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A SYNTHESIS OF OPTICALLY ACTIVE 1,3-DI-t-BUTYLALLENE FROM PROPARGYLIC DERIVATIVES BY HYDRIDE DISPLACEMENT

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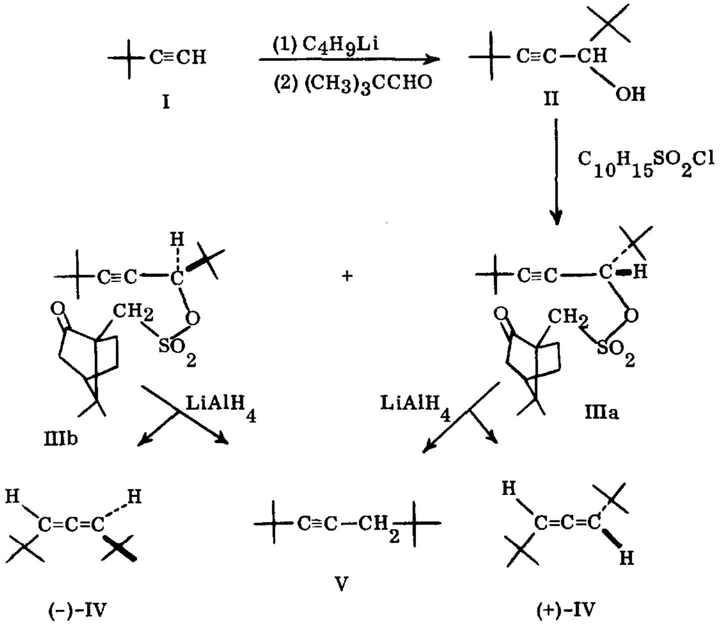
The recent publication of a method for the synthesis of disubstituted optically active allenes (1) prompts us to report our work on the preparation of optically active 1,3-di-t-butylallene. The route employed is shown below.



From pinacolone, t-butylacetylene (I) was prepared by the method of Ivitzky (2) and treated with n-butyllithium in tetrahydrofuran under nitrogen to produce the lithium acetylide. Addition of pivaldehyde, followed by aqueous workup, gave 1,3-di-t-butylpropargyl alcohol (II)* in 90% yield. Esterification of the

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*Each new compound exhibited nmr and infrared spectra consistent with the assigned structure and gave elemental analyses within 0.3% of theory.

alcohol in benzene with d-camphor-10-sulfonyl chloride in the presence of triethylamine led to the corresponding sulfonate ester III in 90% yield. Five recrystallizations from benzene--pentane accomplished separation of the two diastereomers. That the resolution was complete could be determined from the nmr spectra of the diastereomers, which are nearly identical except in the 3.5 δ region where an AB quartet appears. This signal is attributed to the two protons on C_{10} in the camphor moiety. The coupling constant is J = 15 c.p.s. in both diastereomers, but the chemical shift between the protons differs, being 0.43 p.p.m. in diastereomer IIIa, which has $[\alpha]_{578}^{22°} = -27.8°$, and 0.80 p.p.m. in IIIb, which has $[\alpha]_{578}^{22°} = +91.5°$ (c. 1.00, $CHCl_3$).

The diastereomers undergo reduction with lithium aluminum hydride (LAH) in refluxing tetrahydrofuran (THF) to yield a mixture of 1,3-di-t-butylallene (IV) and the isomeric acetylene (V), which can be most conveniently separated by preparative v.p.c. on a 20% fluorosilicone (FSI 1265) column. The proportion of the two reduction products and the magnitude of the rotation of the former differ for the diastereomers IIIa and IIIb. When IIIa was reduced with two moles of LAH in refluxing THF for 18 hr., allene IV and acetylene V were produced in a ratio of 5 : 4. The former had $[\alpha]_{578}^{22°} = +34.6°$ (c. 1.60, benzene). Under the same conditions IIIb gave allene and acetylene in a ratio of 2 : 3, and the rotation of the allene was $[\alpha]_{578}^{22°} = -39.8°$ (c. 1.07, benzene). The yields of the products collected by v.p.c., their ratio, and the rotation of the allene were unchanged when the reaction time was extended by a factor of 2.5.

That these reactions do not proceed by dissociation of the ester into an ion pair which is trapped by hydride is indicated by the reaction of III with three moles of $LiAl[OC(CH_3)_3]_3H$ at reflux in THF for 18 hr., after which the only change is reduction of the carbonyl group in the camphor moiety; no cleavage of the sulfonate group occurs. The inability of this reagent to displace the sulfonate leaving group suggests a second order process in which the acetylene is produced by S_N2 and the allene by S_N2' attack on the sulfonate III (3).

In order to determine the effect of a sulfonate ester leaving group of quite different steric requirements on the product ratio and rotation, the tosylate of fully resolved II was prepared. Optically pure alcohol was obtained from the racemate in 80% yield by three recrystallizations of the brucine salt of the corresponding phthalate half ester (to constant rotation) and subsequent hydrolysis of the half ester half acid by stirring for 48 hr. in aqueous potassium hydroxide. The fully resolved crystalline alcohol from the less soluble diastereomer had $[\alpha]_{578}^{22°} = +4.8°$ (c. 1.00, chloroform) and m.p. 58.8-60.3°. Further evidence of its optical purity came from its conversion in 93% yield to the tosylate, whose rotation $[\alpha]_{578}^{22°} = +64.0°$ (c. 1.00, $CHCl_3$) was unchanged after recrystallization to m.p. 87.5-88.0°.

The results obtained with several different hydride reagents that were used to effect displacement on the tosylate are summarized in the Table. That the allene and acetylene are again produced, respectively, by S_N2' and S_N2 attack of hydride is indicated by the observation that when 2.0 and 4.0 mole equivalents of LAH are used and the reaction interrupted before completion, twice as much product is formed in the reaction with twice as much hydride.

The (+)-II from which the tosylate was synthesized was also converted to the camphor-10-sulfonate

TABLE

NATURE OF PRODUCTS FROM REACTION OF 1,3-DI-t-BUTYLPROPARGYL TOSYLATE WITH VARIOUS HYDRIDE DONORS

Hydride Donor	Ratio Allene IV to Acetylene V	Rotation of Allene IV $[\alpha]_{578}^{22°}$ (benzene)
1.1 mole LAH	1 : 3	-17.0°
3.3 mole AlH_3	1 : 4	-26°
2.2 mole $LiAl(OCH_3)H_3$	1 : 1	-63.5°
2.2 mole $LiAl(OCH_3)_2H_2$	2 : 1	-72.8°

ester, which was shown to be IIIb. Thus, the two sulfonate esters of the same absolute configuration at the asymmetric propargylic carbon atom give, stereoselectively, the same allene enantiomer.

Whether the stereoselectivity favors hydride attack cis or trans to the departing sulfonate anion was ascertained by establishment of the absolute configuration of the propargylic alcohol II and the allene IV. The application of Lowe's highly successful extension of Brewster's rules (4, 5) to (-)-IV assigns it the R configuration, as drawn. Further application of Brewster's rules (5) to the alcohol (+)-II gives the absolute configuration at the asymmetric carbon atom as S, an assignment which was corroborated by the method of Mislow (6). Therefore, since (+)-II leads to the camphor-10-sulfonate ester IIIb, the absolute configuration of this diastereomer is correctly represented in the Figure. Thus, one concludes that in the production of the allene IV from either of the sulfonate esters derived from II, departure of the leaving group trans to the attacking hydride is favored (7).

Optically active allene IV could be obtained as the sole product of reaction in refluxing THF of the resolved alcohol II with LAH in the presence of $AlCl_3$. In this case the sign of rotation of the allene produced depends on the amount of $AlCl_3$ added. From reaction of fully resolved (+)-II with 2 moles of LAH in the presence of 0.15, 0.33, and 0.66 moles of $AlCl_3$, allene IV of rotation $[\alpha]_{578}^{22°}$ (benzene) -32.9°, +5.4°, and +26.4° was obtained. Preliminary experiments on the mechanism of this reaction suggest that the allene is formed, at least in part, from decomposition of an organoaluminum intermediate (8).

Further work on the mechanism and synthetic utility of these reactions is in progress.

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(7) G. Stork and W. N. White, *ibid.*, **78**, 4609 (1956), have found, in contrast, that in a cyclic system with very different nucleophiles and leaving group the S_N2' reaction proceeds in a predominantly *trans* fashion. We are undertaking experiments to determine the stereochemical preference of this reaction in an acyclic system with the same nucleophiles and leaving group as used by these authors.

(8) For the effect of trace amounts of $AlCl_3$ on the LAH reduction of another propargylic system, see E. J. Corey, J. A. Katzenellenbogen, and G. H. Posner, *ibid.*, **89**, 4245 (1967). Some mechanistic work on the reaction with LAH of a 3-phenylallylic alcohol has already been reported, W. T. Borden, *ibid.*, **90**, 2197 (1968).