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THE DIRECT SYNTHESIS OF OPTICALLY ACTIVE trans-CYCLOOCTENE.
OPTICALLY ACTIVE trans-BICYCLO[6.1.0]NONANE

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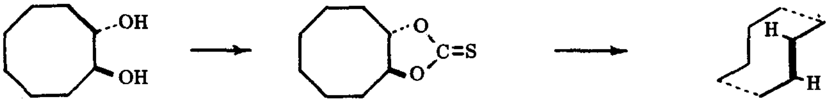
The prediction (1) that medium-sized trans-cyclic olefins should possess molecular dissymmetry was substantiated by Cope and coworkers (2), who resolved trans-cyclooctene via an optically active platinum(II) complex. However, attempts at the direct synthesis of optically active trans-cyclooctene have thus far met with little success (3,4). We report here an efficient, direct synthesis of optically pure trans-cyclooctene which is based on the previously reported (5a) stereospecific conversion of the racemic thionocarbonate (2) to racemic trans-cyclooctene.



1 (+)-antipode

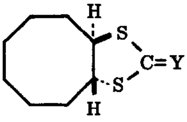
2 (+)-antipode

3 (-)-antipode

Optically active (+)-trans-1,2-cyclooctanediol (1) has been obtained as follows (6). Treatment of a solution of racemic 1 in dry tetrahydrofuran with a slight molar excess of n-butyllithium followed by one equivalent of phthalic anhydride afforded, after recrystallization, the monophthalate half-ester 4, m.p. 167.5-168.5°, in 50-60% yield (7). The strychnine salt of 4 was prepared, then recrystallized by dissolving it in hot chloroform, adding petroleum ether to the cloud point, and cooling to -15°. A second recrystallization from trichloroethylene afforded the salt with rotation $[\alpha]^{21}_{578}$ -29.6° (c 1.826, 95% ethanol), not increased by three additional crystallizations (68% yield). Treatment of the strychnine salt of 4 with aqueous sodium carbonate followed by extraction of the alkaloid, acidification of the basic solution, and filtration and recrystallization of the solid gave (+)-4 in 81% yield, $[\alpha]^{23}_{578}$ +6.2° (c 2.55, 95% ethanol), and m.p. 140.0-140.5°. Saponification of (+)-4 with aqueous potassium hydroxide afforded (+)-1 in 73% yield after distillation (b.p. 88°/0.15 mm). The diol had $[\alpha]^{22}_{578}$ +17.6°, $[\alpha]^{22}_{D}$ +16.9° (c 1.33, absolute ethanol) (6).
The infrared and n.m.r. spectra and refractive index (n^{21}_{D} 1.4990) of (+)-1 were identical to those of racemic 1.

Reaction of the optically active (+)-diol with N,N'-thiocarbonyldiimidazole (5) gave the thionocarbonate (+)-2, m.p. 141.4-142.2°, $[\alpha]_D^{21}$ +17.2° (c 2.27, chloroform), the infrared and n.m.r. spectra of which were identical to those of racemic 2. Treatment of (+)-2 with triisooctyl phosphite at 130° for 17 hr., using a rapid stream of nitrogen through the reaction mixture to remove the olefin as it was formed (5), afforded (-)-trans-cyclooctene in 84% yield and >99% isomeric purity (by v.p.c.). The (-)-3 so obtained had $[\alpha]_D^{21}$ -423° (c 0.650, methylene chloride), identical to the value obtained by Cope (2).

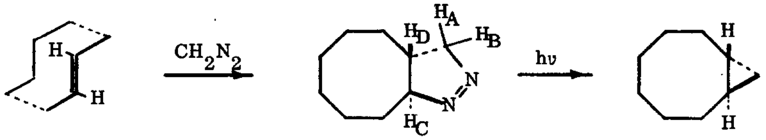
The stereospecific synthesis of trans-cyclooctene via the trithiocarbonate 5b has also been reported (5a). In this route, cis-cyclooctene is converted stereospecifically to trans-1,2-dithiocyanocyclooctane by reaction with thiocyanogen, and thence to the imino dithiocarbonate 5a by refluxing with 48% hydrobromic acid. Treatment of the imino compound with hydrogen sulfide-ethanol affords 5b. We have repeated this synthesis, with the added resolution of 5a, via the salt with (-)-1-phenylethanesulfonic acid (8, 9), which could be brought to constant rotation $[\alpha]_{578}^{26}$ +180.2° after 13 recrystallizations from 2-butanone. After regeneration of (+)-5a, $[\alpha]_{578}^{25}$ +173.6° (c 1.00, absolute ethanol), and conversion to (-)-5b, elimination to trans-cyclooctene was effected in 68% yield by treatment with 1,3-dibenzyl-2-methyl-1,3,2-diazaphospholidine (10) in dry tetraglyme at 30°, removing the olefin under vacuum as it was formed. The (+)-3 so generated was 99% isomerically pure and 96% optically pure. Thus, the formation of optically active trans-cyclooctene via the trithiocarbonate is an alternative to the thionocarbonate route, although the latter is more amenable to a preparative scale synthesis because of the ease with which the precursor is resolved.



5a (+)-antipode, Y = NH

5b (-)-antipode, Y = S

An interesting reaction of trans-cyclooctene, attributable to the reactivity of the strained trans double bond, is the 1,3-dipolar addition of diazomethane to give the 1-pyrazoline 6 (11). The photolytic decomposition of 6 to give trans-bicyclo[6.1.0]nonane (7) (11) suggests a synthesis of this bicyclic structure in optically active form. Toward this end, (-)-3 was treated with an excess of diazomethane; removal of volatile materials and two short-path distillations afforded (-)-6 as a clear, colorless oil (7), n_D^{24} 1.4970,



(-)-3 6 7

$[\alpha]_D^{25}$ -169.5° (c 1.15, carbon tetrachloride). Infrared absorption at 6.50 μ (N=N) and ultraviolet maximum (n-hexane) at 328 mμ (ε = 470) were in accord with the assignment of 6 as a 1-pyrazoline. The n.m.r. spectrum showed a broad band peaking at 1.64 δ (δ = ppm. downfield from tetramethylsilane), 12 H; a broad peak at 2.8 δ (1 H, H_D); a broad peak at 4.0 δ (1 H, H_C); and two groups of ABX quartets, split further into doublets, centered at 4.98 and 3.70 δ (1 H each, H_A and H_B). Coupling constants (in cps.): J_{AB} = 17.0; J_{AC} = 2.4; J_{AD} = 9.0; J_{BC} = 3.2; J_{BD} = 9.5.

Photolysis of an n-hexane solution of (-)-6 in a Pyrex apparatus gave a good yield of (+)-7, contaminated only with 4% (by v.p.c.) of its cis-fused isomer (12). The optically active trans-bicyclo[6.1.0]nonane, n_D^{21} 1.4653, had $[\alpha]_D^{24}$ +25.3° (c 1.10, carbon tetrachloride); its infrared spectrum had bands at 3.29, 3.35, and 9.81 μ (cyclopropane), while the n.m.r. showed two broad bands peaking at 0.20 (6 H) and 1.92 δ (10 H), with no vinyl protons. It seems probable that the optical purity of (+)-7 corresponds to the olefin precursor and is, therefore, high.

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