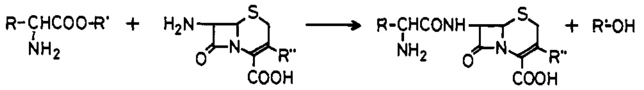
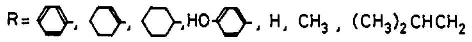
was centrifuged to remove cells and the supernatant fluid thus obtained was chromatographed on an Amberlite XAD-2 column to give 2.2 g of crystals identical in all respects with an authentic sample of cephalexin monohydrate.





R'= CH_3, CH_3CH_2

R''= CH_3, CH_3COOCH_2

In a similar fashion, enzymatic synthesis was also achieved when the D-α-phenylglycine methyl ester was replaced by the esters of other α-amino acids such as glycine, D-alanine, D-leucine, D-α-(1-cyclohexenyl)glycine, D-α-(p-hydroxyphenyl)glycine, and D-α-cyclohexylglycine. However, β-alanine, γ-aminobutyric acid, DL-mandelic acid, phenylacetic acid, and phenoxyacetic acid were not substrates for the enzymatic reaction, the results being given in Table I.

Besides xanthomonads, the like synthesizing ability was found among the strains belonging to the family *Pseudomonadaceae* as shown in Table II which indicates that 7-aminocephalosporanic acid (7-ACA) is also a good substrate for the enzymatic reaction.

Acknowledgment. We wish to thank Dr. T. Miki, Takeda Research Laboratories, for his kind supply of some substrate compounds. We are also indebted to Drs. S. Tatsuoka and R. Takeda of our laboratories for their advice and encouragement.

bance at 260 mμ between before and after treatment of a reaction mixture with the enzyme was proportional to a cephalosporin content in the mixture. The results obtained on samples of cephalexin and cephaloglycine showed good agreement with those recorded by the conventional microbiological method.[12] The spectrophotometric assay was applicable to all the cephalosporins described in this communication. The details of the method will be published elsewhere.

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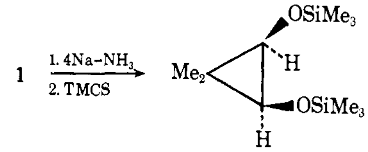
Metal Reduction of Malonates. Formation and Isolation of 3,3-Dimethyl-*cis*-1,2-cyclopropanediol

Sir:

In a recent communication it was recorded that dimethyl dimethylmalonate (**1**) and sodium dispersed in xylene containing trimethylchlorosilane (TMCS) gave dimethylketene methyl trimethylsilyl acetal (**2**) according to the following equation.[1] We now report

$$\underset{\mathbf{1}}{Me_2C(CO_2Me)_2} \xrightarrow[\text{TMCS}]{\text{Na-xylene}} \underset{\mathbf{2}}{Me_2C{=}C(OMe)OSiMe_3} + CO + MeOSiMe_3$$

that the reduction of **1** with 4 equiv of sodium in liquid ammonia followed by TMCS gave five products including **2** and the cyclopropane ring system 3,3-dimethyl-*cis*-1,2-bistrimethylsilyloxycyclopropane[2] (**3**): bp 30° (0.05 mm); nmr ($CDCl_3$) δ 0.12 (18 H), 0.85



3

(3 H), 0.90 (3 H), 2.75 (2 H); ir ($CHCl_3$) 2980, 1460, 1380, 1350, 1170, 1030 cm^{-1}; mass spectrum m/e (rel intensity) 246 (6) M, 73 (100).

Metal reduction of **1** under various conditions formed the products listed in Table I; compounds **4–7** are described below.

Compound **4**, $Me_2C(CH_2OSiMe_3)_2$, displayed the following physical properties: bp 30° (0.05 mm); nmr ($CDCl_3$) δ 0.10 (18 H), 0.80 (6 H), 3.30 (4 H); ir ($CHCl_3$) 2985, 1475, 1400, 1360, 1090 (br), 1010 cm^{-1}; mass spectrum m/e 233 (4, M − 15), 147 (100). Compound **4** was solvolyzed to 2,2-dimethyl-1,3-propanediol.

Compound **5**, $Me_2C(CH_2OSiMe_3)CONHSiMe_3$, showed the following physical properties: bp 45° (0.05 mm); nmr ($CDCl_3$) δ 0.10 (9 H), 0.20 (9 H), 1.10 (6 H), 3.50 (2 H); ir ($CHCl_3$) 3350, 2980, 1660, 1430 (br), 1080 cm^{-1}; mass spectrum m/e 246 (6, M − 15), 73 (100). Compound **5** was hydrolyzed to 2,2-dimethyl-3-hydroxypropionamide, mp 72°.

Compound **6**, $Me_2CHCONHSiMe_3$, displayed the following physical properties: mp 84°; nmr ($CDCl_3$) δ 0.20 (9 H), 1.12 (d, 6 H, J = 6.5 Hz), 2.3 (m, 1 H); ir ($CHCl_3$) 3420, 2980, 1660 (br), 1430 cm^{-1}; mass spectrum m/e 159 (6, M), 73 (100). Hydrolysis of **6** gave isobutyramide.

Compound **7**, $Me_2CHCH_2OSiMe_3$, showed the following physical properties: nmr ($CDCl_3$) δ 0.10 (9 H), 0.85 (d, 6 H, J = 12 Hz), 1.7 (m, 1 H), 3.30 (d, 2 H, J = 12 Hz). Solvolysis of **7** gave isobutyl alcohol.

Candidates as intermediates in the reaction of **1** and sodium–liquid ammonia included $Me_2C(CHO)CO_2Me$ (**8**) and $Me_2C(CONH_2)CO_2Me$ (**9**).[3] Addition of the lithium salt of methyl isobutyrate to methyl formate gave **8**: nmr (CCl_4) δ 1.30 (6 H), 3.7 (3 H), 9.6 (1 H); ir ($CHCl_3$) 3000, 2980, 2715, 1725 (br), 1370 cm^{-1}; mass spectrum m/e 102 (64, M − 28), 41 (100).

Compound **8** was reduced with sodium–liquid ammonia followed by TMCS and gave products in the relative amounts of 25% **3**, 25% **4**, 5% **6**, and 45% **7**, although more residue than normal remained. Under the same conditions **9** gave only **5** and **6** in a ratio of 4:1. Thus, under these conditions **9** is eliminated as an intermediate and **8** is an unlikely intermediate since it gave **7**.

The intermediacy of a three-membered ring enediol dianion in the formation of **3** does not seem likely.[4]

(1) Y. N. Kuo, F. Chen, C. Ainsworth, and J. J. Bloomfield, *Chem. Commun.*, 136 (1971).

(2) The cis stereochemistry of **3** is established from the fact that the methyl groups have different shift values in the nmr spectrum.

(3) W. H. Perkin, *J. Chem. Soc.*, **83**, 1217 (1903).

(4) Reaction of dimethyl succinate with sodium–liquid ammonia at −34° followed by silation using excess TMCS gave 1,2-bistrimethylsilyloxycyclobutene[5] but no 1,2-bistrimethylsilyloxycyclobutane was formed.

(5) J. J. Bloomfield, *Tetrahedron Lett.*, 587 (1968).

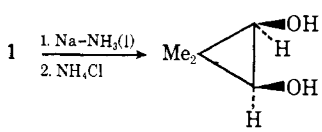
Table I. Products from the Reduction of $Me_2C(CO_2Me)_2$ Followed by Addition of TMCS

Reagents	Temp, °C	% yield[a] (relative % composition of products) 2	3	4	5	6	7
Na–xylene	120	85[b] (100)					
Na–K alloy–ether	25	60[c] (100)					
Na–NH_3(l)	−34	6 (7)	25 (30)	3 (3)	25 (30)	25 (30)	
Na–NH_3(l)	−78	57 (67)	25 (30)	3 (3)			
K–NH_3(l)	−78	38 (50)	25 (35[d])	4 (5)	7 (10)		
Na–NH_3(l)–MeOH[e]	−34		22 (25)	3 (3)		10 (12)	55 (60)

[a] Satisfactory analyses were obtained for the products. Composition established by glc analysis. [b] Reference 1. [c] 40% starting material recovered. [d] No trans isomer of 3 was indicated. This fraction contained another compound tentatively designated as 3-methyl-1-trimethylsilyloxy-2-butanone: nmr (CCl_4) δ 0.15 (9 H), 1.05 (d, 6 H, J = 7 Hz), 2.7 (m, 1 H), 4.1 (2 H). [e] Two equivalents of methanol was used.

The mechanistic pathways for the formation of the products of Table I will be discussed in the context of another publication.[6]

In another experiment, ammonium chloride was added when the reduction was completed and included in the products[7] was a 25% yield of 3,3-dimethyl-*cis*-1,2-cyclopropanediol (**10**): bp 56° (0.05 mm); nmr ($CDCl_3$) δ 0.85 (s, 3 H), 1.00 (s, 3 H), 2.95 (s, 2 H, J = 5.5 Hz from ^{13}C satellite, $J_{^{13}C-H}$ = 180 Hz), and 3.4 (s, 2 H, D_2O removed); mass spectrum[8] *m/e* 102 (5) M, 43 (100).



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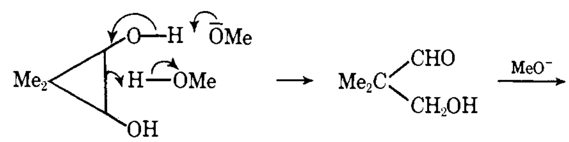
Compound **3** was solvolyzed to **10** with methanol using a silica gel column. Compound **3** and acetyl chloride[9] gave 3,3-dimethyl-*cis*-1,2-diacetoxycyclopropane: bp 85° (15 mm); nmr ($CDCl_3$) δ 1.0 (s, 3 H), 1.1 (s, 3 H), 2.1 (s, 6 H), 3.75 (s, 2 H); ir ($CHCl_3$) 2990, 1735, 1375, 1110, and 1040 cm^{-1}; mass spectrum *m/e* M absent, 43 (100) CH_3CO^+.

Compounds **3** and **10** were unstable to acid, and with sodium methoxide–methanol underwent disproportionation according to the following scheme to give products **11** and **12**.[11] This disproportionation reaction

$$\text{3 or 10} \xrightarrow[\text{MeOH}]{\text{MeO}^-} \underset{\mathbf{11}}{Me_2C(CH_2OH)_2} + \underset{\mathbf{12}}{Me_2C(CO_2Me)(CH_2OH)}$$

catalyzed by methoxide ion may involve the intermediacy of an aldehyde followed by a Cannizzaro reaction. Compound **11** was prepared from **1** and lithium aluminum hydride. Addition of formaldehyde to the lithium salt of methyl isobutyrate gave **12**: nmr (CCl_4) δ 1.11 (s, 6 H), 3.2 (br s, 1 H), 3.4 (s, 2 H), 3.65 (s, 3 H); ir ($CHCl_3$) 3500 (broad), 2985, 1730, 1475, 1370, and 1050 cm^{-1}.



10

11 + 12

Cyclopropanediols as bicyclo compounds are reported[12–14] and O-substituted derivatives of *vic*-cyclopropanediols are also recorded.[10,15–18]

1,2-Cyclopropanediols, through a long history, have been determined to be intermediates in the Clemmensen reduction of 1,3-diketones.[13,19–25] The pathway for their decomposition to products, under the reaction conditions, has been established.[26–29]

Acknowledgment. This work was supported by grants for the National Institutes of Health and the Petroleum Research Foundation, administered by the American Chemical Society. John A. Beel prepared some of the starting materials.

(6) To be published with J. J. Bloomfield.

(7) The reaction products were **10**, 2,2-dimethyl-1,3-propanediol, methyl isobutyrate, and isobutyramide.

(8) The sample contained a small amount of isobutyramide that was subtracted from the spectrum.

(9) A reaction analogous to that of the French workers[10] for compounds closely related to **3**.

(10) M. Audibrand, R. LeGoaller, and P. Arnaud, *C. R. Acad. Sci., Ser. C*, **268**, 2322 (1969).

(11) This redox reaction is similar to that of Reusch and Priddy,[12] who observed an internal redox product when their VI was transformed into IV. Compound **10** reacted with oxygen when air was slowly bubbled through a $CDCl_3$ solution held at 0° for 3 hr. The facile air oxidation of *vic*-cyclopropanediols is recorded by D. B. Priddy and W. Reusch, *Tetrahedron Lett.*, 2637 (1970).

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