(1) was washed with benzene and dried under vacuum.

Triphase Esterification. Procedure D. Sodium 2,4,6-trimethylbenzoate (6.0 mmol), neutralized with sodium hydroxide to a phenolphthalein end point, was dissolved in 6 mL of water, and the solution was placed in a test tube (200-mm o.d.) fitted with a reflux condenser. To this solution was added the triphase catalyst (0.16 g of 1) and the alkyl halide (24 mmol) in 6 mL of organic solvent. The bottom layer was magnetically stirred, but the catalyst at the interface was not visibly disturbed. At the end of the reaction period, the mixture was made strongly acidic with hydrochloric acid and the yield was determined by GLC with the remaining carboxylic acid used as an internal standard. When AG1-8X (chloride form) was used as the catalyst, 0.090 dry g of resin (3.2 mequiv/dry g) was used.

Esterification without Anion-Exchange Resins. Procedure E. Esterification in Methanol. The alkali metal carboxylate salt (6 mmol was dissolved in 20 mL of methanol. Excess alkyl halide (32 mmol) was added. After the reaction period was over, the mixture was analyzed by GLC for both carboxylic acid and ester by use of an internal standard.

Esterification in Acetone with Added Potassium Carbonate. Procedure F. The carboxylic acid (2.0 mmol), the alkyl halide (8.0 mmol), anhydrous potassium carbonate (0.7 g, 5.0 mmol), 15 mL of acetone, and a magnetic stirring bar were placed in a round-bottom flask fitted with a drying tube. After the reaction period was completed (Table III), the cooled reaction mixture was acidified with dilute hydrochloric acid and extracted with CH_2Cl_2. GLC analysis was used to determine the yield with the unreacted acid used as an internal standard.

Alkylation of Potassium Carboxylates with No Excess Base. Procedure G. This procedure is identical with procedure F with the following exceptions. The potassium salt, prepared in advance, recrystallized from ethanol and dried under vacuum, was added to acetone or 95% acetone–water. No potassium carbonate was added.

Potassium *cis*-9,10-epoxyoctadecanoate, prepared from *cis*-9,10-epoxyoctadecanoic acid and KOH in ethanol, was shown to be 100% epoxidized.[27,28] The hydrochloric acid was omitted for the workup of ethyl *cis*-9,10-epoxyoctadecanoate, and the isolated ester was identified by IR, analysis for the oxirane ring, and its mp, 21–22 °C (lit.[33] mp 21 °C), determined without purification.

Kinetic Measurements. The second-order rate constants were determined by the method of Pfeffer and Silbert.[13b] Potassium 2,4,6-trimethylbenzoate (about 0.20 M) in the appropriate acetone–water mixture and ethyl iodide (0.873 M) in 95% acetone were thermostated at 40.0 °C. To each of five flasks containing 2.00 mL of ethyl iodide was pipetted 2.00 mL of the carboxylate salt solution. The flasks were periodically removed, quenched, and titrated over a range of times exceeding 3 half-lives. The rate constants were determined by least squares analysis and the correlation coefficients were 0.997 or greater.

Acknowledgments. We gratefully acknowledge the assistance of Ronald K. Moore (deceased) in the determination of the kinetic data.

Registry No. 2-Ethylhexadecanoic acid, 54240-85-6; 2,2-dimethylhexadecanoic acid, 22890-23-9; 2,4,6-trimethylbenzoic acid, 480-63-7; 3,3-dimethylbutanoic acid, 1070-83-3; *cis*-9,10-epoxyoctadecanoic acid, 24560-98-3; iodoethane, 75-03-6; 1-bromobutane, 109-65-9; 2-iodopropane, 75-30-9; ethyl 2-ethylhexadecanoate, 70116-75-5; ethyl 2,2-dimethylhexadecanoate, 70116-76-6; ethyl 2,4,6-trimethylbenzoate, 1754-55-8; ethyl 3,3-dimethylbutanoate, 5340-78-3; butyl 2,4,6-trimethylbenzoate, 70116-77-7; isopropyl 2,4,6-trimethylbenzoate, 41589-61-1; ethyl *cis*-9,10-epoxyoctadecanoate, 70116-78-8; sodium 2,4,6-trimethylbenzoate, 32642-28-7; potassium hexadecanoate, 2624-31-9; potassium octadecanoate, 593-29-3; potassium *cis*-9-octadecenoate, 143-18-0; potassium 2-ethylhexadecanoate, 70116-79-9; potassium 2,4,6-trimethylbenzoate, 53756-55-1; potassium *cis*-9,10-epoxyoctadecanoate, 70116-80-2; 2-iodooctane, 557-36-8; ethyl hexadecanoate, 628-97-7; ethyl octadecanoate, 111-61-5; ethyl *cis*-9-octadecanoate, 111-62-6; 1-methylheptyl 2,4,6-trimethylbenzoate, 70116-81-3; 1-iodopentane, 628-17-1; pentyl 2,4,6-trimethylbenzoate, 70116-82-4.

(33) G. King, *J. Chem. Soc.*, 1817 (1949).

The Absolute Configuration of (-)-Ethyl α-Formyl-α-methylphenylacetate and (-)-1,2-Diphenyl-2-methyl-1,3-propanedione

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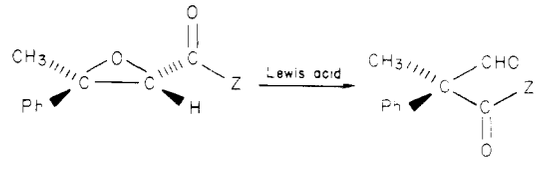
Received January 9, 1979

The absolute configuration and optical purity of (-)-(*S*)-ethyl α-formyl-α-methylphenylacetate and (-)-*S*-1,2-diphenyl-2-methyl-1,3-propanedione have been established. The synthesis and resolution of α-methyltropic acid are described.

We have recently been engaged in a mechanistic investigation of 1,2-carbonyl migrations. In an effort to establish the degree of concertedness of these interesting transformations, we have utilized optically active substrates of known absolute configuration and optical purity. The Lewis acid catalyzed rearrangement of a series of glycidic esters,[2a] epoxy ketones,[2b] and chlorohydrins[2c] has provided experimental evidence that 1,2-carbonyl migration is concerted and proceeds with inversion of configuration at the migration terminus without loss of optical activity (eq 1). These stereochemical studies have required us to determine the optical purity and absolute configuration of (-)-ethyl α-formyl-α-methylphenylacetate (1) and (-)-1,2-diphenyl-2-methyl-1,3-propanedione (2). In



(1)

1, Z = OC_2H_5
2, Z = C_6H_5

(1) National Science Foundation Predoctoral Fellow.

(2) (a) Domagala, J. M.; Bach, R. D.; Wemple, J. *J. Am. Chem. Soc.*, **1976**, *98*, 1975; (b) Domagala, J. M.; Bach, R. D. *ibid*, **1978**, *100*, 1605; (c) Domagala, J. M.; Bach, R. D. *ibid.* submitted for publication.

0022-3263/79/1944-2429$01.00/0

Table I. Optical Purity Determinations for Methyl α-Methyltropate (8), Methyl O-Methyl-α-methyltropate (9), and 1,2-Diphenyl-3-methoxy-2-methyl-1-propanone (10)

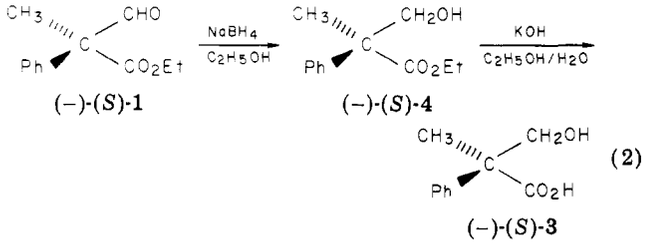
compd	proton type	chemical shifts, Hz (+)-(R)	chemical shifts, Hz (−)-(S)	optical purity, %	$[\alpha]^{25}_D$	$[\alpha]^{25}_D$ for 100% opt pur.[a]
8	OCH_3	330	337	racemic	0	
		332	339	53.4	33.11	62.00
		332	339	54.4	33.11	60.86
			329	100.0	−60.84	−60.84
9	CH_2OCH_3	284	263	racemic	0	
		286	265	52.2	16.79	32.16
		253	240	53.8	16.79	31.21
			286	100.0	−30.79	−30.79
10	OCH_3	374	339	racemic	0	
		369	338	52.8	62.96	119.2
			320	100.0	−122.0	−122.0
	$C-CH_3$	251	260	racemic	0	
			232	100.0	−122.0	−122.0

[a] Calculated by dividing the observed rotation by the optical purity.

the present report we relate the absolute configuration of both 1 and 2 to that of (−)-(S)-α-methyltropic acid (3) of known stereochemistry.[3]

Results and Discussion

The essence of our plan to elucidate the more subtle features of the mechanism of acyl rearrangement was to relate the absolute configurations of all of the rearrangement products (eq 1) to that of α-methyltropic acid. We were fortunate to be able to establish the stereochemistry of 1, which resulted from 1,2-carbethoxy migration,[2a] to α-methyltropic acid (3) by a direct two-step conversion (eq 2).

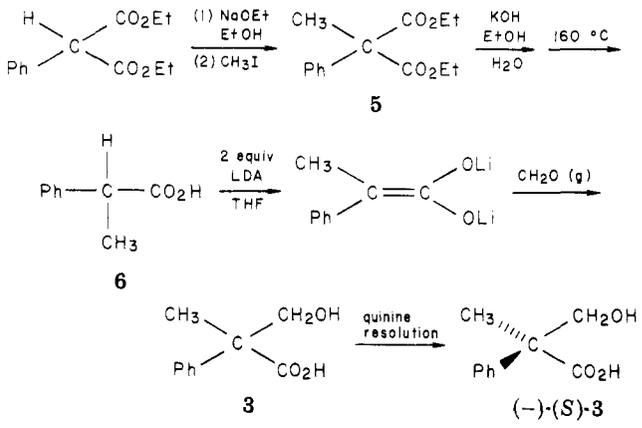


(−)-(S)-1 (−)-(S)-4 (−)-(S)-3 (2)

The aldehyde group in (−)-1 was reduced with sodium borohydride (73%) to (−)-ethyl α-methyltropate (4), $[\alpha]^{25}_D$ −25.7°, which upon saponification afforded (−)-(S)-α-methyltropic acid (3).[3] The acid 3 solidified on standing and had $[\alpha]^{25}_D$ −26.0° which establishes the asymmetric carbon in (−)-1 to have the S configuration. The optical purity of 1 was determined by NMR using the chiral chemical shift reagent EuOPT.[4] A chemical shift difference of 4 Hz was observed for the aldehyde resonances of the two enantiomers of racemic 1. A sample of 1 having $[\alpha]^{25}_D$ −109.2° (c 1.1 $CHCl_3$) showed only a single line of 667 Hz and was therefore optically pure.[5]

Our second objective was to determine the absolute configuration of the keto aldehyde 2 which is obtained upon rearrangement of dypnone oxide (Z = C_6H_5, eq 1). There was no apparent direct approach at our disposal that would allow us to relate the stereochemistry of 2 to α-methyltropic acid (3). We therefore devised an indirect scheme where 2 could be converted to a key intermediate that could subsequently be prepared from optically active 3. This approach appeared to be more practical than degradation of 2 to another compound of known stereochemistry despite the fact that this method required the resolution of 3. Since the reported procedure for the preparation of α-methyltropic acid could only be achieved in low yield, a new synthesis of 3 was developed (Scheme I).

Scheme I



2-Phenylpropionic acid (6) was obtained from diethyl phenylmalonate in high yield (82%) by the malonic ester synthesis. Conversion of 6 to α-methyltropic acid (3) was accomplished by formation of the dianion[6] of 6 with lithium diisopropylamide[7] in tetrahydrofuran and trapping with gaseous formaldehyde that was generated externally from paraformaldehyde at 180 °C.[8] Resolution of the acid 3 with quinine[3a] gave α-methyltropic acid, $[\alpha]^{25}_D$ −29.9° (EtOH). The acid was shown to be optically pure by NMR analysis of methyl esters 8 and 9 derived from 3. The (+)-(R) enantiomer of 3 was isolated from the combined mother liquors in 53% optical purity (Table I).

Inspection of the stereochemically related compounds in Scheme II reveals that the simplest way to interrelate the absolute configurations of 2 and 3 would be to use the β-hydroxy ketone 7 as the key intermediate. Both reduction of 2 and the treatment of α-methyltropic acid (3) with a phenyl anion equivalent converge to this same point.

(3) (a) Melone, G.; Vecchi, A.; Pagani, G.; Testa, E. *J. Org. Chem.* **1960**, *25*, 859; (b) Vecchi, A.; Malone, G. *ibid.* **1959**, *24*, 109; (c) Knabe, J.; Wolf, H.; Juninger, H.; Geismar, W. *Justus Liebigs Ann. Chem.* **1970**, *739*, 15.

(4) The shift reagent employed was "Eu-Opt"; Ventron: Beverly, Mass. See (a) Goering, H. L.; Eikenberry, J. N.; Koermer, G. S. *J. Am. Chem. Soc.* **1971**, *93*, 5913; (b) Whitesides, G. M.; Lewis, D. W.; *ibid*, **1970**, *92*, 6980; **1971**, *93*, 5914.

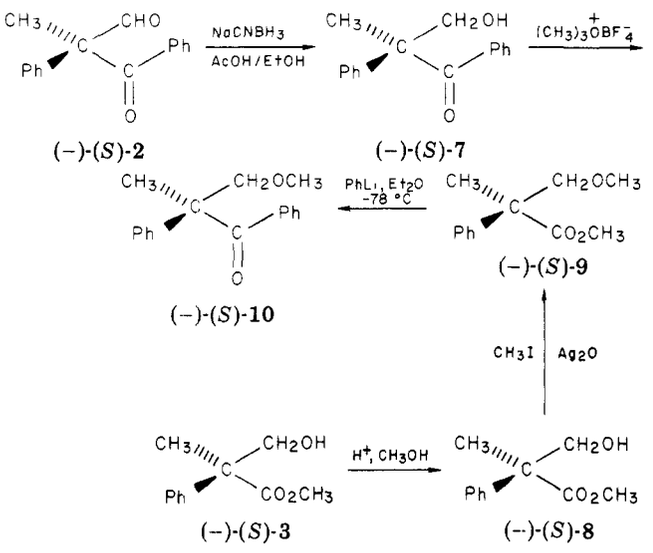
(5) The apparent detectability limit of the NMR spectrometer was 2–3%. The error in determining enantiomer areas was ±2%, which defines an error of ±4% in optical purity values.

(6) (a) Creger, P. L. *J. Am. Chem. Soc.* **1967**, *89*, 2500; (b) Creger, P. L. *ibid.* **1970**, *92*, 1397; (c) Pfeffer, P. E.; Kinsel, E.; Silbert, L. S.; *J. Org. Chem.* **1972**, *37*, 1256.

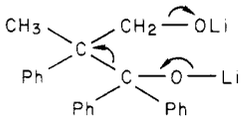
(7) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361.

(8) Gensler, W. J.; Manos, P. T.; Ruks, I. *J. Org. Chem.* **1968**, *33*, 3408.

Scheme II



However, attempts to prepare 7 directly from 3 and 3 equiv of phenyllithium were unsuccessful, although compounds with similar functional groups have been converted to ketones.[9] The main products from this reaction were benzophenone and α-methylstyrene which presumably arise from carbon–carbon bond fragmentation of the dilithium salt 11.[9] Retroaldol reactions, which involve the



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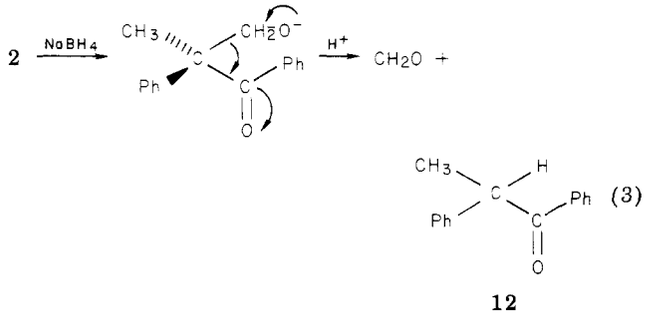
facile deformylation of 2[10a] and the related β-hydroxy ketones like 7,[10b] have also been reported. We therefore sought to find a suitable removable protecting group for the hydroxyl functional group in the keto ester 8 derived from α-methyltropic acid (3).

Using alcoholic solvents and a catalytic amount of sulfuric acid, the methyl and ethyl α-methyltropates 8 and 8a were prepared in quantitative yields. The corresponding *tert*-butyl[11] and trityl esters[12] of these esters could not be prepared in reasonable yield. We were able to prepare the *O*-tetrahydropyranyl[13] derivative of 8a, but it was found to be unstable to base.

Thwarted in our efforts to find a protecting group that could be easily removed, we prepared the methyl ether 10 from the acid 3 (Scheme II) and then converted the target molecule 2 to this same methyl ether via the alcohol 7. The methyl ether functionality was introduced by treatment of methyl α-methyltropate (8) with excess methyl iodide and silver oxide. The protected methyl ester 9 was converted to the desired phenyl ketone 10 (50%) by the action of phenyl lithium at −78 °C. Repeating the sequence with (−)-(*S*)-3, $[\alpha]^{25}_D$ −29.9°, afford (-)-(*S*)-10, $[\alpha]^{25}_D$ −122.0°, which was 100% optically pure (Table I).

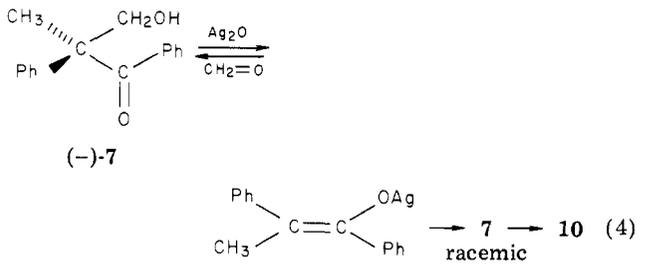
The absolute configurational assignment of 2 was completed by an independent synthesis of 10 from optically pure 2. Reduction of 2 with sodium cyanoborohydride gave the keto alcohol 7, $[\alpha]^{25}_D$ −223.5°. Methylation of 7 with trimethyloxonium tetrafluoroborate in refluxing CH_2Cl_2 gave optically pure 10, $[\alpha]^{25}_D$ −122.0°. These data provide conclusive evidence that the asymmetric center in (−)-2 has the *S* configuration.

Finally, we wish to comment further on the lack of stability toward base of several of the compounds encountered. For example, all efforts to reduce aldehyde 2 with $NaBH_4$ in dimethoxyethane or ethanol produced only α-methyldesoxybenzoin (12) by a retroaldol process (eq 3).



12

When we tried to methylate optically pure 7 with methyl iodide and silver oxide, essentially racemic methyl ether 10 (45%) was obtained. Furthermore, unreacted 7 which was recovered from the reaction mixture after short reaction times had been 99% racemized. That any 7 was reformed to be converted to 10 is indeed surprising, and we offer the reaction sequence given in eq 4 in explanation



of these observations. It should be recalled that methylation, as well as $NaBH_4$ reduction, worked quite well with ester 8 (Scheme II). The problem of racemization of 7 was circumvented by utilizing acidic reaction conditions to effect conversion of 7 to 10. In another surprising reaction, attempts to prepare keto ether 10 directly from *O*-methyl-α-methyltropic acid and phenyllithium again resulted in formation of benzophenone and α-methylstyrene. This process is analogous to the carbon–carbon bond cleavage in 11 and requires the formal elimination of methoxide ion.

In summary, we have provided a series of stereochemical interconversions that relates the absolute configuration of both (−)-(*S*)-1 and (−)-(*S*)-2 to that of (−)-(*S*)-α-methyltropic acid.

Experimental Section

General. Melting points were determined with a Hoover-Thomas Unimelt capillary melting point apparatus and were uncorrected. Infrared spectra were recorded on a Perkin-Elmer instrument Model 267 spectrophotometer. NMR spectral measurements were recorded on Varian Associates A-60 and T-60 models, and peak positions are reported in δ units from tetramethylsilane which was used as an internal standard. More precise NMR shifts were determined using tetramethylsilane as a standard and generating an external signal by a Hewlett Packard 200DB model wide range oscillator and counted on a Hewlett Packard 523B model electronic counter. Optical rotations were measured using a Perkin-Elmer Model 141 polarimeter. Column

(9) Jorgenson, M. J. *Org. React.* **1970**, *18*, 1.
(10) (a) House, H. O. *J. Am. Chem. Soc.* **1954**, *76*, 1235; (b) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: New York, 1972; p 636.
(11) Beyerman, H. C.; Bontekoe, J. S. *Recl. Trav. Chim. Pays-Bas* **1962**, *81*, 691.
(12) Rigby, A. T.; Kim, Y. H.; Crosscup, C. J.; Starkovsky, N. A. *J. Org. Chem.* **1972**, *37*, 956.
(13) Curphy, M. *Org. Synth.* **1971**, *51*, 142.

chromatography and TLC purifications utilize silica gel.

(−)-(*S*)-Ethyl α-Methyltropate (4). To 10 mL of absolute ethanol and 495 mg (1.31 mmol) of sodium borohydride (2.12 equiv of H^-) was added 512 mg (2.46 mmol) of ethyl α-formyl-α-methylphenylacetate (**1**). The mixture was stirred for 30 min, diluted with 5 mL of ethyl ether, and extracted with 5 mL of 10% hydrochloric acid. The aqueous layer was extracted twice with ether and the ethereal fractions were combined, dried ($MgSO_4$), and concentrated affording 478 mg of crude **4**, which was purified by preparative GLC (SE30, 200 °C) to give 278 mg (54%) of the alcohol **4**: NMR (CCl_4) δ 7.31 (s, 5 H, C_6H_5), 4.18 (q, 2 H, J = 7 Hz, OCH_2CH_3), 4.09 (d, 1 H, J = 11 Hz, CH_2OH), 3.50 (d, 1 H, J = 11 Hz, CH_2OH), 2.70 (bs, 1 H, −OH), 1.62 (s, 3 H, CH_3), 1.20 (t, 3 H, J = 7 Hz, OCH_2CH_3); IR (neat) 3480 (broad), 2980, 1725 cm^{-1}.

Following the above procedure, 100 mg (0.490 mmol) of (−)-(*S*)-**1**, $[\alpha]^{25}_D$ −190.2°, was treated with 115 mg (0.304 mmol) of sodium borohydride to give, after purification by GLC, 74 mg (73%) of (−)-(*S*)-**4**, $[\alpha]^{25}_D$ −25.7° (*c* 1.4, $HCCl_3$), whose spectral properties were identical with those of racemic material.

(−)-(*S*)-α-Methyltropic Acid (3). Using the procedure of Vecchi and Malone,[3b] 250 mg (1.20 mmol) of ethyl α-methyltropate (**4**), after treatment with 10% sodium hydroxide, gave 120 mg (55%) of the acid **3**: mp 87–90 °C; NMR (CCl_4) δ 7.53 (bs, 2 H, CO_2H, CH_2OH), 7.39 (s, 5 H, C_6H_5), 4.15 (d, 1 H, J = 11 Hz, CH_2OH), 3.67 (d, 1 H, J = 11 Hz, CH_2OH), 1.64 (s, 3 H, CH_3); IR (neat) 3500–2900, 1708 cm^{-1}. In some cases the acid **3** required purification by column chromatography, before crystallization would occur. Using the conditions above, 116 mg (0.558 mmol) of (−)-(*S*)-**4**, obtained without purification from (−)-(*S*)-aldehyde **1** ($[\alpha]^{25}_D$ −109.2°), was treated with 5 mL of 10% sodium hydroxide at 85 °C for 5 h and gave 49 mg (47%) of (−)-(*S*)-**3**: mp 87–88 °C; $[\alpha]^{25}_D$ −26.0° (*c* 1.6, ethanol) (lit.[3a] mp −27.5 °C). The spectral properties of (−)-(*S*)-**3** were identical with those of racemic material.

Synthesis of α-Methyltropic Acid (3). Diethyl Methylphenylmalonate (5). Sodium (2.44 g; 0.106 g-atom) was added to 150 mL of absolute ethanol while using carefully dried glassware and working under a constant positive pressure of argon. The sodium ethoxide solution was cooled to −10 °C, and 25.0 g (0.106 mol) of diethyl phenylmalonate in 40 mL of absolute ethanol was added over 45 min. The mixture was brought to room temperature, and 20.0 g (0.14 mol) of methyl iodide was added over 20 min with caution, as the reaction was exothermic. The mixture was stirred for 30 min and then quenched by the addition of 100 mL of ethyl ether and 100 mL of aqueous sodium chloride. The organic layer was extracted with aqueous sodium chloride, dried ($MgSO_4$), and concentrated to give 26.3 g (99%) of diethyl methylphenylmalonate (**5**) as a faint yellow oil: NMR (CCl_4) δ 7.50–7.16 (m, 5 H, C_6H_5), 4.13 (q, 4 H, J = 7 Hz, OCH_2CH_3), 182 s, 3 H, CH_3), 1.12 (t, 6 H, J = 7 Hz, OCH_2CH_3); IR (neat) 1740, 1250, 1150 cm^{-1}.

2-Phenylpropionic Acid (6). To a solution of 50 mL of water and 45.6 g of potassium hydroxide in 200 mL of ethanol was added 40.0 g (0.16 mol) of diethyl methylphenylmalonate. The mixture was refluxed for 3 h, and 200 mL of water was added. After the mixture was extracted with 100 mL of methylene chloride, the aqueous layer was acidified with hydrochloric acid to pH 2 and extracted with 100 mL of ether. The ethereal solution was dried ($MgSO_4$) and concentrated to give a yellow-white solid, which was heated, without further purification, to 158 °C. The solid liquified, with the liberation of carbon dioxide, to yield 19.4 g (83% based on **5**) of 2-phenylpropionic acid (**6**): NMR (CCl_4) δ 12.08 (s, 1 H, CO_2H), 7.30 (s, 5 H, C_6H_5), 3.65 (q, 1 H, J = 7 Hz, C–H), 1.45 (d, 3 H, J = 7 Hz, C–CH_3); IR (neat) 3100 (broad), 1710, 1235 cm^{-1}.

α-Methyltropic Acid (3). To 0.04 mol (2.0 equiv) of freshly prepared lithium diisopropylamide (from 5.6 mL of diisopropylamine and 19.2 mL of 2.15 M *n*-butyllithium/hexane) in 30 mL of dry tetrahydrofuran at −7 °C was added 3.0 g (0.02 mol) of 2-phenylpropionic acid (**6**) in 25 mL of dry tetrahydrofuran, and gaseous formaldehyde (from paraformaldehyde at 180 °C) was bubbled through the solution until the precipitate paraformaldehyde became a thick gel. The mixture was stirred for 30 min and then poured over ice containing 10% hydrochloric acid. The organic layer was diluted with 100 mL of ether and extracted with 50 mL of 6 M hydrochloric acid. The ethereal layer was dried ($MgSO_4$) and concentrated to a thick brown oil, which was dissolved in 50 mL of carbon tetrachloride to give 2.05 g (57%) of α-methyltropic acid (**3**) as a white powder, mp 88–90 °C (lit.[2b] mp 91–92 °C). Its spectral properties were identical with those of an authentic sample.

Resolution of α-Methyltropic Acid (3). Using a modification of the literature procedure,[2a] 5.00 g (28.0 mmol) of α-methyltropic acid (**3**) and 9.77 g (28.5 mmol) of quinine was added to 22.5 mL of absolute ethanol and 22.5 mL of distilled water. The mixture was heated until all the solids dissolved. Crystallization was very slow, but seeding or scratching induced too rapid a rate of crystal formation. After 18 h, the crystals were removed by filtration and dried at 50 °C (0.1 mm) to give 3.40 g (46%) of the quinine salt, mp 169–172 °C. Recrystallization of this salt from 40 mL of ethanol and water (50:50) gave, after drying, 2.21 g of quinine salt, mp 178–179 °C.

This entire sequence was repeated twice on a 10-g scale with identical results. The combined batches of quinine salt, 14.08 g, were recrystallized from 400 mL of ethyl acetate–ethanol (9:1). Filtration of the solids and drying for 10 h (0.1 mm) gave 9.3 g of quinine-α-methyltropic salt, mp 183–185 °C (lit.[2a] mp 185–186 °C). Free (−)-(*S*)-α-methyltropic acid was obtained according to the literature procedure.[2a] Thus, 9.26 g of quinine salt afforded 2.56 g (78%) of (−)-(*S*)-α-methyltropic acid, $[\alpha]^{25}_D$ −29.9° (*c* 1.1, absolute EtOH) (lit.[2a], $[\alpha]^{25}_D$ −28°).

In a similar fashion, the quinine salt from the combined first mother liquors gave, after removal of the quinine, 10.83 g (43%) of (+)-(*R*)-**3** $[\alpha]^{25}_D$ 6.14° (*c* 1.1, absolute ethanol).

(−)-(*S*)-Methyl α-Methyltropate (8). To 5.0 g (27.8 mmol) of α-methyltropic acid (**3**) in 100 mL of absolute methanol was added 10 drops of concentrated sulfuric acid. The mixture was refluxed for 28 h, and the methanol was removed under reduced pressure. The remaining oil was diluted with ether and washed with a saturated solution of sodium bicarbonate. The ether was dried ($MgSO_4$) and concentrated to give 5.27 g (98%) of methyl α-methyltropate (**8**): NMR (CCl_4) δ 7.16 (s, 5 H, C_6H_5), 4.00 (d, 1 H, J = 11 Hz, HOCHHR), 3.57 (m, 4 H, CO_2CH_3 and HOCHHR superimposed), 2.93 (s, 1 H, CH_2OH), 1.58 (s, 3 H, CCH_3); IR (neat) 3480, 3090, 3060, 3030, 1730, 1240 cm^{-1}. Using the above procedure 1.50 g (8.33 mmol) of (−)-(*S*)-**3**, $[\alpha]^{25}_D$ −29.8°, gave (−)-(*S*)-**8**, $[\alpha]^{25}_D$ −60.8° (*c* 1.7, $HCCl_3$). Purification by GLC (SE 30, 185 °C) did not alter the rotation.

Ethyl α-Methyltropate (8a). The ethyl ester of α-methyltropic acid was prepared by a method identical with that of the methyl ester. Thus 2.5 g (13.9 mmol) of α-methyltropic acid gave 2.8 g (100%) of ethyl α-methyltropate (**8a**). This material was identical with that prepared from the reduction of **1**.

(−)-(*S*)-Methyl *O*-Methyl-α-methyltropate (9). Using a published procedure,[14] 3.00 g (15.5 mmol) of methyl α-methyltropate (**8**) was added to 30 mL of methyl iodide and 6.0 g (26 mmol) of silver oxide, and the mixture was refluxed for 48 h. The silver salts were removed by filtration and washed with methylene chloride. The filtrate was concentrated and purified by column chromatography using hexane–ethyl acetate (24:1) to give 2.86 g (89%) of methyl *O*-methyl-α-methyltropate (**9**): NMR (CCl_4) δ 7.17 (s, 5 H, aromatic), 3.87 (d, 1 H, J = 8 Hz, CH_3OCHHR), 3.52 (m, 4 H, CO_2CH_3 and CH_3OCHHR superimposed), 3.24 (s, 3 H, OCH_3); IR (neat) 3090, 3060, 3030, 1735, 1240, 1110 cm^{-1}.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69. Found: C, 69.45; H, 7.65.

Using the procedure above, (−)-(*S*)-**8**, $[\alpha]^{25}_D$ −60.8°, was converted to (−)-(*S*)-**9** (65%), $[\alpha]^{25}_D$ −30.8° (*c* 1.4, $HCCl_3$), whose spectral properties were identical with those of racemic material.

***O*-Methyl-α-methyltropic Acid.** In 30 mL of 40% aqueous ethanol, 6 M in potassium hydroxide, was dissolved 1.0 g (4.5 mmol) of methyl *O*-methyl-α-methyltropate (**9**), and the mixture was refluxed for 3 h. The organic layer was diluted with 30 mL of ether and extracted with 75 mL of water. The water layer was acidified to pH 1 and extracted with ethyl ether. The ethereal solution was dried ($MgSO_4$) and concentrated to give 0.76 g (87%): mp 51.5–53.5 °C; NMR ($DCCl_3$) δ 12.15 (s, 1 H, CO_2H), 7.19 (m,

(14) (a) Ferguson, A. C.; Haines, A. H. *J. Chem. Soc. C* **1969**, 2372; (b) Jones, D. N.; Summers, G. H. R. *ibid.* **1959**, 2594.

5 H, C_6H_5), 3.87 (d, 1 H, J = 9 Hz, CH_3OCH_2), 3.48 (d, 1 H, J = 9 Hz, CH_3OCH_2), 3.23 (s, 3 H, OCH_3), 1.59 (s, 3 H, CCH_3); IR (neat) 3300, 2700, 1705, 1110 cm^{-1}.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 68.04; H, 7.22. Found: C, 67.98; H, 7.28.

(-)-(*S*)-1,2-Diphenyl-3-methoxy-2-methyl-1-propanone (10). To 500 mg (2.40 mmol) of methyl *O*-methyl-α-methyltropate (**9**) in 60-mL of dry ethyl ether at −78 °C was added over 2 h 1.34 mL (1.8 M, 1.0 equiv) of phenyl lithium. The mixture was then poured into a cold solution of ammonium chloride. The phases were separated, and the organic layer was dried ($MgSO_4$) and concentrated. Analysis by GLC showed the presence of 1,2-diphenyl-3-methoxy-2-methyl-1-propanone (51%).

(-)-(*S*)-**9** (680 mg; 3.3 mmol) $[\alpha]^{25}_D$ −30.8°, was converted to (-)-(*S*)-**10**, which was purified by preparative TLC to give 310 mg (37%) of (-)-(*S*)-**10**, $[\alpha]^{25}_D$ −122.0° (*c* 1.2, $HCCl_3$), by using the above procedure with slight modification. This material was identical with **10**, prepared from **7**.

(-)-(*S*)-1-Hydroxy-1,2-diphenyl-2-methyl-1-propanone (7). To 2.70 g (11.3 mmol) of the propanedione **2** in 100 mL of absolute ethanol and 14.5 mL of acetic acid was added 334 mg (1.4 equiv H^-) of sodium cyanoborohydride. The solution was stirred for 16 h. The mixture was then poured into cold 10% hydrochloric acid and stirred for 5 min. The acid solution was extracted twice, with 100 mL of ether, and the combined ethereal fractions were extracted with 50 mL of saturated sodium bicarbonate. The ethereal solution was dried ($MgSO_4$) and concentrated to give a thick yellow oil which was purified by chromatography on silica gel using benzene–hexane (4:1), then benzene–ethyl acetate (4.5:5), to give 1.84 g (68%) of 1-hydroxy-1,2-diphenyl-2-methyl-1-propanone (**7**): NMR (CCl_4) δ 7.28 (m, 10 H, aromatic), 4.13 (d, 1 H, J = 11 Hz, CH_2OH), 3.53 (d, 1 H, J = 11 Hz, CH_2OH), 2.83 (s, 1 H, CH_2OH), 1.78 (s, 3 H, $C-CH_3$); IR (neat 3480, 1670 cm^{-1}.

Alcohol **7** could also be purified by preparative TLC using benzene–hexane (4:1) and benzene–ethyl acetate (4.5:0.5).

Using the above procedure, 295 mg (1.24 mmol) of (-)-(*S*)-**2**, $[\alpha]^{25}_D$ −387.3° (*c* 1.08, $HCCl_3$), gave 145 mg (49%) of (-)-(*S*)-**7**, $[\alpha]^{25}_D$ −223.5° (*c* 0.96, $HCCl_3$).

In ethanol, sodium borohydride and **2** gave only a α-methyldesoxybenzoin (**12**, 74%).

Preparation of (-)-(*S*)-1,2-Diphenyl-3-methoxy-2-methyl-1-propanone (10) from 7. A. To 160 mg (0.666 mmol) of 1-hydroxy-1,2-diphenyl-2-methyl-1-propanone (**7**) in 30 mL of methylene chloride was added 248 mg (2.5 eq) of trimethyloxonium tetrafluoroborate.[13] The reaction mixture was refluxed for 16 h followed by the addition of water. The phases were separated, and the organic layer was dried ($MgSO_4$) and concentrated. Analysis by TLC using benzene–hexane (4:1) revealed only two spots with R_f values identical with those of **7** and **10** prepared by an alternate pathway. Purification by preparative TLC using benzene–hexane (4:1) gave 50 mg (31%) of 1,2-diphenyl-3-methoxy-2-methyl-1-propanone (**10**): NMR (CCl_4) δ 7.2 (s, 10 H, aromatic), 3.9 (d, 1 H, J = 9 Hz, CH_2-OCH_3), 3.6 (d, 1 H, J = 9 Hz, CH_2OCH_3), 3.2 (s, 3 H, OCH_3), 1.6 (s, 3 H, CCH_3); IR (neat) 3060, 3020, 1680, 1110 cm^{-1}.

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.32; H, 7.09. Found: C, 80.55; H, 7.00.

(-)-(*S*) alcohol **7**, $[\alpha]^{25}_D$ −223.5° (*c* 0.96, $HCCl_3$) (129 mg; 0.538 mmol), was converted to 60 mg (44%) of (-)-(*S*)-**10**, $[\alpha]^{25}_D$ −122.0° (*c* 1.1, $HCCl_3$), whose spectral properties were identical with those of authentic racemic material, by using the above procedure.

B. To 65 mg (0.27 mmol) of (-)-(*S*)-**7** (53% optically pure) in 3 mL of methyl iodide was added 130 mg of silver oxide. The mixture was gently refluxed for 72 h and then filtered. The filtrate was diluted with methylene chloride and extracted with water. The methylene chloride was dried ($MgSO_4$) and concentrated to give, after purification by preparative TLC, 31 mg (45%) of (-)-(*S*)-**10**, $[\alpha]^{25}_D$ −6.88° (*c* 1.1, $HCCl_3$). Recovered (-)-(*S*)-**7** was 1.1% optically pure, $[\alpha]^{25}_D$ −2.52° (*c* 0.6, $HCCl_3$).

Determination of Optical Purity. All samples whose optical purities were to be determined were weighed directly into the NMR tubes. Typical sample sizes were 30–60 mg. For all determinations, carbon tetrachloride or deuterated chloroform (ca. 0.5 mL, 4% Me_4Si) was used. After preliminary analysis, the europium shift reagent $Eu(C_{11}H_{19}O_2)_3$ was added directly, and the tube was shaken until all solids were dissolved. The spectra were examined for the extent of chemical shift and diastereomeric separation, and then the diastereomeric signals were integrated five times. The chemical shifts were obtained relative to Me_4Si using a side banding technique. From the results of multiple analyses of the same sample, it was found that the relative error in determining optical purities by this method was ±4%.

Acknowledgments. Support of this work by the National Science Foundation (CHE 76 21992) is gratefully acknowledged. R.D.B. would like to thank Professor Roald Hoffmann for his generous hospitality during his sabbatical leave at Cornell where the manuscript was written.

Registry No. (±)-**1**, 70397-71-6; (*S*)-**1**, 59472-41-2; (±)-**2**, 70397-72-7; (*S*)-**2**, 66364-98-5; (±)-**3**, 31917-13-2; (*S*)-**3**, 59492-59-0; (*S*)-**3** quinine salt, 70343-17-8; (*R*)-**3**, 28968-34-5; (*R*)-**3** quinine salt, 70343-22-5; (±)-**4**, 70397-73-8; (*S*)-**4**, 59472-42-3; **5**, 34009-61-5; (±)-**6**, 2328-24-7; (±)-**7**, 70398-00-4; (*S*)-**7**, 66365-01-3; (±)-**8**, 70397-74-9; (*R*)-**8**, 70343-18-9; (*S*)-**8**, 66365-02-4; (±)-**9**, 70397-75-0; (*R*)-**9**, 70343-19-0; (*S*)-**9**, 66365-03-5; (±)-**10**, 70397-99-8; (*R*)-**10**, 70343-20-3; (*S*)-**10**, 66365-04-6; (±)-**12**, 67737-73-9; diethyl phenylmalonate, 83-13-6; methyl iodide, 74-88-4; (±)-*O*-methyl-α-methyltropic acid, 70343-21-4.

Syntheses of Novel Gyrochiral Pentacyclic Systems with C_2 Symmetry. (-)-C_2-Bismethanotwistane and (±)-C_2-Methanoditwistane

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Received October 11, 1978

Diazomethane ring expansion of C_2-bismethanotwistane-8,12-dione (**18**) obtained from the cyclohexadiene–benzoquinone adduct **10** was explored to secure the synthetic route to a novel gyrochiral pentacyclic system, D_3-tritwistane (**7**). Whereas D_3-trishomocubanedione (**22**) was found to afford the single **23** and the double **24** ring expansion products, **18** failed to yield the expected doubly expanded product with a D_3-tritwistane system. Preparation of the new gyrochiral pentacyclic hydrocarbons (-)-C_2-bismethanotwistane (**5**) and (±)-C_2-methanoditwistane (**6**) are reported.

Among groups of rigid pentacyclic hydrocarbons (**1**) which can be conceptually constructed by simultaneous diagonal bridging between the 2,5, 3,7, and 6,8 carbon atoms of twisted D_3-bicyclo[2.2.2]octane, cubane (**2**) (*k* =

0022-3263/79/1944-2433$01.00/0