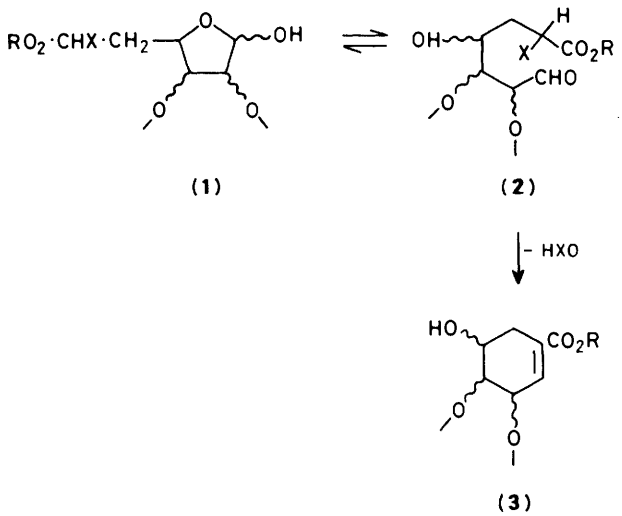
Enantiospecific Synthesis of Shikimic Acid from D-Mannose: Formation of a Chiral Cyclohexene by Intramolecular Olefination of a Carbohydrate-derived Intermediate

George W. J. Fleet,* Tony K. M. Shing, and Steven M. Warr
Dyson Perrins Laboratory, Oxford University, South Parks Road, Oxford OX1 3QY

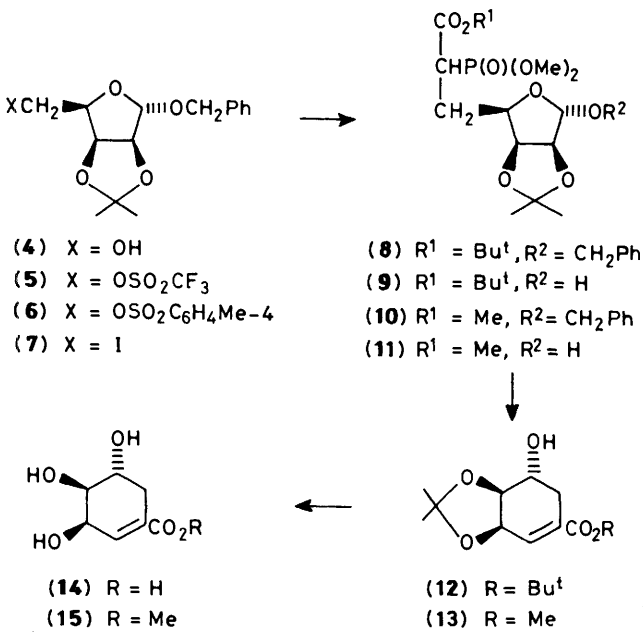
An enantiospecific synthesis of (−)-shikimic acid from D-mannose in an overall yield of 39% is described, in which the key step is an intramolecular Wadsworth–Emmons olefination reaction of a phosphonate. Nucleophilic displacement of triflate from benzyl 2,3-*O*-isopropylidene-5-*O*-trifluoromethylsulphonyl-α-D-lyxofuranoside by the sodium salt of t-butyl dimethoxyphosphorylacetate provides a rare example of substitution at the C-5 position of a furanose derivative by a carbanion.

In spite of the multitude of total syntheses of natural products from carbohydrates, there are only a few examples of the preparation of chiral cyclohexenyl compounds.[1] As part of a programme oriented towards devising a general synthesis of chiral oxygenated cyclohexenes, it was decided to investigate the potential of intramolecular olefination reactions of the type shown in Scheme 1; a furanose derivative (**1**), in equilibrium with an open-chain γ-hydroxyaldehyde (**2**), should be capable of undergoing base-catalysed cyclisation to an oxygenated cyclohexene (**3**) by intramolecular aldol (X = H),[2] Doebner (X = CO_2H),[3] Wittig (X = $^+PPh_3$),[4] or Wadsworth–Emmons[5] [X = P(O)(OMe)$_2$] olefinations. Because of the flexibility of differential protection and easy control of the stereochemistry of oxygen (or indeed other) functional groups in furanose derivatives (**1**), this approach would constitute a powerful and general method for the enantiospecific synthesis of polyfunctional cyclohexenes.



Scheme 1.

Shikimic acid (**14**) is the namesake of a metabolic pathway[6] producing structurally diverse and biochemically important primary and secondary metabolites in plants and micro-organisms. The racemic form of the acid has been the target of several successful syntheses,[7] almost all of which have depended on the construction of a suitable cyclohexenecarboxylic acid by a Diels–Alder reaction; recently a route starting from dihydrobenzoic acid, which features a key bromolactonization, has been reported.[8] In contrast, the two previous enantiospecific syntheses of shikimic acid involve many steps from D-arabinose[9a] or from D-mannose[9b] and both have overall yields of *ca.* 2%; methyl shikimate (**15**) has been prepared from a quinic acid derivative.[10] This paper describes an efficient synthesis of (−)-shikimic acid by an intramolecular olefination reaction of phosphonate (**9**), prepared by a two-carbon-chain extension of the lyxofuranoside (**4**) (Scheme 2); a preliminary report of this work has appeared.[11]



Scheme 2.

2,3:5,6-Di-*O*-isopropylidene-α-D-mannose[12] may be converted into benzyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**4**) without the isolation of any intermediates; the overall yield of (**4**) from D-mannose is 66%.[13] The anomeric position of 2,3-*O*-isopropylidene-α-D-lyxofuranose may be equally readily protected as either the α-benzoyl[14] or α-methyl furanoside.[15] The benzyl protecting group was chosen since it would resist nucleophilic attack during the two-carbon-chain extension (unlike the benzoyl group) and could be removed by hydrogenolysis under conditions which would not affect the phosphonoacetate ester groups (a potential problem in the case of a methyl furanoside). The *lyxo* alcohol (**4**) was treated with

toluene-*p*-sulphonyl chloride in pyridine to produce the toluene-*p*-sulphonate (**6**); compound (**4**) was also converted into the corresponding iodide (**7**) by triphenyl phosphite methiodide. However, neither (**6**) nor (**7**) underwent a nucleophilic substitution reaction with the carbanion derived from methyl dimethoxyphosphorylacetate under a variety of conditions. The resistance to nucleophilic attack of leaving groups in compounds with β-oxygen substituents is well known;[16] there are few, if any, examples of extension of carbon chains by carbanion nucleophilic displacement of derivatives of the 5-hydroxy group in furanosides. The *lyxo* alcohol (**4**) was esterified with triflic anhydride* in the presence of pyridine to give benzyl 2,3-*O*-isopropylidene-5-*O*-trifluoromethylsulphonyl-α-D-lyxofuranoside (**5**) in quantitative yield; unlike many sugar triflates,[17] the trifluoromethanesulphonate (**5**) is relatively stable and can easily be handled at room temperature without decomposition.

Treatment of (**5**) with the sodium salt of t-butyl dimethoxyphosphorylacetate in dimethylformamide (DMF) in the presence of a crown ether at room temperature for 20 h led to the formation of the diastereoisomeric t-butyl (benzyl 5,6-dideoxy-6-dimethoxyphosphoryl-2,3-*O*-isopropylidene-α-D-*lyxo*-heptofuranosid)uronates (**8**) in 81% yield; this provides an illustration of the value of triflate as an excellent leaving group easily displaced under mild conditions in circumstances where more common leaving groups are inert.

Hydrogenolysis of the benzyl protecting groups of the phosphonates (**8**) gave the lactols (**9**) which were treated with sodium hydride in tetrahydrofuran (THF) to form (−)-t-butyl 3,4-*O*-isopropylideneshikimate (**12**) [73% yield from (**8**)]. The t-butyl and isopropylidene protecting groups could be simultaneously and quantitatively removed from compound (**12**) by aqueous trifluoroacetic acid at room temperature to give (3*R*,4*R*,5*R*)-(−)-shikimic acid (**14**). The overall yield of shikimic acid is 59% from the protected *lyxo* alcohol (**4**) and 39% from D-mannose.

Treatment of the triflate (**5**) with the sodium salt of methyl dimethoxyphosphorylacetate gave the dimethoxyphosphorylacetates (**10**) (74%) which, after hydrogenolysis to the lactols (**11**), underwent sodium methoxide-catalysed cyclisation to methyl isopropylideneshikimate (**13**).[11] The isopropylidene protecting group was removed from (**13**) by mild acid treatment (Dowex 50 WX-8 resin, H^+ form; room temperature) to give methyl shikimate (**15**) [62% yield from phosphonate (**10**) and 46% from benzyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**4**)]. However, the conversion of the methyl ester (**15**) into free shikimic acid is not a very high yield process and has frequently been omitted in syntheses of shikimic acid;[7,10] thus the use of the t-butyl ester provides a significant advantage in the synthesis of the free acid (**14**).

The overall yield of (39%) of shikimic acid from mannose in this short sequence is considerably higher than any of the alternatives currently available, and has the additional advantage of producing chiral material; it would be easy to introduce hydrogen isotopes into the C-5 methylene group of *lyxo* alcohol (**4**)—resulting in labelling of the ring methylene of shikimic acid—and/or to introduce other isotopic labels incorporated in the phosphonoacetate fragment.

This approach provides considerable potential for the easy synthesis of chiral analogues of shikimic acid in which the stereochemistry of the oxygens could be controlled or other functional groups introduced; additionally, it indicates a promising route to heavily functionalised chiral cyclohexenes in general, and several other shikimic acid metabolites in particular.

* Trifluoromethanesulphonic anhydride.

Experimental

M.p.s. were recorded on a Kofler block. I.r. spectra were recorded on a Perkin-Elmer 257 or 297 spectrophotometer. ^{1}H N.m.r. spectra were run at 300 MHz on a Bruker WH 300 spectrometer using deuteriochloroform as solvent unless otherwise stated. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Mass spectra were recorded on a VG Micromass 16 F spectrometer; in order to obtain satisfactory mass spectra for these highly polar compounds, it was necessary to use ACE and DCI techniques. Microanalyses were performed by Dr. F. B. Strauss. T.l.c. was performed on glass plates coated with silica gel 'Blend 41,' and compounds were visualised with a spray of 5% v/v sulphuric acid in ethanol. Flash chromatography was carried out using Merck Kieselgel 60, 230—400 mesh. THF was distilled from a solution dried with potassium in the presence of benzophenone under dry nitrogen. D-Mannose, (−)-shikimic acid, t-butyl bromoacetate, and methyl bromoacetate were supplied by the Aldrich Chemical Company. D-Mannose was converted into benzyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**4**)[12,13] as previously described. Shikimic acid was converted into methyl shikimate[18] and into methyl isopropylideneshikimate[19] to provide authentic samples for comparison with synthetic materials. t-Butyl and methyl bromoacetates were converted into the respective alkyl dimethylphosphonates by treatment with trimethylphosphite.[20]

Benzyl 2,3-O-*Isopropylidene*-5-O-*trifluoromethylsulphonyl*-α-D-*lyxofuranoside* (**5**).—A solution of the alcohol (**4**) (1.9 g, 6.8 mmol) in dry dichloromethane (20 ml) containing dry pyridine (1.2 ml, 2.2 equiv.) was cooled to −30 °C and stirred while triflic anhydride (1.49 ml, 1.3 equiv.) was added dropwise during 15 min. The mixture was stirred for a further 15 min at −30 °C, quenched with methanol (1 ml), washed successively with ice–water and cold aqueous potassium dihydrogen orthophosphate (1 M), dried (Na_2SO_4), and filtered through a thin pad of silica topped with Celite. Concentration of the filtrate gave a syrup which was co-distilled with toluene to remove the residual pyridine, and afforded benzyl 2,3-*O*-isopropylidene-5-*O*-trifluoromethylsulphonyl-α-D-lyxofuranoside (**5**) (2.8 g, quantitative) as a pale yellow syrup, $[\alpha]_D^{20}$ +69.8° (*c* 2.0 in $CHCl_3$); R_F 0.6 [ethyl acetate–hexane (1:2 v/v)]; δ(C_6D_6) 0.97 and 1.23 (together 2 s, 2 Me), 3.86 (1 H, dt, $J_{4,3} = J_{4,5} = 3.8$, $J_{4,5'} = 7.6$ Hz, 4-H), 3.99 (1 H, dd, $J_{3,2}$ 5.8 Hz, 3-H), 4.14 (1 H, d, J_{gem} 11.8 Hz, PhC*H*), 4.37 (1 H, d, 2-H), 4.39 [1 H, dd, (obscured by 2-H and PhC*H*′), 5-H], 4.49 (1 H, d, PhC*H*′), 4.56 (1 H, dd, $J_{5',5}$ 10.8 Hz, 5′-H), 5.05 (1 H, s, 1-H), and 7.10—7.17 (5 H, br s, Ph); *m*/*z* (DCI, NH_3) 430 (100%, $M^+NH_4^+$).

t-Butyl (*Benzyl* 5,6-*Dideoxy*-6-*dimethyoxyphosphoryl*-2,3-O-*isopropylidene*-α-D-lyxo-*heptofuranosid*)*uronate*† (**8**).—Sodium hydride (50%; 248 mg, 5.2 mmol) was washed with anhydrous diethyl ether under nitrogen, suspended in dry DMF (15 ml), and the mixture was cooled to 0 °C. A solution of t-butyl dimethoxyphosphorylacetate (1.26 g, 5.6 mmol) in dry DMF (6 ml) was added dropwise to the stirred mixture during 20 min. After the addition the cold bath was removed and the mixture was stirred for 1 h to give a clear solution. A solution of the triflate (**5**) (1.42 g, 3.45 mmol) in DMF (6 ml) was then added, followed by 15-crown-5 (2 drops). The reaction mixture was stirred at room temperature for 20 h, then cooled to 0 °C, quenched with cold aqueous potassium dihydrogen orthophosphate (1 M; 40 ml), and extracted with chloroform (3 × 20 ml). The combined extracts were washed with cold water, dried (Na_2SO_4), and concentrated. The residue was flash chromato-

† The stereochemistry at C-6 is *not* taken into account in assigning α-D-*lyxo* stereochemistry to compounds (**8**)—(**11**). Strictly speaking, the C-6 epimers are mixtures of the α-D-*allo* and β-L-*talo* isomers.

graphed [gradient elution with ethyl acetate–hexane (1:1 ⟶ 2:1 v/v)] to give the isomeric *phosphonates* (**8**) (1.20 g. 81%) as a pale yellow syrup, $[\alpha]_D^{20}$ +55.7° (*c* 2.0 in $CHCl_3$); R_F 0.3 [ethyl acetate–hexane (2:1 v/v)]; $\nu_{max.}$ 1 730 cm^{-1} (ester C=O); δ (*inter alia*) 5.0 (0.57 H, s, 1-H) and 5.02 (0.43 H, s, 1-H of diastereoisomer); *m/z* (DCI, NH_3) 487 (100%, MH^+) and 431 (95%, MH^+ − isobutylene) (Found: C, 56.2; H, 7.5; P, 6.5. $C_{23}H_{35}O_9P$ requires C, 56.8; H, 7.3; P, 6.4%).

t-Butyl (3R,4S,5R)-3,4,5-*Trihydroxy*-3,4,-O-*isopropylidene*-*cyclohex*-1-*enecarboxylate* (**12**).—The phosphonates (**8**) (0.64 g, 1.32 mmol) in methanol (10 ml) were hydrogenated over palladium–charcoal (10%; 210 mg) at room temperature and atmospheric pressure for 30 h. The mixture was filtered through Celite, and the filtrate was concentrated to yield the lactols (**9**) as a syrup. Sodium hydride (50%; 85 mg, 1.3 equiv.) was washed with anhydrous diethyl ether (3 ×) under nitrogen and suspended in dry THF (8 ml). To this stirred suspension was added dropwise a solution of the lactols (**9**) in dry THF (6 ml) during 5 min. The reaction was exothermic; a white gelatinous precipitate was observed. After 45 min, the mixture was cooled to 0 °C, quenched with cold aqueous potassium dihydrogen orthophosphate (1 M; 40 ml), and extracted with chloroform (3 × 20 ml). The combined extracts were dried (Na_2SO_4), filtered through a pad of silica, and the filtrate was concentrated. Flash chromatography of the residue [diethyl ether–hexane (2:1 v/v)] afforded *t-butyl isopropylideneshikimate* (**12**) (260 mg, 73%) as a syrup which crystallised with time at 5 °C, m.p. 44—46 °C, $[\alpha]_D^{20}$ −88.3° (*c* 0.7 in $CHCl_3$); R_F 0.38 [diethyl ether–hexane (2:1, v/v)]; $\nu_{max.}$ 3 420—3 480 (OH), 1 705 (conjugated ester C=O), and 1 655 cm^{-1} (C=C); δ 1.37 and 1.43 (together 2 s, CMe_2), 1.45 (s, Bu^t), 2.13 (1 H, ddt, $J_{6'.6}$ 17.4, $J_{6'.5}$ 10.8, $J_{6'.3} = J_{6'.2}$ = 1.9 Hz, 6'-H), 2.74 (1 H, dd, $J_{6.5}$ 4.7 Hz, 6-H), 2.94 (1 H, d, $J_{OH.5}$ 3.1 Hz, OH), 3.80 (1 H, dddd, $J_{5.4}$ 6.8 Hz, 5-H), 4.03 (1 H, dd, $J_{4.3}$ 7.7 Hz, 4-H), 4.71 (1 H, m, 3-H), and 6.80 (1 H, 2-H); *m/z* (In Beam EI) 255 (95%, $M^+ - CH_3$) (Found: C, 61.8; H, 7.9. $C_{14}H_{22}O_5$ requires C, 62.2; H, 8.2%).

(3R,4S,5R)-3,4,5-*Trihydroxycyclohex*-1-*enecarboxylic Acid* (*Shikimic Acid*) (**14**).—A solution of t-butyl isopropylideneshikimate (**12**) (108 mg, 0.4 mmol) in aqueous trifluoroacetic acid (60% v/v; 5 ml) was kept at room temperature for 12 h. Removal of solvent gave a syrup which was twice concentrated with absolute ethanol to provide white crystalline shikimic acid in quantitative yield, m.p. 184—186 °C (authentic sample,* 184—186 °C); $[\alpha]_D^{20}$ −170° (*c* 0.86 in H_2O) {lit.,[9] $[\alpha]_D$ −179° (*c* 4.0 in water)}. This synthetic material was identical with the authentic sample obtained from Aldrich; R_F 0.5 [ethyl acetate–acetic acid–water (4:1:1 v/v)].

Benzyl 5-*Deoxy*-5-*iodo*-2,3-O-*isopropylidene*-α-D-*lyxo*-*furanoside* (**7**).—A mixture of the alcohol (**4**) (0.69 g, 2.5 mmol) and triphenyl phosphite methiodide (4.2 g, 3.8 equiv.) in dry toluene (25 ml) was heated at reflux under nitrogen for 12 h. Evaporation of the solvent followed by chromatography of the residue [hexane–diethyl ether (4:1)] provided the *title compound* (**7**) (0.67 g, 70%) as a syrup which crystallised with time at 0 °C, m.p. 52—53 °C; $[\alpha]_D^{20}$ +81.1° (*c* 0.8 in $CHCl_3$); R_F 0.60 [hexane–diethyl ether (4:1 v/v)]; δ 1.33 and 1.47 (together 2 s, 2 Me), 3.31 (1 H, dd, $J_{5'.4}$ 6.7, $J_{5'.5}$ 9.7 Hz, 5'-H), 3.39 (1 H, dd, $J_{5.4}$ 9.7 Hz, 5-H), 4.30 (1 H, dt, $J_{4.3}$ 3.5 Hz, 4-H), 4.50 (1 H, d, J_{gem} 11.8 Hz, PhC*H'*), 4.70 (1 H, d, $J_{2.3}$ 5.9 Hz, 2-H), 4.71 (1 H, d, PhC*H*), 4.79 (1 H, dd, 3-H), 5.13 (1 H, s, 1-H), and 7.35 (5 H, br s, Ph); *m/z* (ACE, NH_3) 375 (10%, $M^+ - CH_3$) (Found: C, 46.2; H, 4.9. $C_{15}H_{19}IO_4$ requires C, 46.2; H, 4.9%).

* The m.p. of the synthetic material was identical with that of authentic material obtained from Aldrich Chemical Co.

Benyl 2,3,-O-*Isopropylidene*-5-O-p-*tolylsulphonyl*-α-D-*lyxo*-*furanoside* (**6**).—An ice-cold solution of the alcohol (**4**) (1.3 g, 4.6 mmol) in dry pyridine (8 ml) was mixed with a solution of toluene-*p*-sulphonyl chloride (1.1 g, 1.2 equiv.) in the same solvent (4 ml) at 0 °C. After 48 h at 5 °C the reaction mixture was worked up in the conventional way and chromatographed [hexane–diethyl ether (2:1 v/v)] to give the 5-O-*tosylate* (**6**) (1.9 g, 95%) as a syrup, $[\alpha]_D^{20}$ +52.7° (*c* 1.5 in $CHCl_3$); R_F 0.35 [hexane–diethyl ether (2:1 v/v)]; δ 1.25 and 1.34 (together 2 s, 2 Me), 2.45 (s, ArCH_3),4.22—4.38 (3 H, m, 4-, 5-, and 5'-H), 4.43 (1 H, d, J_{gem} 11.8 Hz, PhC*H'*), 4.62 (1 H, d, $J_{2.3}$ 5.8 Hz, 2-H), 4.64 (1 H, d, PhC*H*), 4.70 (1 H, dd, $J_{3.4}$ 3.2 Hz, 3-H), 5.06 (1 H, s, 1-H), 7.32—7.37 (7 H, m, ArH), and 7.84 (2 H, d, ArH) (Found: C, 60.8; H, 5.9. $C_{22}H_{26}O_7S$ requires C, 60.8; H, 6.0%).

Methyl (*Benzyl* 5,6-*Dideoxy*-6-*dimethoxyphosphoryl*-2,3-O-*isopropylidene*-α-D-lyxo-*heptofuranosid*)*uronate* (**10**).—Sodium hydride (50%; 122 mg, 1.5 equiv.) was washed with dry diethyl ether (2 ×) under dry nitrogen, suspended in dry DMF (12 ml), and the mixture was cooled to 0 °C. A solution of methyl dimethoxyphosphorylacetate (485 mg, 1.6 equiv.) in DMF (1 ml) was added dropwise to the stirred suspension. After 1 h, a solution of the triflate (**5**) (684 mg, 1.66 mmol) in the same solvent (2 + 2 ml) was introduced, followed by 18-crown-6 (2 drops). The resulting mixture was stirred at room temperature for 16 h, then cooled to 0 °C, quenched with cold aqueous potassium dihydrogen orthophosphate (1 M; 20 ml), and extracted with chloroform (3 × 10 ml). The combined extracts were washed with cold water, dried (NA_2SO_4), and concentrated. Flash chromatography of the residue [gradient elution with ethyl acetate–hexane (2:1 ⟶ 3:1 v/v)] furnished the isomeric *phosphonates* (**10**) (552 mg, 75%) as a pale yellow syrup, $[\alpha]_D^{20}$ +57.0° (*c* 0.5 in $CHCl_3$); R_F 0.3 [ethyl acetate–hexane (3:1 v/v)]; $\nu_{max.}$ 1 735 cm^{-1} (ester C=O); δ (*inter alia*) 1.30, 1.31, 1.45, and 1.46 (together 4 Me, 4 s of *ca.* equal intensity); *m/z* (DCI, isobutane) 445 (100%, MH^+) and 337 (97%, $MH^+ - C_7H_7O$) (Found: C, 54.3; H, 6.2; P, 7.0. $C_{20}H_{29}O_9P$ requires C, 54.1; H, 6.6; P, 7.0%).

Methyl (3R,4S,5R)-3,4,5-*Trihydroxycyclohex*-1-*enecarboxylate* (*Methyl Shikimate*) (**15**).—The phosphonates (**10**) (132 mg, 0.29 mmol) in methanol (5 ml) were hydrogenated over palladium–charcoal (10%; 24 mg) at room temperature and atmospheric pressure for 8 h. The mixture was filtered through Celite and methanolic sodium methoxide (1.048 M; 0.9 ml, 3 equiv.) was added to the filtrate. After 2 h, the reaction was quenched with saturated aqueous ammonium chloride and extracted with chloroform (3 ×). The combined extracts were concentrated and residue was dissolved in methanol containing Dowex 50 WX-8 resin (H^+; 1 g, prewashed with methanol). After being stirred at room temperature for 20 h, the mixture was filtered. Removal of the solvent from the filtrate gave white crystals (35 mg, 62%) with m.p. 104—108 °C. Recrystallisation from ethyl acetate yielded fluffy needles of methyl shikimate (**15**), m.p. 115—116.5 °C (lit.,[18] 113—114 °C); $[\alpha]_D^{20}$ −125° (*c* 1.8 in EtOH) {lit.,[18] $[\alpha]_D^{20}$ −130° (*c* 1.88 in EtOH)}, identical with an authentic sample prepared from shikimic acid (Aldrich).

Acknowledgements

We are pleased to acknowledge an S.E.R.C. postdoctoral fellowship (to T. K. M. S.) in support of this work.

References

1 R. J. Ferrier, P. Prasit, and P. C. Tyler, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1641 and references cited therein; S. Hanessian, 'Total

Synthesis of Natural Products: The Chiron Approach,' Pergamon, Oxford, 1983.
2 A. T. Nielsen and W. J. Houlihan, *Org. React.*, 1968, **16**, 47.
3 G. Jones, *Org. React.*, 1967, **15**, 204; P. M. Collins, W. G. Overend, and T. K. M. Shing, *J. Chem. Soc., Chem. Commun*, 1982, 297.
4 L. D. Cama and B. D. Christensen, *J. Am. Chem. Soc.*, 1978, **100**, 8006.
5 W. S. Wadsworth, *Org. React.*, 1977, **25**, 73.
6 U. Weiss and J. M. Edwards, 'The Biosynthesis of Aromatic Compounds,' Wiley, New York, 1980; E. Haslam, 'The Shikimate Pathway,' Wiley, New York, 1974.
7 B. Ganem, *Tetrahedron*, 1978, **34**, 3353; M. Koreeda and M. A. Ciufolini, *J. Am. Chem. Soc.*, 1982, **104**, 2308; C. D. Snyder and H. Rapoport, *ibid.*, 1974, **95**, 7821.
8 K. E. Coblens, V. B. Muralidharen, and B. Ganem, *J. Org. Chem.*, 1982, **47**, 5041.
9 (*a*) H. J. Bestmann and H. A. Heid, *Angew. Chem., Int. Ed. Engl.*, 1971, **10**, 336; (*b*) M. Yoshikawa, Y. Ikeda, H. Kayakiri, and I. Kitagawa, *Heterocycles*, 1982, **17**, 209.
10 J. Cleophax, J. Leboul, D. Mercier, A. Gaudemer, and S. DovGero, *Bull. Soc. Chim. Fr.*, 1973, 2992.
11 G. W. J. Fleet and T. K. M. Shing, *J. Chem. Soc., Chem. Commun.*, 1983, 849.
12 R. L. Whistler and M. L. Wolfrom, *Methods Carbohydr. Chem.*, 1963, **2**, 319.
13 J. S. Brimacombe, F. Hunedy, and L. C. N. Tucker, *J. Chem. Soc. C*, 1968, 1381.
14 H. Ohrui and S. Emimoto, *Tetrahedron Lett.*, 1975, 2765.
15 R. L. Whistler and J. N. BeMiller, *Methods Carbohydr. Chem.*, 1980, **8**, 173.
16 S. S. Shaik, *J. Am. Chem. Soc.*, 1983, **105**, 4359.
17 V. K. Iyer and J. P. Horwitz, *J. Org. Chem.*, 1982, **47**, 644 and references cited therein.
18 H. O. L. Fischer and G. Dangschat, *Helv. Chim. Acta*, 1934, **17**, 1196, 1200.
19 H. O. L. Fischer and G. Dangschat, *Helv. Chim. Acta*, 1935, **18**, 1206.
20 J. Boutagy and R. Thomas, *Chem. Rev.*, 1974, **74**, 87.

Received 2*nd September* 1983; *Paper* 3/1529