Selective Brominative Cyclization of Polyenes assisted by Acetonitrile. Application to the Synthesis of Acoratriene[1]

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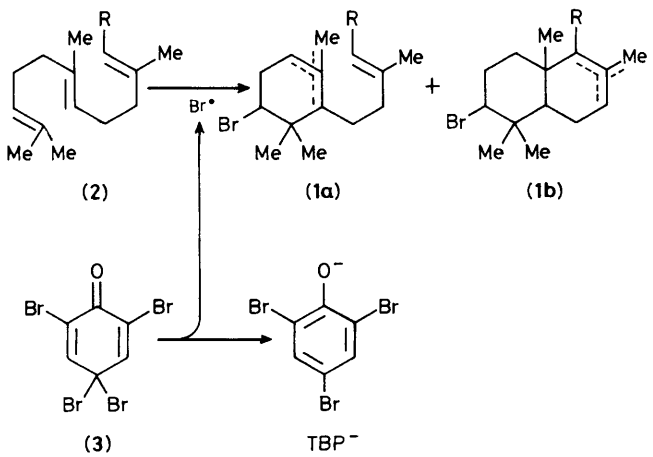
Reaction of polyenes (**4a, b**) with 2,4,4,6-tetrabromocyclohexa-2,5-dienone at −20 °C in the presence of MeCN and subsequent quenching with water gives monocyclic amides (**8a, b**) and (**9a, b**), while the cycloalkene (**7a, b**) was formed during the reaction at room temperature; acoratriene (**12**) was elaborated from (**7b**) *via* a ring contraction product (**10b**).

The construction of structures of type (**1a**) or (**1b**) by Br^+-induced cyclization of acyclic polyene progenitors (**2**) is of special interest from biomimetic considerations. In connection with our efforts to synthesise bromine-containing cyclic terpenoids,[2] we have explored the reactivity of 2,4,4,6-tetrabromocyclohexa-2,5-dienone (**3**) and found that MeCN controls the reaction of polyenes.

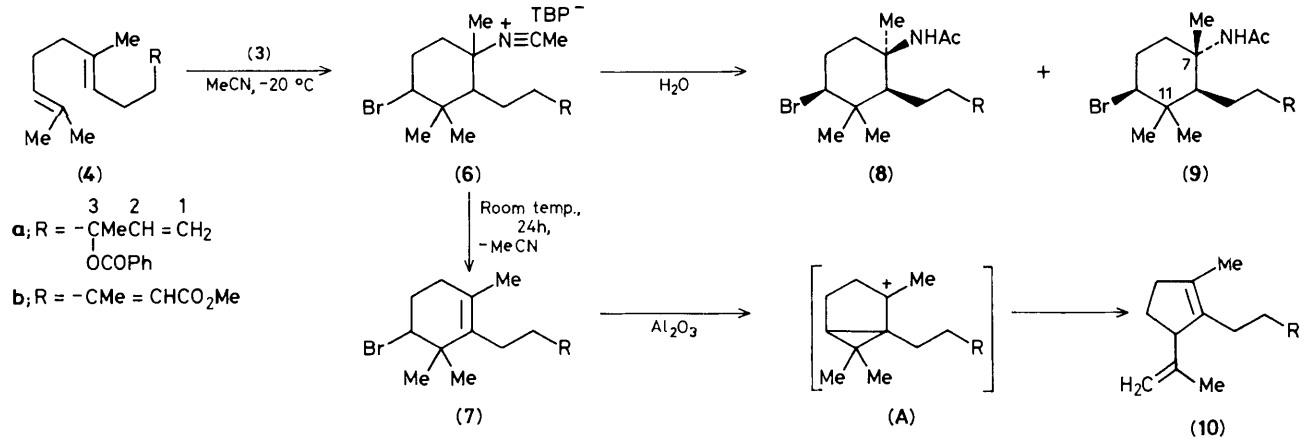


(2) (1a) (1b)

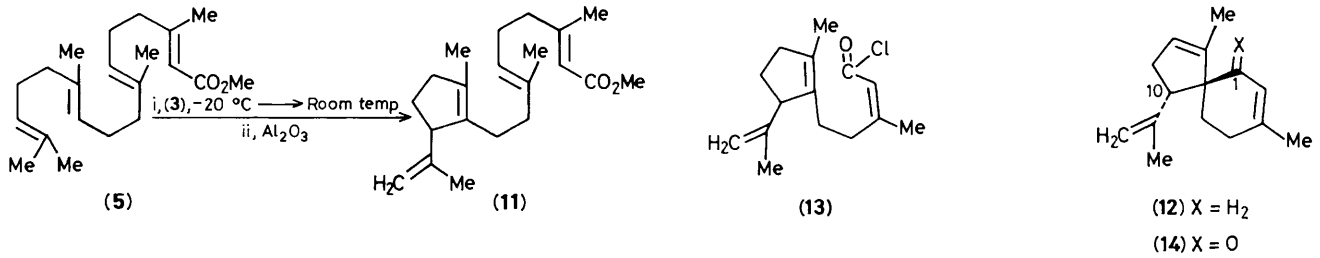
(3) TBP⁻

Treatment of (**4a**) with (**3**) (1.1 equiv.) in MeCN at room temperature afforded a mixture of monocyclic bromides in 75% yield. ^{13}C and ^1H n.m.r. analyses indicated that the major component of the mixture was (**7a**) and a minor isomeric product was also formed (ratio *ca.* 5 : 1). This mixture could not be separated by conventional chromatographic techniques. When stirred with Al_2O_3 in hexane at room temperature, (**7a**) was selectively converted into the cyclopentene derivative (**10a**) in 45% yield from (**4a**) (the transformation conditions were not optimized). No double bond isomer of (**10a**) was detected in the ring contraction product. Although the exact reaction mechanism from (**7**) to (**10**) is obscure, a bicyclo[3.1.0]hexyl cation (A) may be a plausible intermediate in the ring contraction.†

† It has been reported recently that 1-substituted 2-methylene-6,6-dimethylbicyclo[3.1.0]hexanes undergo smooth cyclopropane ring opening with formation of 3-isopropenyl-1,2-disubstituted cyclopentenes in the presence of electrophilic agents, ref. 3.



Scheme 1



The reaction of (**4a**) with (**3**) in MeCN at −20 °C (12 h) was then studied. To half of the reaction mixture was added water at the same temperature and then the mixture was kept at room temperature overnight. Two amides, (**8a**) and (**9a**), were obtained in 39 and 43% yield, respectively.‡ Meanwhile, the remainder was allowed to warm to room temperature and kept overnight whereupon standard work-up gave the mixture of monocyclic bromides [(**7a**) and isomer] in 75% yield.

The ester (**4b**) was allowed§ to react with (**3**) as in the case of (**4a**). Again, amide formation, (**8b**) and (**9b**), was observed when the reaction was quenched with water at −20 °C while (**7b**) was obtained by warming the reaction mixture to room temperature. Compound (**7b**) was transformed into (**10b**) in 40% yield from (**4b**).¶

These reactions are best rationalized by a mechanism involving a nucleophilic attack of the MeCN molecule onto a carbonium ion intermediate and the formation of (**6**) as illustrated in Scheme 1. The participation of MeCN is well documented in the reaction involving a carbonium ion intermediate.[4] However, the present observation concerning capture and elimination of MeCN, which is dependent on the reaction temperature, is of interest with regard to the solvent effect of MeCN. The sequence of the above reaction is also applicable to the higher homologue (**5**), providing the ring contraction product (**11**) in 40% yield.

Thus the present method represents a general route for the preparation of cyclopentene rings possessing the required alkenyl substituents.[3] The reaction was applied to the synthesis of acoratriene (**12**).[5] The acid chloride (**13**), prepared from (**10b**) by usual procedures, was allowed to react with $SnCl_4$ in CH_2Cl_2 at −78 °C,[6] giving the spiro ketone (**14**) in 64% yield. The relative stereochemistry of (**14**) was the one expected from stereochemical considerations and was confirmed by its ^1H n.m.r. spectrum, in which the C(10)-proton resonance appeared at relatively low field, δ 3.45 (t, *J* 8 Hz), because of the anisotropic effect of the carbonyl group. Reduction of the carbonyl group of (**14**) with AlH_3 at −78 °C followed by acetylation with Ac_2O in pyridine in the presence of 4-(dimethylamino)pyridine furnished a stereoisomeric mixture (*ca.* 1 : 1) of the acetate in 75% yield. Treatment of the mixture with Li in ethylamine at −78 °C afforded a hydrocarbon in 54% yield, the physical data of which were completely compatible with the acoratriene (**12**).

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References

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‡ The stereochemistry of (**8a**) and (**9a**) were deduced by comparison of the ^1H n.m.r. chemical shifts of C(7)- and C(11)-methyls [δ 1.13 (Me × 2) and 1.43 (Me) in (**8a**); 0.97 (Me) and 1.12 (Me × 2) in (**9a**)], respectively.

§ The reaction was carried out separately using both 2*Z*- and 2*E*-isomers of (**4b**).

¶ ^{13}C, ^1H n.m.r., and i.r. spectra and (a) combustion or (b) high resolution mass spectral analyses of all the products were consistent with each structure assigned.