Preparation of Cyclo-octyn-3-ol, Cyclononyn-3-ol, and Derivatives

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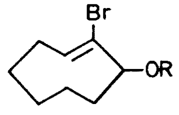
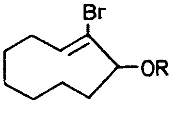
Summary Cyclo-octyne and cyclononyne derivatives have been prepared by the action of KOBu^t–Me$_2$SO on the corresponding 1-bromo-*trans*-cyclo-octenes and -cyclononenes: the elimination reaction was very fast at 20°, and high yields of products were generally obtained.

WE recently found[1] that the dibromocarbene adducts of cycloheptene and cyclo-octene reacted with AgClO$_4$–MeOH to give virtually quantitative yields of *trans*-cyclo-octene and -cyclononene derivatives (Ia and IIa, respectively). The corresponding alcohols (Ib and IIb) were similarly prepared by the Ag$^+$-assisted hydrolysis of the same substrates. We now report that when the latter *trans*-cycloalkene derivatives are treated with potassium t-butoxide in anhydrous dimethyl sulphoxide solution at room temperature, extremely rapid elimination of the elements of hydrogen bromide occurs, and the corresponding cycloalkyne derivatives can usually be isolated from the products in good yields.

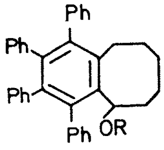


(I) a, R = Me
b, R = H



(II) a, R = Me
b, R = H

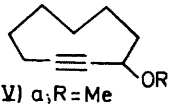
(III) a, R = Me
b, R = H



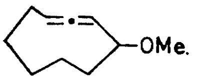
(IV) a, R = Me
b, R = H

In a typical experiment, 3 mol equiv. of *ca.* 1·5M-KOBu^t–Me$_2$SO were added to a stirred solution of 2-bromo-3-methoxy-*trans*-cyclo-octene[1] (Ia) in Me$_2$SO at 20°, and the reaction quenched within 5 s by the addition of cold aqueous AcOH. 3-Methoxycyclo-octyne (IIIa), characterized by mass, i.r., and n.m.r. spectroscopy, was then isolated from the products as a colourless liquid, b.p. 48—50°/6 mm, in 74% yield; it reacted with tetracyclone to give the expected product (IVa), m.p. 228·5—229·5°. In contrast to the behaviour of (Ia), 1-bromo-*cis*-cyclo-octene[3] was recovered in *ca.* 85% yield after it had been treated with KOBu^t–Me$_2$SO under the same conditions for 10 min at 20°.†

Treatment of 2-bromo-*trans*-cyclo-octen-3-ol (Ib) with KOBu^t–Me$_2$SO gave several products but no detectable amount of cyclo-octyn-3-ol (IIIb). However, the latter compound was obtained by the acidic hydrolysis of its tetrahydropyranyl ether (III; R = C$_5$H$_9$O), which was in turn obtained in high yield by the action of KOBu^t–Me$_2$SO on the corresponding 2-bromo-*trans*-cyclo-octene derivative (I; R = C$_5$H$_9$O). Cyclo-octyn-3-ol (IIIb) was characterized by spectroscopic methods and as its crystalline, analytically pure phenylurethane derivative (III; R = CONHPh), m.p. 98—99°; (IIIb) also reacted with tetracyclone to give the expected product[3] (IVb).



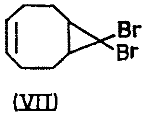
(V) a; R = Me
b; R = H



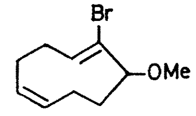
(VI)

3-Methoxycyclononyne (Va), free from the isomeric allene (VI), was obtained as a colourless liquid, b.p. 40—42°/0·3 mm, in 70% yield from 2-bromo-3-methoxy-*trans*-cyclononene[1] (IIa); it was characterized by elemental analysis and by spectroscopic methods. When (IIa) was treated with KOBu^t–Me$_2$SO for 10 min at 20°, pure 4-methoxycyclonona-1,2-diene (VI)‡ could be isolated from the products as a colourless liquid, b.p. 55—58°/0·8—0·9 mm, in 69% yield. As expected,[5] 2-chloro-3-methoxy-*trans*-cyclononene[1] reacted more slowly with KOBu^t in Me$_2$SO solution than its bromo-analogue (IIa), but it was *ca.* 75% converted into (Va) after 5 s at 20°. Under the same conditions, however, 2-bromo-3-methoxy-*cis*-cyclononene[6] remained over 60% unchanged after 10 min.

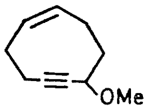
Unlike cyclo-octyne-3-ol (IIIb), cyclononyn-3-ol (Vb) could be obtained in 60% yield directly from the corresponding *trans*-bromo-alcohol (IIb).[1] Pure cyclononyn-3-ol was isolated by distillation as a colourless viscous liquid, b.p. 70°/0·7 mm; it was characterized by spectroscopic methods and as its crystalline phenylurethane derivative, m.p. 80—81°.



(VII)



(VIII)



(IX)

Finally, the preparation of 7-methoxycyclonon-1-en-5-yne (IX) was undertaken. Reaction between 9,9-dibromobicyclo[6,1,0]non-4-ene[7] (VII) with AgClO$_4$–MeOH under the usual conditions[1] gave 2-bromo-3-methoxy-*trans,cis*-cyclonona-1,6-diene (VIII) in 89% yield. Treatment of (VIII) with KOBu^t–Me$_2$SO for *ca.* 5 s at 20° gave 7-methoxycyclonon-1-en-5-yne (IX), which was isolated from the products as a colourless liquid, b.p. 44—46°/0·5 mm, in 67% yield. The latter compound was characterized by elemental analysis and by the usual spectroscopic methods.

The procedure described in this communication has led to the preparation of some previously undescribed derivatives of cyclo-octyne and cyclononyne from readily accessible starting materials. The yields obtained compare

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† The base-catalysed conversion of vinyl halides into acetylenes has been reported, in several instances,[4] to proceed more slowly when *cis*- rather than *trans*-elimination is involved.

‡ It is noteworthy that 3-methoxycyclononyne (VIIIa) is much less stable to KOBu^t–Me$_2$SO than 3-methoxycyclo-octyne (Va).

favourably with the usually quite low yields§ reported for cyclo-octyne and cyclononyne derivatives prepared by other routes. It seems reasonable to conclude that the present procedure for the synthesis of strained cycloalkynes is general and depends only on the availability of the corresponding *trans*-1-bromocycloalkene derivatives.

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§ The yields obtained by other routes[3,8] have usually ranged from less than 10% to *ca.* 40%. We are aware of only one literature report[3] of a good yield of a strained monocyclic cycloalkyne: thus, cyclo-octyne was obtained in 77% yield by treatment of the corresponding 1-aminotriazole derivative with lead tetra-acetate.

[1] C. B. Reese and A. Shaw, *J. Amer. Chem. Soc.*, 1970, **92**, 2566.
[2] F. G. Willey, *Angew. Chem. Internat. Edn.*, 1964, **3**, 138.
[3] G. Wittig and H.-L. Dorsch, *Annalen*, 1968, **711**, 46.
[4] G. Köbrich, *Angew. Chem. Internat. Edn.*, 1965, **4**, 49; S. J. Cristol and R. S. Bly, *J. Amer. Chem. Soc.*, 1961, **83**, 4027; D. R. Kelsey and R. G. Bergman, *ibid.*, 1970, **92**, 228.
[5] S. I. Miller and W. P. Noyes, *J. Amer. Chem. Soc.*, 1952, **74**, 629.
[6] M. S. Baird and C. B. Reese, *J. Chem. Soc.* (*C*), 1969, 1803.
[7] L. Skattebøl, *Tetrahedron Letters*, 1961, 167.
[8] A. T. Blomquist, R. E. Burge, jun., L. H. Liu, J. C. Bohrer, A. C. Sucsy, and J. Kleis, *J. Amer. Chem. Soc.*, 1951, **73**, 5510; A. T. Blomquist, L. H. Liu, and J. C. Bohrer, *ibid.*, 1952, **74**, 3643; A. T. Blomquist and L. H. Liu, *ibid.*, 1953, **75**, 2153; V. Prelog, K. Schenker, and W. Küng, *Helv. Chim. Acta*, 1953, **36**, 471; A. C. Cope, P. T. Moore, and W. R. Moore, *J. Amer. Chem. Soc.*, 1960, **82**, 1744; G. Wittig and A. Krebs, *Chem. Ber.*, 1961, **94**, 3260; A. Krebs, *Tetrahedron Letters*, 1968, 4511.