The Synthesis of Isobullvalene

Sir:

The hydrocarbon I, for which the name isobullvalene has been proposed,[1] was suggested[2] to be a unifying intermediate accounting for a number of reactions yielding II as a product. One of these is the reaction of lithium cyclononatetraenide[3] in ether[4] with methylene chloride and n-butyllithium in n-hexane, which gives after distillation as the major product the hydrocarbon II and as a minor product *trans*-dihydronaphthalene.[2] As indicated in Scheme I these products should arise from the likely intermediate cyclononatetraenyl carbene (III).[5] *trans*-Dihydronaphthalene could result from the ring expansion[6] of III since *cis,cis,cis,cis,trans*-cyclodecapentaene is known to thermally cyclize to *trans*-dihydronaphthalene at −25°,[7] and the product II could result from the intramolecular addition of the carbene in III to a double bond[5d,6a,8] if isobullvalene (I) undergoes a facile Cope rearrangement.[9] We are reporting below the synthesis of I.[10]

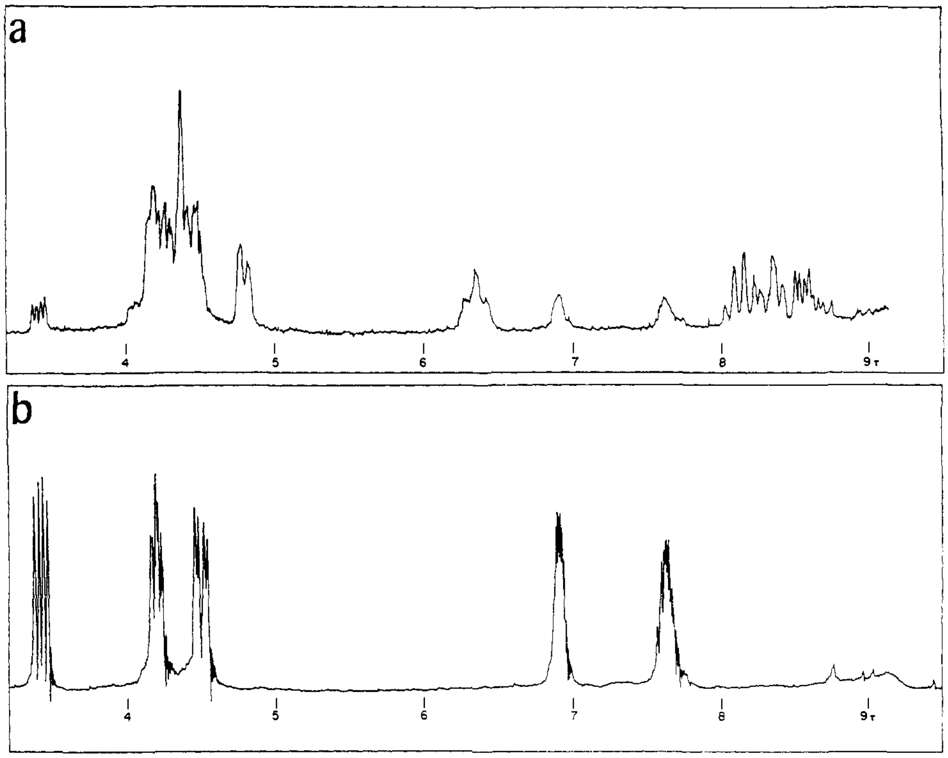
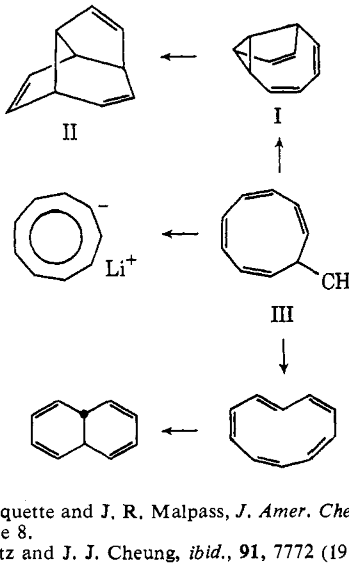


Figure 1. Nmr spectra (100 MHz) in CCl_4: (a) top spectrum, isobullvalene; the small peaks at τ 3.45, 6.90, and 7.62 are due to small amounts of II; (b) bottom spectrum, the same sample after warming at room temperature overnight.

Scheme I



When the reaction of lithium cyclononatetraenide in ether with methylene chloride and n-butyllithium is conducted as previously described,[11] except that instead of being allowed to warm to room temperature the reaction mixture is stirred at −30 to −50° for 4.5 hr, worked up with ice water and cold ether, and the ether removed by rotary evaporation at 0°, the resulting residue contains isobullvalene (I) in place of II as the data below indicate.

(1) The crude product was purified by chromatography at 3° on a short alumina column using n-pen-

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(1) L. A. Paquette and J. R. Malpass, *J. Amer. Chem. Soc.*, **90**, 7151 (1968), footnote 8.

(2) T. J. Katz and J. J. Cheung, *ibid.*, **91**, 7772 (1969).

(3) (a) T. J. Katz and P. J. Garratt, *ibid.*, **86**, 5194 (1964); (b) E. A. LaLancette and R. E. Benson, *ibid.*, **87**, 1941 (1965).

(4) Prepared using 9-chlorobicyclo[6.1.0]nonatriene and Li (1% Na) dispersion.

(5) (a) G. L. Closs, *J. Amer. Chem. Soc.*, **84**, 809 (1962); (b) G. L. Closs and L. E. Closs, *ibid.*, **85**, 99 (1963); (c) W. Kirmse and B.-G. von Bülow, *Chem. Ber.*, **96**, 3316 (1963); (d) W. Kirmse and D. Grassman, *ibid.*, **99**, 1746 (1966); (e) M. J. Goldstein and S. J. Baum, *J. Amer. Chem. Soc.*, **85**, 1885 (1963).

(6) (a) G. L. Closs and R. B. Larrabee, *Tetrahedron Lett.*, 287 (1965); (b) W. Kirmse and K.-H. Pook, *Chem. Ber.*, **98**, 4022 (1965).

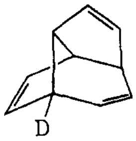
(7) S. Masamune and R. T. Seidner, *Chem. Commun.*, 542 (1969).

(8) (a) W. R. Moore and H. R. Ward, *J. Org. Chem.*, **25**, 2073 (1960); (b) H. Tsuruta, K. Kurabayashi, and T. Mukai, *J. Amer. Chem. Soc.*, **90**, 7167 (1968).

(9) W. von E. Doering, *et al.*, *Tetrahedron*, **23**, 3943 (1967).

(10) A recent attempt to synthesize I yielded II instead [E. Vedejs, R. A. Shepherd, and R. P. Steiner, *J. Amer. Chem. Soc.*, **92**, 2158 (1970)].

(11) The solvent for the n-butyllithium was changed to n-pentane.



IV

tane as the eluent. The nmr spectrum of the purified material was determined in CCl$_4$ solution at $-12°$ and is shown in Figure 1a. When the nmr spectrum was redetermined after the sample had been allowed to remain at room temperature overnight, the spectrum changed to that shown in Figure 1b. The latter spectrum is that of II;[12] the former we attribute to I.

(2) When the purified material was hydrogenated at -5 to $-15°$ in methanol with 5% rhodium on carbon catalyst,[13] the gas chromatogram of the distilled product showed only two major peaks accounting for 86% of the area of the chromatogram. The components accounting for these peaks were collected by preparative glpc, and the major one, accounting for 61% of the original glpc trace, was identified as the saturated hexahydro derivative of I; it was identical (ir, nmr, glpc) with the hydrocarbon obtained upon Wolff–Kishner reduction of tricyclo[5.3.0.0^{2,10}]decan-9-one.[9] The minor product of the hydrogenation, accounting for 25% of the glpc trace, was identified as the hexahydro derivative of II by comparing it with the product obtained by hydrogenating (with rhodium on carbon) an authentic sample of II.

(3) When the product of the reaction of lithium cyclononatetraenide with methylene chloride plus *n*-butyllithium at low temperature[14] is allowed to react in liquid ammonia with a large amount of sodium and then methanol,[15] the major product isolable by distillation and preparative glpc is a *cis*-bicyclo[5.3.0]decadiene, identified by the parent peak in its mass spectrum (m/e 134, the base peak at 75 V) and the product of its hydrogenation in methanol over PtO$_2$, *cis*-bicyclo[5.3.0]decane,[16] identical (ir, nmr) with the hydrogenation product (PtO$_2$ in HOAc) of azulene.[16a] The sodium–ammonia–methanol reduction of II under the conditions described gave none (nmr and glpc) of the bicyclo[5.3.0]decadiene.

The simplest explanation for 1, 2, and 3 above, as well as for the previous observation[2] that lithium cyclononatetraenide reacts with CD$_2$Cl$_2$ plus *n*-butyllithium to give, after warming, IV is that the initial product is isobullvalene.

The conversion of isobullvalene (I) to II was monitored in CCl$_4$ solution by proton nmr spectroscopy.[17] From the rate constants for the reaction determined at 20, 25, and 35° the enthalpy of activation was determined to be 19.5 ± 0.8 kcal/mol and the entropy of activation to be -9.1 ± 3 eu. This means that the half-life for the conversion of isobullvalene to II is 35 min at 25° and 13 hr at 0°.

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(12) (a) M. Jones, Jr., *J. Amer. Chem. Soc.*, **89**, 4236 (1967); (b) M. Jones, Jr., S. D. Reich, and L. T. Scott, *ibid.*, **92**, 3118 (1970).

(13) *Cf.* ref 7, footnote 4.

(14) For this experiment the product was purified by distillation at low temperature.

(15) *Cf.* the reduction of bullvalene: G. Schröder, *Chem. Ber.*, **97**, 3140 (1964).

(16) (a) F. Šorm and M. Romaňuk, *Collect. Czech. Chem. Commun.*, 22, 779 (1957); (b) E. Korvåts, A. Fürst, and Hs. H. Günthard, *Helv. Chim. Acta*, 37, 534 (1954); (c) N. L. Allinger and V. B. Zalkow, *J. Amer. Chem. Soc.*, **83**, 1144 (1961).

(17) The intensity of the resonance of II at τ 3.45 was measured.

Acknowledgments. We are grateful to the National Institutes of Health (MH-08912) for its support, Badische Anilin und Sodafabrik, A. G., for gifts of cyclooctatetraene, and Professor S. Masamune for informing us of similar experiments performed in his laboratory.[18]

(18) K. Hojo, R. T. Seidner, and S. Masamune, *J. Amer. Chem. Soc.*, **92**, 6641 (1970).

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Syntheses *via* 2-Oxazolines. II. A Versatile Synthesis of Aliphatic Carboxylic Acids and Esters. Mono- and Dialkylation of Acids Masked by a Simple Protecting Group

Sir:

The recent reports[1,2] concerning the elaboration of aliphatic carboxylic acids through their dianions prompts us to describe our preliminary results which offer a potentially useful synthesis of carboxylic esters and acids. During our studies involving dihydro-1,3-oxazines which have shown considerable utility as precursors to aldehydes[3] and ketones,[4] we routinely examined the analogous 2-oxazoline system (**1**) which has long been known[5] and readily prepared[6] from 2-aminoethanol derivatives and carboxylic acids. After investigation of a host of 2-oxazolines we chose the 2-substituted 4,4-dimethyl-2-oxazoline (**1**) as a potential precursor for elaborated carboxylic acids due to (a) ease of formation,[6] (b) ready availability of starting materials, and (c) stability toward a wide variety of temperatures and reagents. Although we found that the 2-methyl group can be smoothly metalated with butyllithium (THF, $-78°$) and the resulting lithio derivative alkylated with various electrophiles (alkyl halides, carbonyl compounds, epoxides) to **2**, no conditions could be found to effect an efficient reduction of the C=N link which would provide aldehyde precursors.[7] On the other hand we observed that the 2-oxazoline ring could be easily transformed into the corresponding ethyl esters (**3**) by heating in 5–7% ethanolic sulfuric acid. Thus a method to elaborate carboxylic acid derivatives and convert them directly to their ethyl esters was at hand. The simplest 2-oxazoline derivative **1** (R = H) can be made in quantity by the method previously described[6] and can be utilized as a $>$CHCO$_2$Et

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(1) P. L. Creger, *J. Amer. Chem. Soc.*, **89**, 2500 (1967); *ibid.*, **92**, 1396 (1970).

(2) P. E. Pfeffer and I. S. Silbert, *Tetrahedron Lett.*, 699 (1970).

(3) H. W. Adickes, I. R. Politzer, and A. I. Meyers, *J. Amer. Chem. Soc.*, **91**, 2155 (1969), and earlier references cited.

(4) A. I. Meyers and A. C. Kovelesky, *ibid.*, **91**, 5857 (1969); A. I. Meyers and E. M. Smith, *ibid.*, **92**, 1084 (1970).

(5) J. W. Cornforth, *Heterocycl. Compounds*, **5**, 386 (1957).

(6) H. L. Wehrmeister, *J. Org. Chem.*, **27**, 4418 (1962); P. Allen and J. Ginos, *ibid.*, **28**, 2759 (1963); commercially available from Columbia Organic Chemicals, Columbia, S. C.

(7) Recent reports [R. M. Srivastara, K. Weissman, and L. B. Clapp, *J. Heterocycl. Chem.*, **4**, 114 (1967); J. V. Paukstelis and R. M. Hammaker, *Tetrahedron Lett.*, 3557 (1968)] have described the facile tautomerism of oxazolidines and imines as a function of temperature, solvents, and substituents. Since the imine form is more prevalent than that observed in the tetrahydro-1,3-oxazines, overreduction to the saturated amino alcohols cannot be circumvented [A. I. Meyers and A. Nabeya, *Chem. Commun.*, 1163 (1967)].