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REACTION OF IODINE WITH NON-CONJUGATED DIENES; IODOCYCLIZATION PROMOTED BY A REMARKABLE GEM-DIALKYL EFFECT

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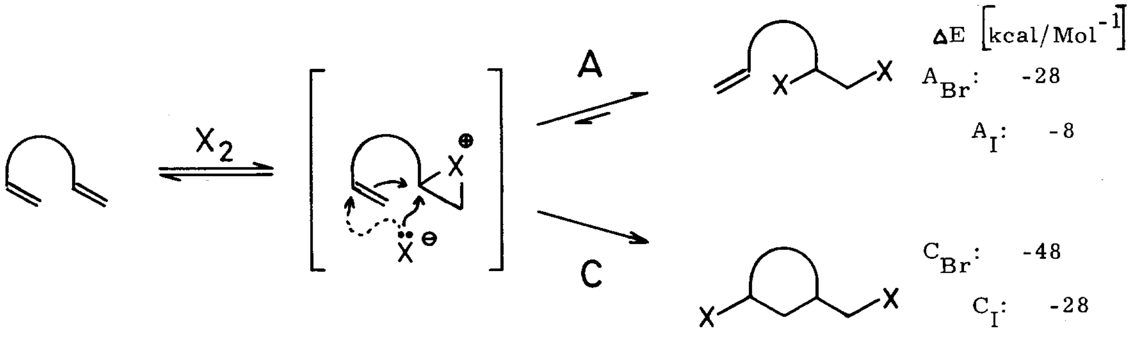
Bromonium ion induced cyclizations of polyene derivatives have received considerable attention recently, both with respect to synthesis and biosynthesis of halogenated terpenes[1]. However, mostly low to moderate yields of cyclized products have been reported. The attack of bromide or other external nucleophiles on the intermediate bromonium ion in these cases is an important – or even dominating – side reaction leading to 1,2 addition products.

The addition of iodine to 1-alkenes is a comparatively slow, low enthalpy process with unfavourable entropy change; the result is an equilibrium mixture with high olefin conversion.[2] Internal attack upon the intermediate iodonium ion, i.e. cyclization, therefore should be more favoured than in the case of bromine-induced reactions[3] (see scheme 1):



Scheme 1: Halogen addition (A) vs. cyclization (C)[a] with 1, n-dienes

Pursuing our studies on reactions of non-conjugated dienes[5], the homologous dienes 1 were treated with one equivalent of iodine in CCl_4 at room temperature for ~ 2 days.

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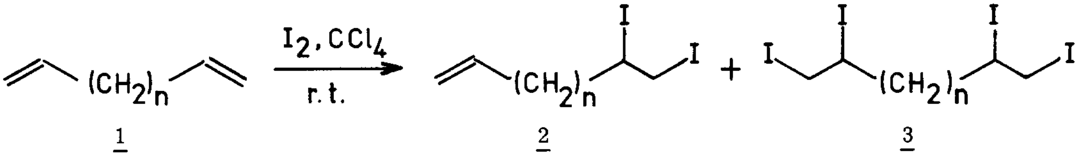
[a] a) One mode of ring closure shown only which may be termed Exo-Tet, Endo-Trig[4].

Following the reaction course by vinyl-H NMR integration indicated that regardless of chain length (C_6 to C_8) only addition to the double bonds had occurred. The mono/bis adduct ratio 2:3 obtained by NMR analysis of the crude products after work-up[6] varied slightly from 2.1 (C_6; 2a:3a) to 2.8 (C_8; 2c:3c). This was confirmed by separate weight determination of C_6 mono and bis adducts, the latter – 1,2,5,6-tetraiodohexane 3a [7], a stable, crystalline solid with m.p. 86° (dec.) – precipitating from the reaction mixture[8].



a: n=2; b: n=3; c: n=4

Contrary to the above results, 4,4-dimethyl-1,6-heptadiene[9] 4a with one equivalent of iodine after ~30 h at room temperature shows complete disappearance of vinyl proton signals in the NMR spectrum. After work-up[10], in 85% yield a ~3:1 mixture of cyclized diiodo compounds 5a is isolated the structure of which is evident from some further transformations:

1. treatment of 5a with KOH in triethylene glycol (r.t. → 200°) affords a mixture of hydrocarbons in ~60% yield. The main constituent (~60% of mixture) was separated by preparative GLC and identified as 1,1-dimethyl-3-methylene-4-cyclohexene[11,12] 6a.
2. deiodination of 5a is smoothly effected by heating with tributyltin hydride and the resulting hydrocarbon identified as 1,1,3-trimethylcyclohexane[11,13] 7a (97% yield).
3. reacting 5a with sodium cyanide in DMSO at 90° for 20 min. leads to double bond isomers of allocyclo-geranonitrile 8a (1:1 mixture, 94-95% yield).

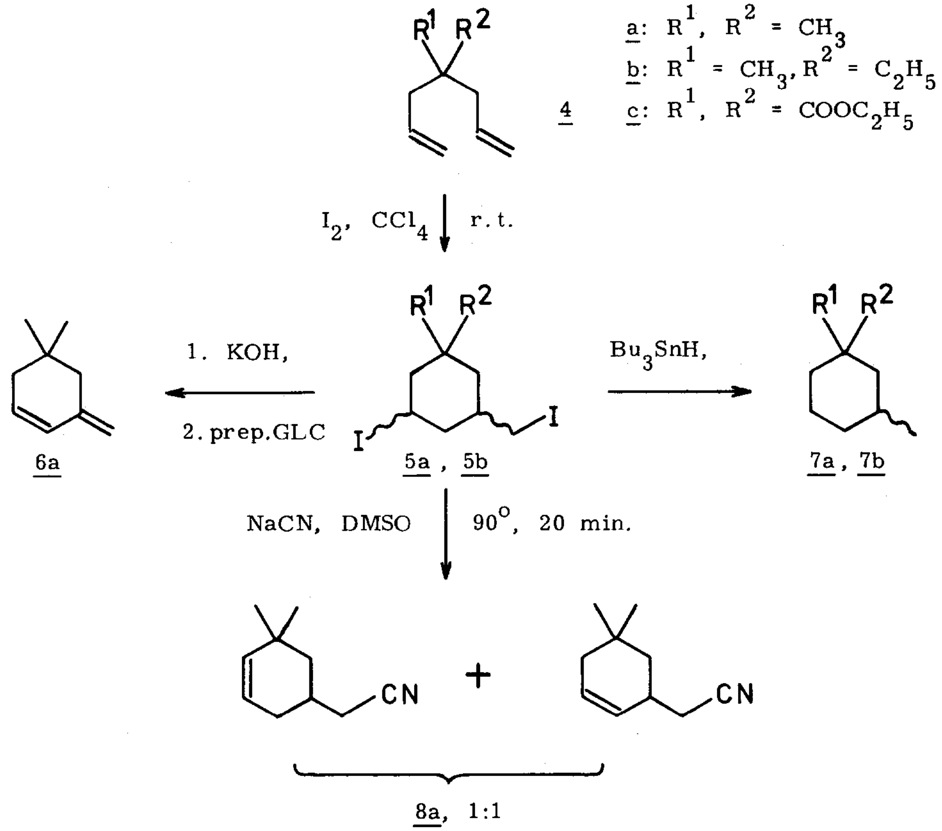
The iodocyclization product of 4a thus represents a mixture of cis/trans-1,1-dimethyl-5-iodo-3-iodomethyl-cyclohexanes; the major isomer is attributed the cis configuration (CHI multiplet centred at ~4,35 ppm vs. 4.75 ppm for the minor component).

Two aspects of this work deserve particular attention:

1. introduction of dialkyl substituents[14] into the 4-position of 1,6-heptadiene completely changes the reaction path towards cyclization;
2. iodine indeed is superior to bromine in effecting cyclization, at least of 4a: by similar treatment of 4a with bromine only addition is observed (NMR).

In order to define the scope of iodocyclization, several other dienes were reacted with iodine as described above:

a) 4-ethyl-4-methyl-1,6-heptadiene[15] 4b iodocyclizes likewise as expected (99% yield of crude product 5b, 93% of cis/trans-1-ethyl-1,3-dimethyl-cyclohexanes 7b after deiodination);



b) 4-monosubstituted 1,6-heptadienes (Br, OH, OTs), diallyl ether and 4-vinyl-cyclohexene furnish acyclic addition products only (NMR);

c) cyclic dienes with double bonds appropriately situated for transannular interactions[16] are similarly amenable to iodocyclization; f.e. cis,trans-1,5-cyclodecadiene (90% – presumably trans – 1,4-diiodo-cis-decalin; 90% of cis-decalin after tributyltin hydride treatment) and, reported recently by Yurchenko et al.[17], 3-methylene-7-isopropylidene-bicyclo[3.3.1]nonane (65% of 2,2-dimethyl-3-iodo-1-iodomethyl-adamantane).

d) the presence of internal nucleophiles even as weak as ethoxycarbonyl oxygen in δ-position to a double bond (4-pentenoate subunit) as in 4c precludes iodocyclization; instead, iodolactonization is preferred[18].

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