Bougot and B. Potteau, *Compt. Rend.*, **259**, 2859 (1964); *Chem. Abstr.*, **62**, 2704 (1965).



Scheme II. Mechanism of the formation of the epoxylactone.

epoxylactone (**6**) are depicted in Scheme II. The presence of the carbethoxy group at the β-position of the lactone ring would have effected a rapid transformation of the transient intermediates (**19** and **20**) to the α-hydroxyaminoaconate (**7**), which may be stabilized by forming a conjugated ring system in an acidic media. It is considered that the compound (**7**) would be the key intermediate for the present reaction, since **7** can be converted into the α-diazolactones (**4** and **5**) by the action of excess nitrous acid *via* **21** and **22**, which were affected by phosphoric acid to afford the epoxylactone (**6**), as a result of electrophilic attack of a proton to the α-carbon atom along with the elimination of a nitrogen molecule, followed by the intramolecular nucleophilic attack of the oxygen atom attached to the β-position of **4** and **5**.

Experimental[19]

Ethyl α-Hydroxyamino-γ,γ-dimethylaconate (7). To a solution of α-carboxy-β-carbethoxy-γ,γ-dimethylbutyrolactone (**3**)[3] (5 g) in glacial acetic acid (10 m*l*) sodium nitrite (1.5 g) in water (3 m*l*) was added. The reaction mixture was stirred for 30 min at 0—2°C and then diluted with water (34 m*l*) with stirring for 1 hr. The mixture was extracted with ether and the extract was washed with aqueous sodium chloride. After drying over Na_2SO_4 and concentrating by evaporation, the residue, when scrubbed, solidified and afforded 3.2 g (68.1%) of **7**, mp 71.5°C (*n*-hexane - benzene); IR (Nujol mull) 3280, 3100, 1778, 1700, 1655, 1400, 1375, 1340, 1260, 1195, 1090, 990, 910, 870, and (ethanol or chloroform) 1780—1775 (lactone C=O), 1745—1740 (ester C=O), 1660 cm^{-1} (C=C); UV max (95% EtOH) 224 mμ (ε 11000) and 258 mμ (ε 760); NMR ($CHCl_3$) τ −0.90 (m, NH), 5.77 (q, C-CH$_2$-O), 6.10 (s, OH), 8.44 (s, CH$_3$), 8.50 (s, CH$_3$), and 8.72 (t, CH$_3$-C-O).

Found: C, 50.18; H, 6.08; N, 6.47%. Calcd for $C_9H_{13}NO_5$: C, 50.23; H, 6.09; N, 6.51%.

Nitrosation of α-Carboxy-β-carbethoxy-γ,γ-dimethylbutyrolactone (3). A solution of sodium nitrite (10 g) in water (20 m*l*) was added to a solution of **3** (20 g)[3] in glacial acetic acid (36 m*l*) with stirring at 0—5°C. After the mixture had been stirred for 30 min at 10—15°C, it was diluted with water (170 m*l*), stirred for an additional 1 hr, and the organic layer was taken up in ether. The extract was washed several times with aqueous sodium chloride, once with a small portion of 5% aqueous sodium bicarbonate, twice with aqueous sodium chloride, and dried over Na_2SO_4. Removal of the solvent gave 16.0 g of slightly greenish yellow, neutral liquid (Mixture I), which showed a strong band at 2100 cm^{-1}. The tlc of the Mixture I showed four spots (R_f values: 0.70, 0.35, 0.26, and 0.16).

Separation of each components of the Mixture I was carried out as follows: the ethereal solution of the Mixture I (16.0 g) extracted several times with 5% aqueous sodium bicarbonate (2.5 *l*), washed with aqueous sodium chloride, and dried over Na_2SO_4. Evaporation of the solvent gave 4.0 g of pale greenish yellow liquid (Mixture II) which was chromatographed on thin layer

19) All melting and boiling points are uncorrected. Infrared spectra were determined on a Hitachi EPI-S$_2$ and ultraviolet spectra on a Hitachi ESP-3T spectrophotometer. Thin layer chromatography (tlc) on baked silica gel G (E. Merck) as the support with acetone-benzene (1 : 8) as the solvent and with iodine for detection purposes was employed throughout the experiments. The NMR spectra were obtained on Japan Electron Optics Laboratory spectrometer (JNM-C-60) in chloroform with TMS as internal standard. The molecular weight determinations were made on a Hitachi RMU-6E mass spectrometer using a cold injection port. Microanalyses were performed by Miss H. Nisino of our laboratory.

plate to give two spots (R_f: 0.70 and 0.16). The Mixture II (4.0 g) dissolved in ether was extracted with aqueous sodium carbonate (100 ml), washed with aqueous sodium chloride, and dried over Na_2SO_4. Removal of the ether gave slightly colored liquid (**4**) (2.5 g) which gave a spot (R_f 0.70) on silica gel plate. Analytically pure sample of **4** was obtained from the spots (R_f 0.70) on silica gel plates arranged to 0.8 mm thickness. The spectral data were as follows: IR 3000—2850, 2100, 1765—1740, 1390, 1375, 1360, 1305, 1240, 1080, 1050, 1020, 980, 930, 910, 730 cm^{-1}; UV max (95% EtOH) 217 mμ (ε 4230) and 255 mμ (ε 7050); NMR ($HCCl_3$) τ 5.27 (q, C-C$\underline{H}_2$-O), 7.84 (s, C$\underline{H}_3$COO), 8.40 (s, C$\underline{H}_3$), 8.62 (s, C$\underline{H}_3$), 8.68 (t, C$\underline{H}_3$-C-O).

Found: C, 49.26; H, 5.42; N, 9.97%. Calcd for $C_{11}H_{14}N_2O_6$: C, 48.89; H, 5.22; N, 10.37%.

The extracts with aqueous sodium carbonate were acidified with dilute sulfuric acid to pH 6.5—7 and extracted with ether. The extracts were washed with aqueous sodium chloride and dried over sodium sulfate, and the solvent was removed *in vacuo*. The remaining viscous oil (1.0 g) (Mixture III) gave an elongated elliptical spot (R_f 0.16). From the head part of the tlc spot of the Mixture III, α-nitrolactone (**8**) (0.3 g), white solid, mp 66.5°C was obtained, after repeated purification by tlc on silica gel G plates (0.8 mm thickness). The spectral data of **8** were as follows: IR (Nujol mull): 1785, 1727, 1656, 1470—1445, 1395—1390, 1375, 1315, 1300, 1265, 1245—1220, 1200, 1175, 1115, 1095, 1025, 955, 900, 860, 845, 820, 790, 765, 705 cm^{-1}; NMR ($HCCl_3$) τ 4.11 (d, $\underline{H}_\alpha$), 5.62 (q, C-C$\underline{H}_2$-O), 5.92 (d, $\underline{H}_\beta$), 8.22 (s, C$\underline{H}_3$), 8.60 (s, C$\underline{H}_3$), and 8.67 (t, C$\underline{H}_3$-C-O).

Found: C, 46.63; H, 5.84%. Calcd for $C_9H_{13}NO_6$: C, 46.75; H, 5.60%.

From the tail part of the tlc spot (R_f 0.16) of the Mixture III, azoxylactone (**9**) (0.7 g), pale yellow solid, mp 120—123°C, was obtained, after repeated purification by tlc on silica gel G plates (0.8 mm thickness). The spectral data of **9** were as follows: IR (Nujol mull): 1785, 1750, 1640, 1480, 1470, 1450, 1395, 1375, 1305—1200, 1105—1010, 960, 935—930, 900, 865, 830, 780, 740 cm^{-1}; NMR ($HCCl_3$) τ 8.9—8.2 (*gem* C$\underline{H}_3$, C$\underline{H}_3$-C-O) and 5.4—6.1 (C-C$\underline{H}_2$-O).

Found: C, 52.77; H, 5.65; N, 6.86%. Calcd for $C_{15}H_{24}N_2O_9$: C, 52.42; H, 5.86; N, 6.79%.

The alkaline extracts (2.5 *l*) from the Mixture I were neutralized with dilute sulfuric acid to pH 6.5—7 and extracted with ether. The ethereal extracts were washed with aqueous sodium chloride, dried, and concentrated. The tlc of the residual pale yellow oil (Mixture IV) (11.0 g) showed the presence of two components (R_f 0.35 and 0.26). Separation was carried out by extracting the ethereal solution of the Mixture IV with aqueous sodium carbonate. From the ether layer there was obtained 1.0 g of pale yellow, neutral oil (R_f 0.35). The analytical sample was obtained by passing the crude oil through an aluminum oxide G (E. Merck) column using acetone to remove a trace of the impurity (R_f 0.26). The spectral data of **5** were as follows: IR 3500—3000 (broad), 3000—2800, 2100, 1740—1715, 1470, 1385, 1355, 1255, 1190, 1090—1070, 1027, 905, 735 cm^{-1}; NMR ($HCCl_3$) τ 5.60 (s, O$\underline{H}$), 5.62 (q, C-C$\underline{H}_2$-O), 8.46 (s, C$\underline{H}_3$), 8.65 (s, C$\underline{H}_3$), and 8.65 (t, C$\underline{H}_3$-C-O).

Found: C, 47.61; H, 5.55; N, 11.70%. Calcd for $C_9H_{12}N_2O_5$: C, 47.37; H, 5.35; N, 12.28%.

On the other hand, the alkaline layer was neutralized with dilute sulfuric acid, washed, and dried over Na_2SO_4. Removal of the solvent gave 8.0 g of slightly colored oil (R_f 0.26), which was solidified upon standing for several days, to white crystals (**7**), mp 71.5—73°C (benzene - *n*-hexane). The structure was confirmed by comparison of the infrared spectrum with that of authentic **7**.

Ethyl α-Diazoparaconates (4 and 5). These were obtained from the α-hydroxyaminolactone (**7**) in 85—90% yield by treating with sodium nitrite (2 mol) in an aqueous acetic acid at 3—7°C for 3 hr. Separation of **4** and **5** was carried out in a manner described above. Both **4** and **5** (estimated to be 5 : 1) were identified by their R_f values of tlc and their infrared spectra, which were in good agreement with those of the reference compounds (**4** and **5**) obtained in the above experiment.

Ethyl α-Nitro-γ,γ-dimethylparaconate (8). To a solution of concentrated nitric acid (0.3 ml) and glacial acetic acid (3 ml) ethyl α-hydroxyamino-γ,γ-dimethylaconate (**7**) (200 mg) was added at 2—5°C with stirring for 20 min. The cooled mixture was poured into 50 ml of ice water. After 15 min of stirring, the precipitate was filtered, washed with water, and dried. Recrystallization from *n*-hexane - benzene (4 : 1) gave 65 mg (*ca.* 30%) of **8**, white crystal, mp 66.0—66.5°C, whose infrared spectrum was identical with that of the reference compound obtained as described in the above paragraph.

Azoxylactone (9) from Ethyl α-Hydroxyamino-γ,γ-dimethylaconate (7). A mixture of **7** (200 mg) and manganese dioxide[20] (1.0 g) in acetone (10 ml) was kept at room temperature for 2 days. The manganese dioxide was filtered off and the filtrate was concentrated under vacuum to give 150 mg of **9**, pale yellow solid, mp 118—123°C, identified by comparison with the authentic sample obtained as described in the preceding paragraph.

Ethyl α,β-Epoxy-γ,γ-dimethylparaconate (6) from α-Diazolactones (4 and 5). A mixture of **4** and **5** (5 : 1) (500 mg) was dissolved in phosphoric acid (0.5 ml) at room temperature, and immediately colorless gas was evolved. When the gas evolution was ceased, the mixture was poured into 50 ml of saturated aqueous sodium chloride with stirring, and extracted with ether. The extract was washed with water, dried over Na_2SO_4 and the solvent was stripped *in vacuo*. Upon distillation of the residual oil, there was obtained 340 mg (89.1%) of **6**, bp 100°C/2 mmHg, n_D^{20} 1.4458; IR 1780 (lactone C=O), 1740 (ester C=O), and 1250 and 865 (epoxy) cm^{-1}; NMR ($HCCl_3$) τ 5.63 (q, C-C$\underline{H}_2$-O), 5.83 (s, $\underline{H}$), 8.33 (s, C$\underline{H}_3$), 8.42 (s, C$\underline{H}_3$), and 8.67 (t, C$\underline{H}_3$-C-O).

Found: C, 54.03; H, 6.16%. Calcd for $C_9H_{12}O_5$: C, 54.00; H, 6.04%.

α,β-Epoxy-γ,γ-dimethylparaconic Acid (11). To a solution of γ,γ-dimethylaconic acid (**10**)[13] (2.4 g) in methanol (36.6 ml) and 15% hydrogen peroxide solution (20.4 ml) 16% aqueous sodium hydroxide (34.2 g) was added at 20—25°C. The mixture was kept at room temperature for overnight, then poured into water (200 ml), acidified with diluted sulfuric acid,

20) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, *J. Chem. Soc.*, **1952**, 1094.

and extracted with ether. The extracts were washed with water, dried over Na_2SO_4, and evaporated to dryness to give 1.8 g (71%) of **11**, white needles, mp 120°C (methanol-benzene); IR 1740 (lactone, carboxylic acid C=O) and 1250, 920, and 860 (epoxy) cm^{-1}.

Found: C, 48.49; H, 4.79%. Calcd for $C_7H_8O_5$: C, 48.84; H, 4.68%.

Esterification of α,β-Epoxy-γ,γ-dimethylparaconic Acid (11). A solution of α,β-epoxyparaconic acid (**11**) (300 mg) in ethyl orthoformate (2 m*l*) was refluxed for 8 hr and then distilled *in vacuo* to give **6** (250 mg), bp 100°C/2 mmHg, whose infrared spectrum was in good agreement with that of the reference compound **6** obtained as described in the preceding paragraph.

Ethyl α-Hydroxy-γ,γ-dimethylaconate (12). Method A. A solution of ethyl α-hydroxyamino-γ,γ-dimethylaconate (**7**) (2.0 g) in concentrated hydrochloric acid (20 m*l*) was kept at 25—30°C for 3 days. Then, the mixture was neutralized with 2 N aqueous sodium hydroxide to pH 4—5 and extracted with ether. The extracts were washed with saturated aqueous sodium chloride, dried over $MgSO_4$, and evaporated to dryness to give **12** (1.0 g, 55%), mp 71.0°C (lit.[15] mp 73.0—73.5°C); IR (Nujol mull) 1750 (lactone C=O), 1710 (ester C=O), and 1660 (C=C) cm^{-1}; NMR ($HCCl_3$) 2.62 (s, O<u>H</u>), 5.62 (q, C–C<u>H</u>$_2$–O), 8.38 (s, *gem* C<u>H</u>$_3$), and 8.60 (t, C<u>H</u>$_3$–C–O), 8.38 (s, *gem* C<u>H</u>$_3$), and 8.60 (t, C<u>H</u>$_3$–C–O). The microanalysis of **12** gave good result for carbon and hydrogen.

Method B. A mixture of ethyl α, β-epoxy-γ,γ-dimethylparaconate (**6**) (500 mg) and sodium trichloroacetate (500 mg) was heated to 97—135°C for 15 min, then poured into water (30 m*l*), and extracted with ether. The aqueous layer was acidified to pH 4—5 with diluted sulfuric acid and extracted with ether. This extracts were washed with saturated aqueous sodium chloride, dried over $MgSO_4$, and evaporated to dyness to afford **12** (300 mg, 60%), mp 71°C, which was identified by its infrared spectrum and by comparison with that of the authentic specimen obtained by Method A.

Preparation of the Derivatives (13, 14, and 15) of 12. The compounds (**13**, **14**, and **15**) were prepared as follows: **13** was obtained by treating **12** with diazomethane; **14** was prepared by refluxing **12** with ethyl orthoformate; **15** was prepared by refluxing **12** with acetic anhydride. The physical constants, microanalyses, and spectral data of these compounds are listed in Table 1.

Thermal Decomposition of Ethyl α-Hydroxyamino-γ,γ-dimethylaconate (7). The thermal decomposition of **7** (1.0 g) carried out at 140—160°C/25 mmHg for 3 hr and then the mixture was taken up in ether. The ether layer was extracted with aqueous sodium bicarbonate, washed with water, and dried over Na_2SO_4. After removal of the solvent, the residue was distilled to give 380 mg (53%) of ethyl isopropylidenecyanoacetate (**17**), M^+ 153 *m/e*, bp 99—100°C/8.5 mmHg (lit.[17] 116—118°C/11 mmHg), which was identical in all respects with authentic specimen (**17**).[17] Small amount of the distillate, bp 100—130°C/2 mmHg, solidified in the side tube of Claisen flask or in the receiver as colorless needles. This was recrystallized from ethanol to afford ethyl α-amino-γ,γ-dimethylaconate (**16**) as colorless needles, yield 160 mg (17%), M^+ 199 *m/e*, mp 120°C; UV max (95% EtOH) 297.5 mμ (ε 11600); IR (Nujol mull) 3450 and 3350 (NH_2), 1760 (lactone C=O), 1690 (ester C=O), 1635 (C=C), and 1583 (NH_2) cm^{-1}; NMR ($HCCl_3$) τ 4.42 (broad N<u>H</u>$_2$), 5.71 (q, C–C<u>H</u>$_2$–O), 8.40 (s, *gem* C<u>H</u>$_3$), and 8.65 (t, C<u>H</u>$_3$–C–O).

Found: C, 54.22; H, 6.63; N, 7.11%. Calcd for $C_9H_{13}NO_4$: C, 54.26; H, 6.58; N, 7.03%.

The alkaline extract was acidified with dilute sulfuric acid to pH 6.5—7 and extracted with ether. The extracts were washed with saturated aqueous sodium chloride and dried over Na_2SO_4. After removal of the solvent, there was obtained 130 mg (23%) of isopropylidenecyanoacetic acid (**18**), mp 129—130.5°C (lit.[18] 137°C). The confirmation of the structure was made based on the spectral data and from the conversion of **18** into **17** by the action of ethyl orthoformate.[14]

Ethyl α-(*N*-Acetoxy-*N*-acetyl)amino-γ,γ-dimethylaconate (19). A solution of **7** (500 mg) in acetic anhydride (3 m*l*) was refluxed for 4 hr. The solvent was removed under reduced pressure. Distillation of the residue gave 700 mg (*ca.* 95%) of **19**, bp 145°C/2.5 mmHg; IR 1805 and 1775 (lactone C=O), 1725 (ester C=O), and 1650 (C=C) cm^{-1}; NMR ($HCCl_3$) τ 5.81 (q, C–C<u>H</u>$_2$–O), 7.75 (s, C<u>H</u>$_3$–CO–O–N), 7.88 (s, C<u>H</u>$_3$CO–N), 8.37 (s, *gem* C<u>H</u>$_3$), and 8.68 (t, C<u>H</u>$_3$–C–O).

Found: C, 52.39; H, 5.97%. Calcd for $C_{13}H_{17}NO_7$: C, 52.17; H, 5.73%.

Thermal Decomposition of 19. The thermal decomposition of **19** (500 mg) was carried out at 140—160°C/ 25 mmHg for 2 hr to give exclusively a fraction boiling at 98—100°C/8.5 mmHg, whose infrared spectrum was superimposable in very fine detail with that of the authentic sample (**17**) obtained in the above paragraph.

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