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SYNTHESIS OF OXABETWEENALLENES

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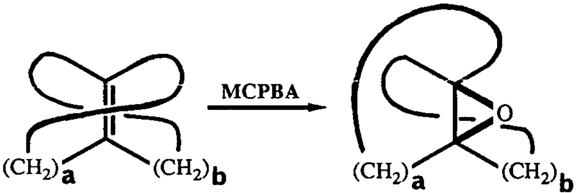
Abstract: A new route to heterocyclic doubly bridged allenes has been developed starting from cycloalkynones. Addition of 4-pentenylmagnesium bromide followed by acetylation and S_N2' addition of 4-pentenylmagnesium bromide-CuI affords symmetrically substituted cycloallenes. Selective hydroboration-oxidation of the terminal alkenes followed by phase-transfer promoted cyclization of the monotosylate derivatives yields the oxabetweenallenes.

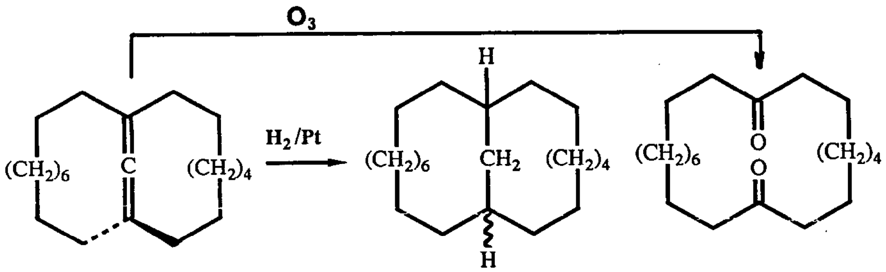
The influence of molecular environment on chemical reactivity is nicely illustrated by the striking rate differences observed for additions to the double bond of homologous [a.b] betweenanenes.[1] For example, both [10.8] and [10.10] betweenanene (I, a = 10; b = 8, 10)[2] fail to react with *m*-chloroperoxybenzoic acid, even after prolonged (3 week) reaction times.[1] The [22.10], [24.10], and [28.10] analogs, on the other hand, are smoothly converted to the epoxides at rates that increase with increasing ring size.[3] These trends indicate that a bridging chain of 8 or 10 carbons effectively shields the internal face of a double bond but the effect is diminished as the chain length increases.



I II

a	b	time (h)
10	8	N.R.
10	10	N.R.
22	10	22
24	10	10.5
28	10	6

A similar effect would be expected for the allenic moiety of an [a.b] betweenallene,[2] although the orthogonal relationship of the 1,3-bridges should attenuate the degree of shielding for a given chain length in comparison to the corresponding betweenanene. To date, only the [10.8] member (III) of the doubly bridged allene family has been described.[4] Unlike its alkene counterpart, the [10.8] allene underwent hydrogenation and ozonolysis to the expected products.[4]

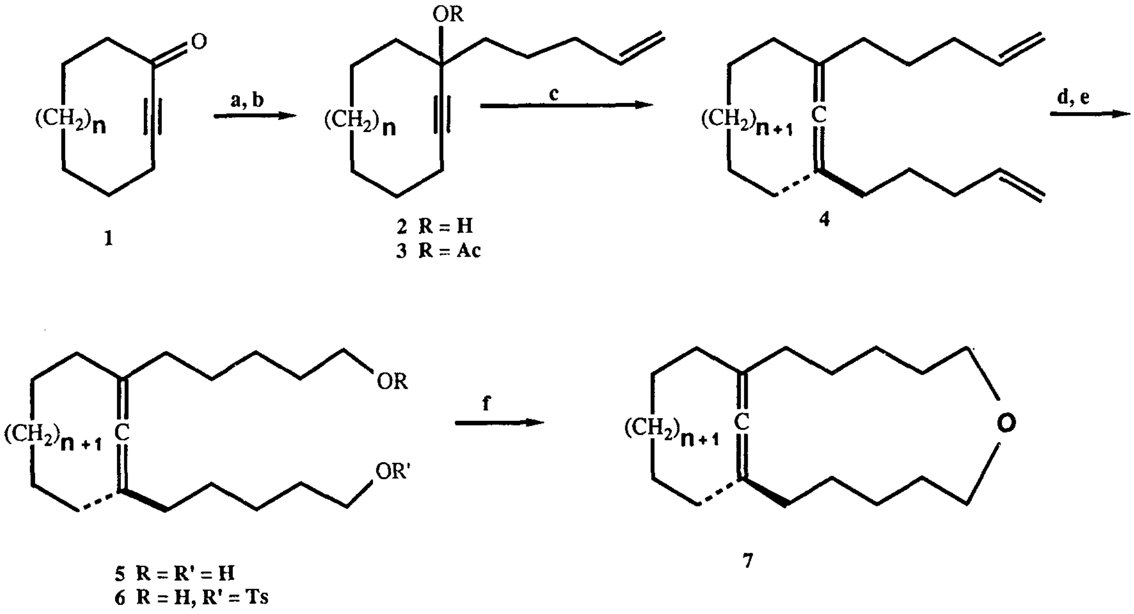


III IV V

With a view to exploring the chemistry of both carbocyclic and heterocyclic betweenallenes we have been working on efficient synthetic access to this unusual class of bridged compounds. In this report we describe a new general route to oxabetweenallenes along with some preliminary studies on the reactivity of the [11.9] and [12.11] systems **7a** and **7b**.[5]

Our sequence utilizes cycloalkynones 1, prepared by Friedel-Crafts cyclization of ω-TMS alkynyl carboxylic acid chlorides according to the method of Utimoto, *et al.*[6] Addition of 4-pentenylmagnesium bromide to the ketones **1a** and **1b** in the presence of $MgBr_2$ to suppress enolization afforded the alcohols **2a** (90%) and **2b** (91%), respectively.[7] The derived acetates **3a** (95%) and **3b** (98%) underwent smooth S_N2' displacement with 4-pentenylmagnesium bromide in the presence of CuI and Me_2S to give the allenic dienes **4a** (92%) and **4b** (90%).[8] The structures of these products were fully supported by the ^{13}C NMR spectra which showed the central allenic carbon at 200.4 (**4a**) and 198.2 ppm (**4b**) in addition to the remaining sp^2 and sp^3 carbons in the proper ratios. Selective hydroboration was effected with disiamylborane to give, after oxidation of the intermediate borane, the crystalline diols **5a** (90%, mp 60-61°C) and **5b** (88%, mp 52-53°C). Cyclization to the oxabetweenallenes **7a** (51%, mp 37-38°C) and **7b** (48%, mp 68-70°C) was effected by slow addition of the mono tosylate derivatives **6a** (52%) and **6b** (70%) to 40% aqueous $NaOH-C_6H_6$ under phase-transfer conditions.[9]

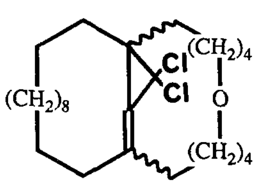
Scheme^{a,b}



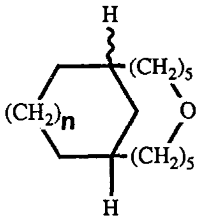
[a] *a* series, n = 4; *b* series, n = 7

[b] a) C_5H_9MgBr, $MgBr_2 \cdot Et_2O$, THF; H_2O, NH_4Cl; b) Ac_2O, Et_3N, DMAP; c) C_5H_9MgBr, CuI, Me_2S, THF, -78° to 20°C; d) $(Me_2CHCHMe)_2BH$, THF; H_2O_2, NaOH; e) *p*-TsCl, Et_3N, DMAP; f) NaOH, $(n\text{-}Bu)_4NHSO_4$, C_6H_6, slow addition over 24 h at room temp, then 16 h at room temp

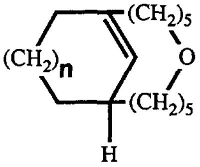
The [11.9] oxabetweenallene **7a** gave no reaction with dichlorocarbene[10] or with hydrogen in the presence of Wilkinson's catalyst[11] under conditions where the higher homolog **7b** afforded a monoadduct **8** and a mixture of tetrahydro products **9b**. Both **7a** and **7b** were hydrogenated over Pd-C to a mixture of tetrahydro and dihydro products **9** and **10**.[12]



8



9a n = 7
9b n = 10



10a n = 7
10b n = 10

Thus the 9-carbon bridging chain of betweenallene **7a** diminishes the reactivity of the central allene relative to that of the larger ring bicyclic **7b**. The effect, however, is considerably less than is found in betweenanenes where a 10-carbon bridge completely blocks reaction with dichlorocarbene or hydrogen.[1]

Finally, it should be noted that the present synthetic route is amenable to a variety of hetero betweenallenes of varying ring sizes as well as the parent carbocyclics. Further extensions are planned.[13]

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References and Notes

1. Reviews: a) Nakazaki, M.; Yamamoto, K.; Naemura, K. In *Topics in Current Chemistry, 125. Stereochemistry*. Vogtle, F.; Weber, E., Ed.; Springer-Verlag: Berlin, 1984; pp 2-25. b) Marshall, J. A. *Acc. Chem. Res.* **1980**, *13*, 213.

2. The nomenclature is related to the familiar Baeyer convention for bridged systems in which numerical prefixes are used to indicate the length of chains connecting the bridgehead atoms.[1b]

3. Marshall, J. A.; Black, T. H. *J. Am. Chem. Soc.* **1980**, *102*, 7581.

4. Nakazaki, M.; Yamamoto, K.; Maeda, M.; Sato, O.; Tsutsui, T. *J. Org. Chem.* **1982**, *47*, 1435.

5. By analogy with the betweenanene-Baeyer system of nomenclature **7a** and **7b** would be named 7-oxa[11.9]betweenallene and 20-oxa[12.11]betweenallene, respectively.[1b]

6. Utimoto, K.; Tanaka, M.; Kitai, M.; Nozaki, H. *Tetrahedron Lett.* **1978,** 2301.

7. In the absence of added $MgBr_2$ the yield of addition products was near 50% and starting ketones were recovered. *Cf.* House, H. O.; Traficante, D. D. *J. Org. Chem.* **1963,** *28,* 355.

8. *Cf.* Baret, P.; Barreiro, E.; Greene, A. E.; Luché, J. L.; Teixeire, M-A.; Crabbé, P. *Tetrahedron* **1979,** *35,* 2931.

9. Freedman, H. H.; Dubois, R. A. *Tetrahedron Lett.* **1975,** 3251. *Ca.* 20% of diol **5** was also formed in each of the cyclizations. The yields are calculated accordingly.

10. *Cf.* Skattebol, L. *Tetrahedron Lett.* **1965,** 2175.

11. Smaller ring cycloallenes have been found to afford dihydro products upon hydrogenation using Wilkinson's catalyst. Bhagwat, M. M.; Devaprabhakara, D. *Tetrahedron Lett.* **1972,** 1391.

12. For a review of allene chemistry, see Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; Wiley-Interscience: New York, 1984.

13. All new compounds have been fully characterized by ^{1}H and ^{13}C NMR analysis and by C, H combustion analysis and/or gc-mass spectral analysis.

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