The Absolute Configuration of *trans*-2-Methylcyclopropanecarboxylic Acid[1]

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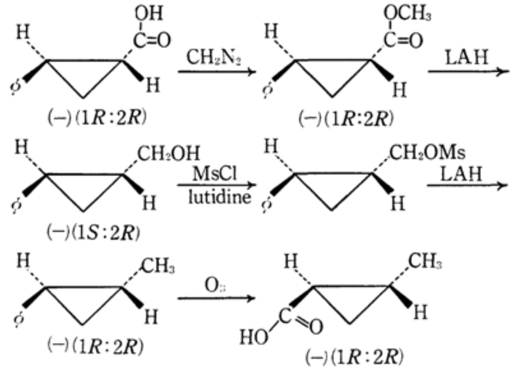
In the course of our studies of asymmetric syntheses in Simmons-Smith reactions, it was necessary to establish the absolute configuration of *trans*-2-methylcyclopropanecarboxylic acid.[2] We wish, at this time, to report the absolute assignment of the configuration of this acid by means of a direct chemical transformation. In a previous paper[3], the absolute configurations of (−)-*trans*-1, 2-cyclopropanedicarboxylic acid and (+)-*trans*-2-phenylcyclopropanecarboxylic acid were established as $1R:2R$ and $1S:2S$ respectively by an unequivocal correlation with *trans*-1, 2-dimethylcyclopropane of a known configuration. This provides us with the mean of correlating *trans*-2-methylcyclopropanecarboxylic acid with *trans*-2-phenylcyclopropanecarboxylic acid.

Methyl *trans*-2-phenylcyclopropanecarboxylate, $[\alpha]_D^{12}$ −171.9°, of a 51.3% optical purity, which had resulted from the quantitative esterification with diazomethane of the corresponding (−)-acid, was reduced with lithium aluminum hydride to the carbinol, $[\alpha]_D^{12}$ −46.6°. The carbinol was then converted with methanesulfonyl chloride in lutidine into the mesylate; then due to the instability of the mesylate, it was immediately reduced with lithium aluminum hydride to 1-methyl-2-phenylcyclopropane, $[\alpha]_D^{16}$ −57.7°. The ozonolysis of the laevorotatory hydrocarbon produced (−)-*trans*-2-methylcyclopropanecarboxylic acid, $[\alpha]_D^{19}$ −42.9° (chloroform), $[\alpha]_D^{19}$ −39.7° (ethanol). On the basis of this chemical conversion, (−)-*trans*-2-methylcyclopropanecarboxylic acid can be assigned the $1R:2R$ absolute configuration.



The predictions of the direction and the magnitude of rotation by the Brewster calculation of conformational asymmetry[4] show a good agreement with the observed values of (−)-($1R:2R$)-1-methyl-2-phenylcyclopropane, $[M]_D$ −148.7° (Found; chloroform), $[M]_D$ −140° (Calcd.) and (−)-($1R:2R$) - 2 - methylcyclopropanecarboxylic acid, $[M]_D$ −83.7° (Found; chloroform), $[M]_D$ −90° (Calcd.).

Experimental

Methyl (—)-*trans*-2-Phenylcyclopropanecarboxylate.—(−)-*trans*-2-Phenylcyclopropanecarboxylic acid ($[\alpha]_D^{22}$ −200.8° (c=3.168, 1 dm., ethanol); optical purity 64.4% based on $[\alpha]_D$ 311.7°[3]; 6.8 g.) was esterified by the standard method with diazomethane to give the methyl ester, b. p. 128—131°C/10 mmHg; n_D^{20} 1.5292; $[\alpha]_D^{12}$ −215.7° (c3.786, 1 dm., ethanol). Yield, 7.1 g. (95%).

(—) - *trans* - 1-Hydroxymethyl-2-phenylcyclopropane.—Methyl (—)-*trans*-2-phenylcyclopropanecarboxylate, $[\alpha]_D^{12}$ −171.9°; of a 51.3% optical purity, 12.4 g.; 0.07 mol., was stirred drop by drop into a slurry of lithium aluminum hydride (1.9 g.; 0.05 mol.) in 200 ml. of dry ether at room temperature. After the addition had been completed, the reaction mixture was gently refluxed by stirring it for 30 min. To the reaction mixture chilled in ice water, there was then added enough dilute hydrochloric acid (*ca.* 30 ml. of concentrated hydrochloric acid in 200 ml. of ice water) to effect a clear solution. The acidic solution was extracted with ether, and the ethereal extract was washed with aqueous sodium bicarbonate and sodium chloride solutions and dried over sodium sulfate. After ether had been removed, the residue was distilled under reduced pressure to give the carbinol, b. p. 133—135°C/10 mmHg; n_D^{21} 1.5502;

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[2] Asymmetric syntheses of this acid have been achieved by Simmons-Smith reactions in our laboratory and will be described in detail later elsewhere.

[3] Y. Inouye, T. Sugita and H. M. Walborskv, *Tetrahedron*, **20**, 1695 (1964).

[4] J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5483 (1959).

$[\alpha]_D^{12}$ −46.6° (c=2.640, 1 dm., ethanol). Yield, 10.4 g. (quantitative).

***trans*-1-Mesyloxymethyl-2-phenylcyclopropane.**—Into a solution of the (−)-carbinol (10.4 g.; 0.07 mol.) in 40 g. of dry lutidine (freshly distilled over barium oxide) methanesulfonyl chloride (10 g.; 0.096 mol.) was effectively stirred under a nitrogen atmosphere so as to maintain the reaction temperature at −10—0°C. After the addition had been completed, stirring was continued for an additional 3 hr. under cooling. The pasty product was then poured onto a mixture of concentrated hydrochloric acid (35 ml.) and crushed ice. The oily product which separated was collected with ether and dried over anhydrous magnesium sulfate. The ether was removed in vacuo and an oily product was obtained which solidified on dry-ice cooling. Because of the instability, no further purification of the crude mesylate (16.8 g.; 106%) was attempted. The infrared spectrum of the crude mesylate indicated SO_3-bands at 1172 and 1350 cm^{-1}, while the OH-band originally present in the carbinol had disappeared.

(−)-*trans*-1-Methyl-2-phenylcyclopropane.—The mesylate (16.8 g.) in 100 ml. of dry ether was stirred into a slurry of lithium aluminum hydride (7.6 g.; 0.2 mol.) in dry ether (500 ml.) at room temperature. The reaction mixture was then gently refluxed for an additional 3 hr. After ice water containing 70 ml. of concentrated hydrochloric acid had been added to the chilled reaction mixture, the ethereal solution was separated and the aqueous layer was extracted with ether. The combined extract was washed with an aqueous sodium bicarbonate solution and dried over sodium sulfate. Upon distillation, a crude hydrocarbon was obtained, b. p. 184—192°C; (6.7 g.) Since this product was colored a dark wine-red, it was percolated through an alumina column using petroleum ether as the eluent. The colorless effluent was redistilled under reduced pressure to give the (−)-hydrocarbon, b. p. 77—78°C/18 mmHg; n_D^{20} 1.5181; $[\alpha]_D^{13}$ −49.2° (c 3.432, 1 dm., ethanol); $[\alpha]_D^{13}$ −52.8° (c 1.60, 1 dm., chloroform). Yield, 6.69 g. (72% based on the carbinol). Since the v. p. c. analysis of the product indicated contamination by a by-product, the product was fractionated by means of preparative v. p. c. to give pure (−)-*trans*-1-methyl-2-phenylcyclopropane, b. p. 74—76°C/18 mmHg; n_D^{21} 1.5185; $[\alpha]_D^{16}$ −57.7° (c 3.676, 1 dm., chloroform) (lit.⁵⁾ b. p. 78—79°C/20 mmHg; n_D^{25} 1.5204 for a racemic sample). Yield, 3.2 g. The infrared spectrum of the contaminant fraction showed a nonconjugated C=C band at 1641 cm^{-1} and CH_2=CH– bands at 911, 995 and 1414 cm^{-1}; these bands suggested 3-phenylbutene-1 and/or 4-phenylbutene-1, but no further investigation was attempted.

(−)-*trans*-2-Methylcyclopropanecarboxylic Acid.—A stream of crude ozone was passed through a solution of the (−)-hydrocarbon (2.8 g.; 0.021 mol.) in carbon tetrachloride (70 ml.) at 40°C for 29 hr. After the reaction mixture had been allowed to stand still overnight at room temperature with 30 ml. of 10% hydrogen peroxide, another 10 ml. of 30% hydrogen peroxide was added and the mixture was gently refluxed for 1 hr. The acid was taken up a dilute sodium hydroxide solution and the alkaline solution, free from neutral substances, was acidified with dilute hydrochloric acid and distilled in steam. The distillate was thoroughly extracted with ether and dried over sodium sulfate. The distillation of the extract under reduced pressure gives (−)-*trans*-2-methylcyclopropanecarboxylic acid, b. p. 97—100°C/18 mmHg; n_D^{20} 1.4331; $[\alpha]_D^{19}$ −42.9° (c 3.625, 2 dm., chloroform); $[\alpha]_D^{19}$ −39.4° (c 3.060, 2 dm., ethanol); (lit.⁶⁾ b. p. 96.0—97.0°C/16 mmHg; n_D^{25} 1.4348 for a racemic sample). Yield, 1.0 g. (47%). The infrared spectrum was identical in every respect with that of an authentic specimen.⁶⁾ *p*-Phenylphenacylester, m. p. 105—106°C, laths (from methanol) $[\alpha]_D^{14}$ −33.4° (c 1.065, 2 dm., chloroform).

Found: C, 77.25; H, 6.22, Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16%.

(±)-*trans*-2-Methylcyclopropanecarboxylic acid prepared from (±)-*trans*-2-phenylcyclopropanecarboxylic acid by the same route as above had a b. p. of 96—102°C/18 mmHg, n_D^{21} 1.4350, and was identified by means of its infrared spectrum as well as by its amide, m. p. 108—108.5°C, needles (from chloroform and petroleum ether) (lit.⁶⁾ m. p. 111.3—112.0°C).

Found: C, 60.35; H, 9.26. Calcd. for C_5H_9ON: C, 60.59; H, 9.15%.

Since the starting material used in the correlation work was of a 51.3% optical purity, the maximum rotations of (−)-*trans*-2-methylcyclopropanecarboxylic acid and (−)-*trans*-1-methyl-2-phenylcyclopropane should be $[\alpha]_D$ −83.6° and $[\alpha]_D$ −112.5° respectively in chloroform.

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5) H. D. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959).

6) D. E. Applequist and A. H. Peterson, ibid., **82**, 2372 (1960).