References and Notes

(1) For an application of this approach to the synthesis of dictyopterenes, see K. C. Das and B. Weinstein, *Tetrahedron Lett.*, 3459 (1969).
(2) (a) J. P. Marino and T. Kaneko, *Tetrahedron Lett.*, 3971 (1973); (b) J. P. Marino and T. Kaneko, *J. Org. Chem.*, **39**, 3175 (1974); (c) Y. Tamura, T. Miyamoto, T. Nishimura, and Y. Kita, *Tetrahedron Lett.*, 2351 (1973); (d) R. W. LaRochelle, B. M. Trost, and L Krepski, *J. Org. Chem.*, **36**, 1126 (1971); (e) J. R. Neff, R. R. Gruetzmacher, and J. E. Nordlander, *ibid.*, **39**, 3814 (1974).
(3) B. M. Trost and D. E. Keeley, *J. Am. Chem. Soc.*, **98**, 248 (1976), and references cited therein.
(4) (a) K. Kitatani, T. Hiyama, and H. Nozaki, *J. Am. Chem. Soc.*, **97**, 949 (1975); (b) M. Braun and D. Seebach, *Angew. Chem.*, **86**, 279 (1974); (c) A. Schmidt and G. Kobrich, *Tetrahedron Lett.*, 2561 (1974); (d) D. Seyferth and H. M. Choen, *J. Organomet. Chem.*, **1**, 15 (1963); (e) H. M. Walborsky, *Rec. Chem. Prog.*, **23**, 75 (1962); (f) H. Hart and R. A. Cipriani, *J. Am. Chem. Soc.*, **84**, 3697 (1962); (g) D. E. Appliquist and A. H. Peterson, *ibid.*, **83**, 862 (1961); (h) H. M. Walborsky and F. M. Hornyak, *ibid.*, **77**, 6026 (1955).
(5) Several reports have appeared on the intermediacy of cyclopropylcopper reagents: (a) K. Kitatani, T. Hiyama, and H. Nozaki, *J. Am. Chem. Soc.*, **98**, 2362 (1976); (b) E. J. Corey and G. Posner, *ibid.*, **89**, 3911 (1967); (c) M. P. Periasamy and H. M. Walborsky, *ibid.*, **97**, 5930 (1975); (d) R. G. Carlson and W. S. Mardis, *J. Org. Chem.*, **40**, 817 (1975); (e) R. C. Hahn and G. W. Jones, *J. Am. Chem. Soc.*, **93**, 4232 (1971). These authors reported the only previous conjugate addition of a cyclopropylcopper reagent to an enone.
(6) H. O. House, C.-Y. Chu, J. M. Wilkins, and M. J. Umens, *J. Org. Chem.*, **40**, 1460 (1975).
(7) T. S. Sorensen and K. Rajeswari, *J. Am. Chem. Soc.*, **93**, 4222 (1971).

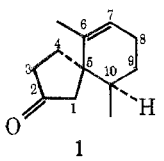
A Convenient Photochemical Synthesis of a Precursor to the Spirovetivanes[1]

Drury Caine,* Anibal A. Boucugnani, and William R. Pennington

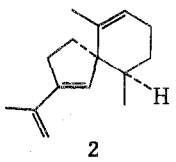
School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

Received May 26, 1976

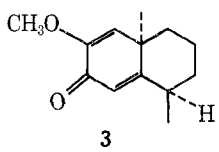
Recently, we reported the synthesis of the spiro enone **1**,[2] and its conversion into (±)-α-vetispirene (**2**)—a member of the spirovetivane family of sesquiterpenes.[3] In the better of the two routes to **1** employed previously,[2] the methoxy dienone **3** was converted into the spiro[4.5]decenone derivative **4** by photochemical rearrangement in glacial acetic acid. The



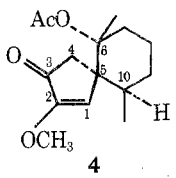
1



2



3

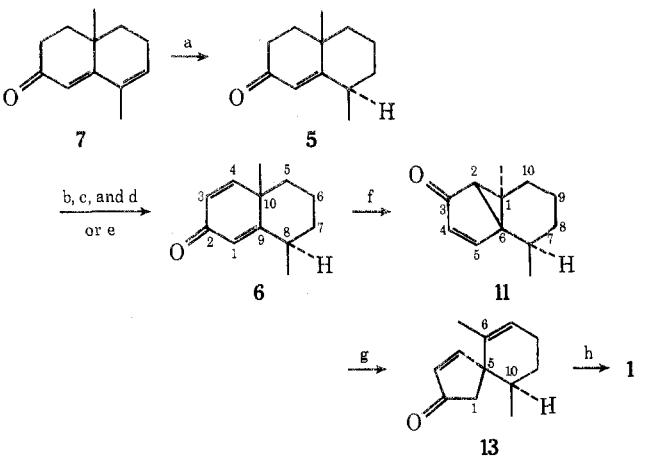


4

cis relationship between the 1-methylene group and the 10-methyl group was established by removal of the 3-carbonyl group and hydrolysis of the enol ether function. These conditions also converted the 6-acetoxyl group into a hydroxyl group and the 6,7 double bond was introduced by dehydration. Although this approach was completely stereospecific, the synthesis of **3** and its conversion into **1** required a rather large number of steps. Since **1** appeared to be a useful intermediate for the synthesis of other spirovetivanes, the development of a shorter route to this compound was of interest.

We felt that a simple approach to **1** would involve as a key step the photoisomerization of the *cis*-dimethyl cross-conjugated dienone **6** into the tricyclodecenone derivative **11** which has a cis relationship between C-2 of the cyclopropane ring and the secondary methyl group. Selective electrophilic cleavage of the external (1,2) bond of the cyclopropane ring of **11** would then yield a spiro[4.5]decane derivative readily

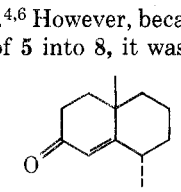
Scheme I



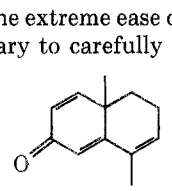
a, Pd/C, cyclohexene, C_2H_5OH; b, LDA, THF, −70 °C; c, PhSeCl, −70 °C; d, H_2O_2, e, DDQ, dioxane, reflux; f, *hν* (2537 Å), dioxane, 25 °C; g, H_2SO_4, HOAc–Ac_2O; h, Pd/C, 95% C_2H_5OH NaOH.

convertible into **1**. These transformations have been accomplished as shown in Scheme I.

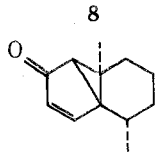
Selective reduction of the 7,8 double bond of the known transannular dienone **7**[4] was carried out by transfer hydrogenation using palladium on carbon and cyclohexene in refluxing ethanol.[5] This procedure led to the formation of the thermodynamically unstable *cis*-8,10-dimethyl octalone **5** in 90% yield. The reaction was highly selective and under carefully controlled conditions GLC analysis of the product indicated that it contained less than 5% of the more stable trans isomer **8**.[4,6] However, because of the extreme ease of isomerization of **5** into **8**, it was necessary to carefully avoid the



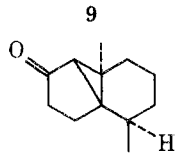
8



9



10



12

presence of acidic or basic impurities. Best results were obtained when the starting material and all reagents were carefully purified just prior to use and when the reduction was carried out on a relatively small scale, i.e., 5–10 g. The cross-conjugated dienone **6** could be obtained by conventional oxidation of **5** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in benzene or dioxane.[7] However, the desired product was contaminated with a significant amount of the trienone **9**, even when only 1 equiv of the oxidizing agent was employed. The formation of **9** would be expected to occur via the trienol resulting from proton transfer from C-8. Enolization of **5** would be expected to occur rather readily because it would lead to relief of a severe 1,3-diaxial methyl–methyl interaction. In order to avoid the formation of the trienone, the selenoxide elimination procedure of Reich and co-workers[8] was employed for the conversion of **5** into **6**. Treatment of the enone with lithium diisopropylamide (LDA) in THF at −70 °C gave the homoannular lithium enolate resulting from kinetic deprotonation at C-3.[9] This enolate was trapped with phenylselenenyl chloride at −70 °C and the crude phenylseleno ketone was oxidized with hydrogen peroxide in ethyl acetate–THF to give **6** in approximately 55% yield.

Kropp has reported the conversion of the trans dimethyl

dienone related to **6** into the corresponding bicyclohexenone derivative **10** by irradiation in dioxane at 2537 Å.[10] Under similar conditions **6** gave **11** in 70% yield. Compound **11** was almost quantitatively converted into the known tricyclodecane derivative **12**[11] by catalytic hydrogenation with 5% palladium on carbon in 95% ethanol.

On treatment of **11** with sulfuric acid in acetic acid–acetic anhydride under the conditions developed by Marshall and Johnson[12] for cleavage of the cyclopropane ring in **10**, the spiro dienone **13** was obtained in 92% yield. Selective catalytic hydrogenation of the conjugated double bond in 95% ethanol containing sodium hydroxide gave **1** in ca. 90% yield. The five-step sequence from **7** to **1** was accomplished in ca. 30% overall yield.

Experimental Section[13]

***cis*-8,10-Dimethyl-1(9)-octal-2-one (5).** To a stirred solution of 5.0 g (0.028 mol) of the transannular dienone **7**[4] in 40 ml of cyclohexene and 200 ml of 95% ethanol was added 2.0 g of 5% palladium on carbon. The reaction mixture was stirred at reflux temperature under nitrogen for 2 h. After cooling to room temperature the catalyst was removed by filtration, and the solvent was removed in vacuo. Distillation of the residue gave 4.58 g (90%) of a colorless liquid, bp 51–53 °C (0.04 mm), which was greater than 95% one component by GLC (column A). The product was identified as the enone **5** on the basis of its spectral properties: uv max (95% ethanol) 240 nm (ϵ 13 832); ir (CCl_4) 1670 (conjugated C=O) and 1610 cm^{-1} (conjugated C=C); NMR (CCl_4) δ 1.22 (d, J = 7.3 Hz, 3 H, 8-CH_3), 1.30 (s, 3 H, 10-CH_3), and 5.59 (s, 1 H, 1-H); mass spectrum (70 eV) *m/e* 178 (M^+).

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.85; H, 10.19.

***cis*-8,10-Dimethyl-1(9),3-hexal-2-one (6). A. From Enone 5 by the Selenoxide Elimination Procedure.** To a stirred solution of 1.13 ml (0.008 mol) of dry diisopropylamine, 20 mg of α,α-bipyridyl, and 12.0 ml of dry THF at ca. 0 °C was added dropwise from a syringe 5.64 ml of a 1.42 M solution of *n*-butyllithium in hexane under nitrogen. The solution was stirred for 30 min and then cooled to −70 °C and 0.95 g (0.005 mol) of the enone **5** in 12.0 ml of dry THF was added dropwise with stirring under nitrogen over a 25-min period. The reaction mixture was stirred for an additional 15 min and 1.64 g (0.0086 mol) of phenylselenenyl chloride in 13.0 ml of dry THF was added dropwise over an 8-min period. The reaction mixture was then allowed to warm to room temperature and poured into 25 ml of a saturated aqueous solution of ammonium chloride. After stirring the layers were separated and the aqueous layer was extracted with two 25-ml portions of ethyl acetate. The combined organic layers were washed with 40 ml of cold 5% hydrochloric acid, two 30-ml portions of a saturated aqueous solution of sodium bicarbonate, and two 30-ml portions of a saturated aqueous solution of sodium chloride, and dried with anhydrous magnesium sulfate. After filtration, 1.54 g (0.014 mol) of 30% aqueous hydrogen peroxide was added to the filtrate and the mixture was stirred for 3 h at room temperature. The solution was then poured into 30 ml of cold water and after shaking the layers were separated. The organic layer was washed with two 30-ml portions of a saturated aqueous solution of sodium bicarbonate and two 30-ml portions of a saturated aqueous solution of sodium chloride, and dried with anhydrous magnesium sulfate. The mixture was filtered and the solvent removed in vacuo to give 0.79 g of crude product. Distillation of the residue gave 0.49 g (52%) of dienone **6**, bp 79–88 °C (0.10 mm), which was greater than 90% pure by GLC (column A). An analytical sample which was collected by preparative GLC (column B) showed uv max (95% ethanol) 239 nm (ϵ 11 600); ir (CCl_4) 1660 (conjugated C=O), 1630 (conjugated C=C), 1607 (conjugated C=C), and 1587 cm^{-1} (conjugated C=C); NMR (CCl_4) δ 1.30 (d, J = 7.5 Hz, 3 H, 8-CH_3), 1.32 (s, 3 H, 10-CH_3), 5.97 (d, J = 1.5 Hz, 1 H, 1-H), 6.00 (d of d, J = 1.5 and 10.1 Hz, 1 H, 3-H), and 6.62 (d, J = 10.1 Hz, 1 H, 4-H); mass spectrum (70 eV) *m/e* 176 (M^+).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.52; H, 9.16.

B. From Enone 5 by Oxidation with DDQ. To a solution of 6.75 g (0.038 mol) of enone **5** in 400 ml of dry benzene was added 11.17 g (0.05 mol) of DDQ and the solution was refluxed under nitrogen for 25 h. The reaction mixture was cooled to ca. 10 °C and filtered, and the filtrate was washed with two 200-ml portions of cold 2% aqueous sodium hydroxide, two 200-ml portions of water, and two 200-ml portions of a saturated aqueous solution of sodium chloride, and dried over anhydrous magnesium sulfate. After filtration the solvent was removed in vacuo to afford 5.11 g of an oil which was shown to contain 3% enone **5**, 68% dienone **6**, and 29% of the trienone **9** by GLC (column A).

A similar run conducted in dioxane gave almost identical results.

A similar run conducted in benzene using 1 equiv of DDQ gave a mixture which was shown to contain 23% **5**, 60% **6**, and 17% **9** by GLC (column A).

A sample of trienone **9**, collected by preparative GLC (column B), showed uv max (95% ethanol) 224 nm (ϵ 12 170), 247 (8650), and 300 (10 890); ir (CCl_4) 1656 (conjugated C=O), 1618 (conjugated C=C), and 1581 cm^{-1} (conjugated C=C); NMR (CCl_4) δ 1.18 (s, 3 H, 10-CH_3), 1.90 (d, J = 1.7 Hz, 3 H, 8-CH_3), 5.92 (m, 1 H, 7-H), 6.03 (m, 1 H, 1-H), 6.07 (q, J_{AB} = 10.2, J_{BC} = 1.5 Hz, 1 H, 3-H), and 6.71 (d, J_{AB} = 10.2 Hz, 1 H, 4-H); mass spectrum (70 eV) *m/e* 174 (M^+).

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.49; H, 8.20.

***trans*-1,7-Dimethyltricyclo[4.4.0.0^{2,6}]dec-4-en-3-one (11).** A solution of 0.45 g of **6** in 95 ml of anhydrous dioxane was irradiated for 6 h using a Hanau NK 6/20 low-pressure mercury lamp. The solution was stirred with a stream of nitrogen for 10 min prior to and during the entire irradiation period. Removal of the solvent in vacuo and distillation of the residue gave 0.315 g (70%) of **11**, bp 63–70 °C (0.1 mm), which was greater than 90% pure by GLC (column A). The analytical sample was collected by preparative GLC (column B) and showed uv max (95% ethanol) 234 nm (ϵ 4820); ir (CCl_4) 1695 cm^{-1} (conjugated cyclopentenone); NMR (CCl_4) δ 0.96 (d, J = 6.7 Hz, 3 H, 7-CH_3), 1.18 (s, 3 H, 1-CH_3), 5.82 (q, J_{AB} = 5.5, J_{BX} = 1.1 Hz, 1 H, 4-H), and 7.19 (q, J_{AB} = 5.5, J_{AX} = 0.8 Hz, 1 H, 5-H); mass spectrum (70 eV) *m/e* 176 (M^+).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.84; H, 9.21.

6,10-*c*-Dimethyl-*r*-5-*C*^{1}-spiro[4.5]deca-3,6-dien-2-one (13). To a solution of 2.36 g (0.014 mol) of the tricyclodecenone **11** in 47 ml of glacial acetic acid containing 0.94 ml of acetic anhydride was added dropwise with stirring at room temperature 0.94 ml of concentrated sulfuric acid. Stirring was continued for 25 h at room temperature and the reaction mixture was poured into 370 ml of an ice-cold solution of 10% aqueous sodium hydroxide. The mixture was extracted with three 100-ml portions of ether and the combined ethereal extracts were washed with 100 ml of a saturated aqueous solution of sodium chloride and dried with anhydrous magnesium sulfate. Removal of the solvent gave 2.17 g (92%) of **13** as an oil which crystallized on standing. Recrystallization of the product from hexane gave an analytical sample: mp 53.5–54.5 °C; uv max (95% ethanol) 223 nm (ϵ 9493); ir (CCl_4) 3028, 1715 (conjugated cyclopentenone), 1584 (conjugated C=C), 1457, and 1376 cm^{-1}; NMR (CCl_4) δ 0.78 (d, J = 5.5 Hz, 3 H, 10-CH_3), 1.54 (m, 3 H, 6-CH_3), 2.10 (AB quartet, J_{AB} = 19 Hz, 2 H, 1-CH_2), 5.55 (br s, $W_{1/2}$ = 4 Hz, 1 H, 7-H), 6.15 (d, J_{AB} = 5.5 Hz, 1 H, 3-H), and 7.21 (d, J_{AB} = 5.5 Hz, 1 H, 4-H); mass spectrum (70 eV) *m/e* 176 (M^+).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.75; H, 9.19.

6,10-*c*-Dimethyl-*r*-5-*C*^{1}-spiro[4.5]dec-6-en-2-one (1). A solution of 1.97 g (0.012 mol) of **13** in 15 ml of 95% ethanol containing 2.2 ml of 10% aqueous sodium hydroxide was hydrogenated at atmospheric pressure in the presence of 0.2 g of 5% palladium on carbon. The reaction was stopped after 288 ml (0.012 mol) of hydrogen had been absorbed and the catalyst was removed by filtration. Water (15 ml) was added to the filtrate and the aqueous phase was extracted with three 30-ml portions of ether. The ether layer was washed with one 25-ml portion of saturated aqueous sodium chloride and dried with anhydrous magnesium sulfate. Removal of the solvent in vacuo gave 1.81 g (91%) of **1**, bp 65–70 °C (0.2 mm), which showed identical physical and spectral properties with those of an authentic sample.[2]

***trans*-1,7-Dimethyltricyclo[4.4.0.0^{2,6}]decan-3-one (12).** To a solution of 0.177 g of **11** in 50 ml of 95% ethanol was added 0.031 g of 10% palladium on carbon and the mixture was hydrogenated in a Parr apparatus for 3 h at 25 psi hydrogen pressure. Removal of the solvent in vacuo and distillation of the residue gave 0.168 g (94%) of **12**: bp 65–70 °C (0.025 mm); ir (CCl_4) 1715 cm^{-1} (C=O); NMR (CCl_4) δ 0.96 (d, J = 6.5 Hz, 3 H, 7-CH_3) and 1.16 (s, 3 H, 1-CH_3).

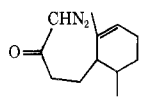
Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.85; H, 10.26.

The spectral properties of **12** were in agreement with those reported by McCurry.[11b]

Registry No.—**1**, 58406-60-3; **5**, 60102-91-2; **6**, 60047-55-4; **7**, 60047-56-5; **9**, 60047-57-6; **11**, 60132-24-3; **12**, 60102-92-3; **13**, 60047-58-7.

References and Notes

(1) This investigation was supported by Grant CA 12193, awarded by the National Cancer Institute, DHEW.
(2) D. Caine, A. A. Boucugnani, S. T. Chao, J. B. Dawson, and P. F. Ingwalson, *J. Org. Chem.*, **41**, 1539 (1976).
(3) For an excellent review, see J. A. Marshall, S. F. Brady, and N. H. Andersen, *Fortschr. Chem. Org. Naturst.*, **31**, 283 (1974).
(4) J. A. Marshall and D. J. Schaeffer, *J. Org. Chem.*, **30**, 3642 (1965).
(5) D. Burn, D. N. Kirk, and V. Petrow, *Tetrahedron*, **21**, 1619 (1965).
(6) D. Caine and F. N. Tuller, *J. Org. Chem.*, **34**, 222 (1969).
(7) D. Walker and J. D. Hiebert, *Chem. Rev.*, **67**, 153 (1967).
(8) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975).
(9) R. A. Lee, C. McAndrews, K. M. Patel, and W. Reusch, *Tetrahedron Lett.*, 965 (1973).
(10) P. J. Kropp, *J. Am. Chem. Soc.*, **87**, 3914 (1965).
(11) (a) McCurry[11b] has reported that a mixture of **12** and the corresponding 7-α-methyl epimer[10] is produced in a 1:9 ratio on copper-catalyzed decomposition of the diazo ketone i. (b) P. M. McCurry, Jr., *Tetrahedron Lett.*, 1845 (1971); P. M. McCurry, Jr., Ph.D. Dissertation, Columbia University, 1970.



i

(12) J. A. Marshall and P. C. Johnson, *J. Org. Chem.*, **35**, 192 (1970).
(13) Melting points and boiling points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 457 infrared spectrophotometer. Ultraviolet spectra were taken on a Beckman DBGT recording spectrophotometer using 1-cm matched quartz cells. NMR spectra were determined at 60 MHz with a Varian T-60 spectrometer. Signals are reported in parts per million (δ) downfield from internal tetramethylsilane. Mass spectra were obtained using a Hitachi Perkin-Elmer RNU-7 or a Varian M-66 spectrometer. Microanalyses were obtained by Atlantic Microlab, Inc., Atlanta, Ga. Gas–liquid chromatography was carried out using a Perkin-Elmer 881 or an Aerograph A-90-P3 gas chromatograph. The following columns were used: A (6 ft × 0.125 in., 20% Carbowax K-20M on Chromosorb W); B (10 ft × 0.25 in., 20% Carbowax K-20M on Chromosorb W).

Amino Acids and Peptides. 44. Synthesis of DL-γ-Carboxyglutamic Acid, a New Amino Acid

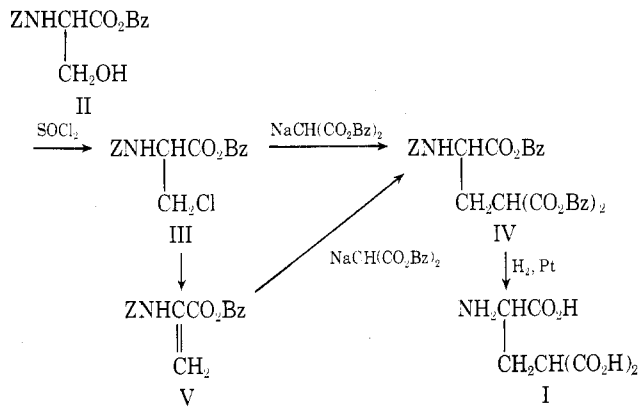
Boris Weinstein,* Kerry G. Watrin, H. Jeff Loie, and Joseph C. Martin

Department of Chemistry, University of Washington, Seattle, Washington 98195

Received April 27, 1976

Vitamin K dependent blood clotting proteins, such as prothrombin and factor X, have been found to contain a novel amino acid, L-γ-carboxyglutamic acid (I),[1-3] which is implicated in the formation of calcium binding sites.[4,5] The initial formulation relied exclusively on spectral data, so a synthesis seemed desirable, both to confirm the structure and to obtain a larger quantity for other biochemical activities.

Benzyl N^{α}-benzyloxycarbonyl-L-serinate (II)[6] was refluxed with thionyl chloride in benzene to give benzyl N^{α}-benzyloxycarbonyl-3-chloro-L-alaninate (III). Addition of chloride III to a solution of monosodium dibenzyl malonate in tetrahydrofuran then afforded tribenzyl 3-benzyloxycarbonylamino-DL-1,1,3-propanetricarboxylate (IV). Ester IV was optically inactive, which suggested that its mode of formation must have involved a racemization step. To clarify this situation, a solution of chloride III on stirring with sodium hydride formed benzyl N^{α}-benzyloxycarbonyl-2-methyleneglycinate (V). The readdition of monosodium dibenzyl malonate to the unsaturated ester V went smoothly and furnished the condensation product IV. Thus, the actual conversion of III to IV goes by way of a β-elimination sequence, which was first reported to occur on alkaline treatment of (di-*O*-phenylphospho)serine derivatives.[7] Hydrogenation of compound IV in methanol afforded DL acid I and a comparison with a natural specimen showed common chromatographic behavior.[8] A tentative pK_a value indicates that it is the most acidic natural amino acid.



While this work was in progress (or at an end), five other approaches to this amino acid appeared in the literature. The first procedure began with DL-serine and proceeded via the same intermediates described here, but the report did not provide any experimental details.[9] The second route involved the preparation of methyl N^{α}-benzyloxycarbonyl-3-iodo-L-alaninate or methyl N^{α}-benzyloxycarbonyl-*O*-tosyl-L-serinate, followed by condensation with di-*tert*-butyl malonate. The resulting ester was subjected to sequential deprotection involving hydrogen, base, and acid treatment. Methyl N^{α}-benzyloxycarbonyl-2-methyleneglycinate was identified, but only as a by-product of the alkylation step. A low rotation was tabulated for the condensation ester, but this observation must be erroneous, as the final amino acid had no rotation.[10] One of the intermediates in this synthesis has now been crystallized[11] and used in a resolution.[12] The third path started with the tosylate mentioned above and several DL derivatives of blocked I were generated, but there was no report of the free amino acid.[13] The fourth preparation used a condensation between ethyl N^{α}-acetyl-2-methyleneglycinate and diethyl malonate to yield triethyl DL-acetamidopropane-1,1,3-tricarboxylate. Alkaline hydrolysis, desalting, and treatment with ammonium hydroxide formed the monoammonium salt of the DL amino acid I.[14] The last scheme required the synthesis of benzyl-di-*tert*-butyl N^{α}-butyloxycarbonyl-DL-γ-carboxyglutamate, which after a two-step removal of the protecting groups was changed into the trifluoroacetate salt of I.[15]

In summary, the synthesis described here is the simplest and most direct for the preparation of free DL-γ-carboxyglutamic acid.

Experimental Section[16]

Benzyl N^{α}-Benzyloxycarbonyl-3-chloro-L-alaninate (III). A mixture of magnesium oxide (0.160 g, 4 mmol) and benzyl N^{α}-benzyloxycarbonyl-L-serinate (0.624 g, 2 mmol) in benzene (20 ml) was treated with thionyl chloride (0.440 g, 4 mmol) and refluxed for 3 h. The solvent was removed in vacuo, the residue was extracted with hot benzene (3 × 10 ml), and the pooled organic phase was washed with water and dried (Na_2SO_4). Evaporation of the benzene gave the desired product, which was crystallized from ethanol–water: mp 90–92 °C (0.232 g, 33%); R_f 0.26; ν_{max} 3410 (NH), 3045, 3030 (aromatic CH), 2960 (aliphatic CH), 1740, 1715 (CO), 1640 (C=C), and 697 cm^{-1}; $[\alpha]^{21.0}D$ −20.0° (*c* 1.0); δ_{Me_4Si} 7.45 (aromatic), 5.75 (NH), 5.25 ($CH_2C_6H_5$), 5.20 ($OCH_2C_6H_5$), 4.80 (CH), and 3.90 (CH_2Cl), J = 2 Hz. Anal. Calcd for $C_{18}H_{18}ClNO_4$ (347.79): C, 62.16; H, 5.22; Cl, 10.20; N, 4.03. Found: C, 62.17; H, 5.22; Cl, 10.68; N, 3.94.

Tribenzyl 3-Benzyloxycarbonylamino-DL-1,1,3-propanetricarboxylate (IV). A suspension of sodium hydride (50% in mineral oil, 0.149 g, 31 mmol) in tetrahydrofuran (15 ml) under a nitrogen atmosphere was stirred with dibenzyl malonate (0.966 ml, 34 mmol) for 5 min, after which the now cloudy solution was diluted with more tetrahydrofuran (30 ml) and agitated for 2 h. A solution of the