a or b should be favored. Since UV absorption spectra of these ethers well coincide with those of corresponding alcohols, a direct through-space interaction between two phenyl groups in ether presumably does not operate. On the basis of the information presently available a possible explanation for *dl* preference is that a conjugative destabilization which has been suggested by Bingham favors conformation a or b.

Experimental Section

Preparation of Ethers. Bis(ethylphenylcarbinyl) ether was obtained as follows. A mixture of water, concentrated sulfuric acid, and ethylphenylcarbinol (obtained by the reaction of benzaldehyde with ethylmagnesium iodide[19]) in the ratio of 2:3:15 by volume was stirred for 2 h at room temperature and was washed with water several times and then distilled under reduced pressure. Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.71. Found: C, 85.22; H, 8.36.

The preparation procedure for bis(*n*-butylphenylcarbinyl) ether was similar to that for Ia using *n*-butylmagnesium chloride instead of ethylmagnesium iodide.[20] Anal. Calcd for $C_{22}H_{30}O$: C, 85.11; H, 9.76. Found: C, 85.24; H, 9.66.

Bis(cyclohexylphenylcarbinyl) ether was obtained as follows. A mixture of water, concentrated sulfuric acid, and cyclohexylphenylcarbinol (obtained by the reaction of benzaldehyde with cyclohexylmagnesium chloride) in the ratio 2:3:15 by volume was stirred for 30 min at 40 °C and was dissolved in diethyl ether. The solution was washed with water prior to the ether being removed under reduced pressure. Anal. Calcd for $C_{26}H_{34}O$: C, 86.13; H, 9.45. Found: C, 85.88; H, 9.33.

General Procedure of Epimerization. The procedure of epimerization was described in the preceding paper.[1] The composition of starting ethers used is listed in Table I. Separation and analyses of isomers were carried out by GLC using a 4.5-m ethylene glycol adipate polyester, 20% on Chromosorb W, column at 180 °C (for Ia) or at 200 °C (for Ib). In these analyses the isomers which had shorter retention time were assigned the *dl* configuration as described in the preceding paper.[1] Since the two isomers of Ic did not sufficiently separate in GLC, these were analyzed by NMR, in which the isomer with the methine protons signal at higher field was assigned the *dl* configuration as described in the preceding paper.[1]

Registry No.—Ethylphenylcarbinol, 93-54-9; *n*-butylphenylcarbinol, 583-03-9; cyclohexylphenylcarbinol, 945-49-3.

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An Improved Procedure for the Preparation of Bicyclo[2.2.2]octa-2,5,7-triene (Barrelene)

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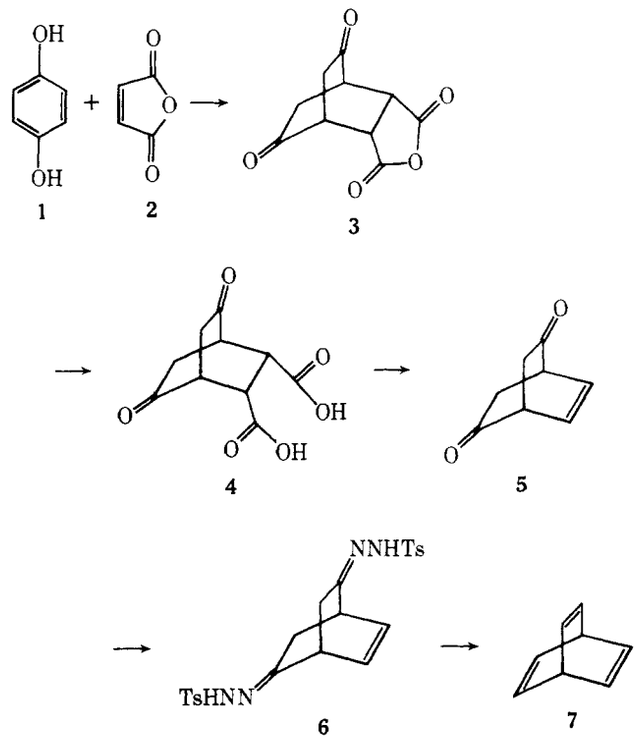
Barrelene (7) is a molecule of considerable theoretical and experimental interest.[1] However, each of the methods for its preparation [2-4] has its disadvantages. The recently published method of Dauben et al.[4] is undoubtedly the most efficient, but requires the rare and costly cyclooctatetraene as starting material.[5] The method of Taylor[3] is simple in that bicyclo[2.2.2]oct-2-ene is essentially halogenated and dehalogenated to give **7** together with bicyclo[2.2.2]octa-2,5-diene. Nevertheless, the manipulation is bothersome as the starting olefin has to be prepared in an autoclave and the products, which are only obtained in low yields, need to be separated by programmed gas–liquid chromatography. We report another method of preparation, which is short, easy to carry out, and makes use of cheap, readily available starting materials.

The key step, namely the construction of the bicyclo[2.2.2]-octane skeleton, is achieved readily, but in low yield, by simply melting together maleic anhydride (**2**) with hydroquinone (**1**) at 200 °C for 2 h.[6] From the mixture, the adduct (**3**) is isolated and immediately hydrolyzed to the corresponding acid (**4**) in an overall yield of 7%. Oxidative decarboxylation of **4** is crucial, as yields tend toward the low side.[7,8] However, heating **4** with lead tetraacetate in pyridine and dioxane under nitrogen for 10 min gives bicyclo[2.2.2]oct-2-ene-5,7-dione (**5**) in 42% yield. Subsequent conversion to the bistosylhydrazone **6** is



1 2 3 4 5 6 7

straightforward (98% yield). Submission of **6** to methyllithium leads to barrelene (**7**) in 12% yield accompanied by benzene.[9,10] The latter probably arises by competitive fragmentation; in any event its presence will not interfere with any chemical reactions which might be done with **7** and it can be simply removed if needs be.

Experimental Section

5,7-Dioxobicyclo[2.2.2]octane-2,3-dicarboxylic Anhydride (3).[6] A mixture of hydroquinone (**1**, 607.0 g, 5.52 mol) and maleic anhydride (**2**, 1097.0 g, 11.2 mol) are heated in an atmosphere of carbon dioxide under strong reflux in a 2-L round-bottom three-neck flask for 2 h. The mixture, at about 70 °C, just above its solidification point, is carefully poured with stirring into ethyl ether (3.2 L) in a 5-L beaker and left overnight. The Diels–Alder adduct (**3**) is collected on a Buchner funnel and washed with cold ether. The beige crystals, 170.0 g, are used directly.

5,7-Dioxobicyclo[2.2.2]octane-2,3-dicarboxylic Acid (4). The crude anhydride (**3**, 170.0 g) is dissolved in water (1 L) and warmed to 80 °C with mechanical stirring for 2 h. Activated charcoal is added and heating continued for 15 min. Filtration over Celite followed by

recrystallization during 2 days in a cold room gives the diacid (**4**, 87.0 g) as colorless crystals in a 7% yield starting from **1**.

5,7-Dioxobicyclo[2.2.2]oct-2-ene (5). The diacid (**4**, 27.0 g, 0.12 mol) and lead tetraacetate (102.0 g, 0.23 mol) in dioxane (260 mL) are purged with nitrogen for 15 min and then placed in a water bath at 12–15 °C. The mixture is vigorously stirred while nitrogen continues to be passed through it. Pyridine (250 mL) is next admixed. The mixture is kept in a bath of water at 60 °C for 10 min, when the carbon dioxide should all be released. The mixture is then rapidly cooled and poured into nitric acid (2 N, 1350 mL). The acid solution is extracted with chloroform (8 × 100 mL). The organic phase is washed with water (1 × 100 mL), with saturated aqueous sodium bicarbonate (2 × 100 mL), and with saturated sodium chloride solution (1 × 100 mL). Drying over Na_2SO_4 and evaporation gives practically pure (as judged by NMR) diketone (**5**, 7.2 g, 53 mmol) in 42% yield.

The Bistosylhydrazone (6) of 5. The diketone (**5**, 3.8 g, 28 mmol) in ethanol (10 mL) is added dropwise to tosylhydrazine (10.4 g, 56 mmol) in ethanol (64 mL) over 10 min. The solution is then heated under reflux for 4 h; the resulting precipitate is filtered warm, washed with ethanol, and dried in vacuo giving the bistosylhydrazone (13.0 g, 27.5 mmol) as pure product in 98% yield.

Bicyclo[2.2.2]octa-2,5,7-triene (Barrelene, 7). To a solution of bistosylhydrazone (**7**, 5.7 g, 12 mmol) in 1,2-bis(dimethylamino) ethane (70 mL) cooled to −23 °C is added dropwise during 1 h a solution of methyllithium (2 M) in ether (48 mL).[9,10] The mixture is stirred under nitrogen for 4 h at −23 °C and then overnight at 20 °C. Excess reagent is decomposed carefully with water (ca. 150 mL). Ether extraction (5 × 30 mL) followed by washing with water (1 × 50 mL), hydrochloric acid (2 N, 2 × 50 mL), water (1 × 50 mL), and saturated aqueous sodium chloride (1 × 50 mL) and drying (over $NaSO_4$) affords a solution which must be carefully evaporated. Most solvent can be removed by distilling at atmospheric pressure using a Vigreux column 20 cm long. In the residue, barrelene (**7**) is present (190–200 mg, 15% yield). Separation of pure **7** can be effected by GLC using a column of 20% SE-30 or 10% OV-17 on Chromosorb W at 150 and 100 °C, respectively. On average, 120 mg (10% yield) of pure barrelene (**7**) is isolated.[11]

Registry No.—**1**, 123-31-9; **2**, 108-31-6; **3**, 61586-14-9; **4**, 61543-84-8; **5**, 17660-74-1; **6**, 61543-85-9; **7**, 500-24-3; tosylhydrazine, 1576-35-8.

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Preparation and Reactivity of a New Spin Label Reagent

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In the course of developing a reagent which could be used to selectively attach a nitroxide spin label to tyrosine residues in proteins, we have prepared *N*-(2,2,5,5-tetramethyl-3-carbonylpyrrolidine-1-oxyl)imidazole (I), a stable, crystalline solid. Preliminary studies indicate that this reagent may be generally useful for attaching the nitroxide spin label to molecules of biological interest. In this communication, we report the preparation of I, its hydrolytic reactivity, and its utility as a reagent for synthesis of spin-labeled molecules.

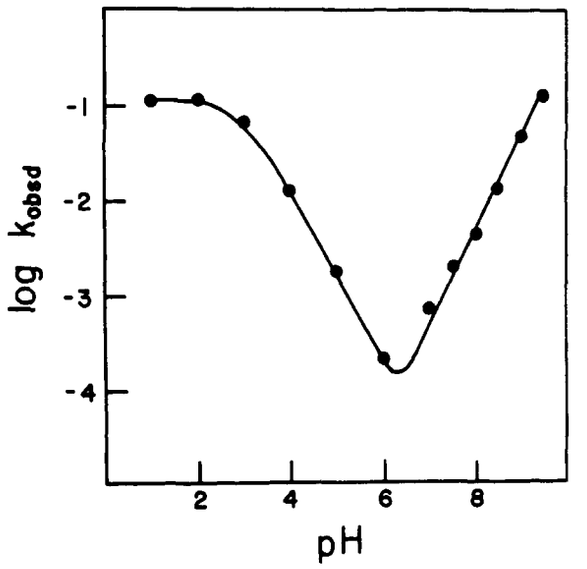
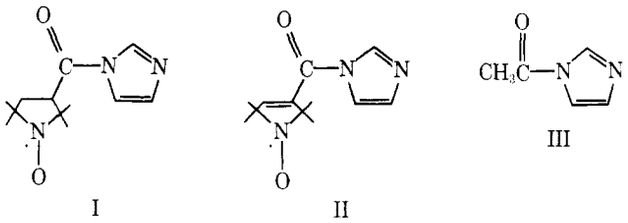


Figure 1. pH profile for hydrolysis of I.



I II

Preparation of I was achieved by allowing equimolar amounts of *N,N'*-carbonyldiimidazole and *N*-(2,2,5,5-tetramethylpyrrolidine-1-oxyl)-3-carboxylic acid[1] to react for several hours at room temperature as a suspension in dry benzene. After workup and two crystallizations from ether, a 57% yield of I was obtained. This product gave satisfactory elemental analysis, IR spectrum, and EPR spectrum. Several previous attempts to prepare I using various methods and conditions led to either destruction of the nitroxide function or to mixtures of products which could not be readily characterized. Use of solvents which afforded homogeneous solutions did not yield isolable amounts of I.

Preparation of the unsaturated analogue (II) of I has been reported.[2] This material was unstable and decomposed rapidly. In contrast, we have stored crystals of I at 4 °C for more than 1 year without noticeable decomposition.

Hydrolysis of I in aqueous solution was studied over the pH range 1.0–9.5. The results are plotted in Figure 1, where the points are experimental and the solid curve is the computer fit of the data to eq 1.

$$k_{obsd} = \frac{K_a^{SH}}{(H^+) + K_a^{SH}}\left[\frac{k_0^{SH}(H^+)}{K_a^{SH}} + \frac{k_{OH}^{S}K_w}{(H^+)}\right] \quad (1)$$

The values of the parameters of eq 1 are listed in Table I, where K_a^{SH} is the acid dissociation constant of the conjugate acid (SH) of I, k_0^{SH} is the water-catalyzed reaction of SH, and k_{OH}^{S} is the hydroxide-catalyzed reaction of S.

The rate parameters obtained for hydrolysis of I are compared to those of Jencks[3] for hydrolysis of *N*-acetylimidazole (III). Both the acid term k_0^{SH} and the base term k_{OH}^{SH} are

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