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TOWARDS A SYNTHESIS OF (±)MODHEPHENE VIA CASCADE REARRANGEMENT: SYNTHESIS AND REARRANGEMENT OF DISPIRO[3.0.4.2]UNDECANES TO [3.3.3]PROPELLANES[1)]

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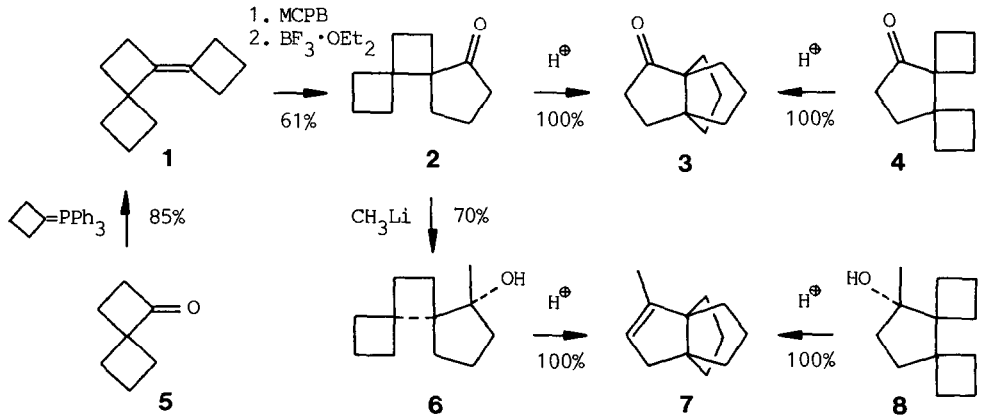
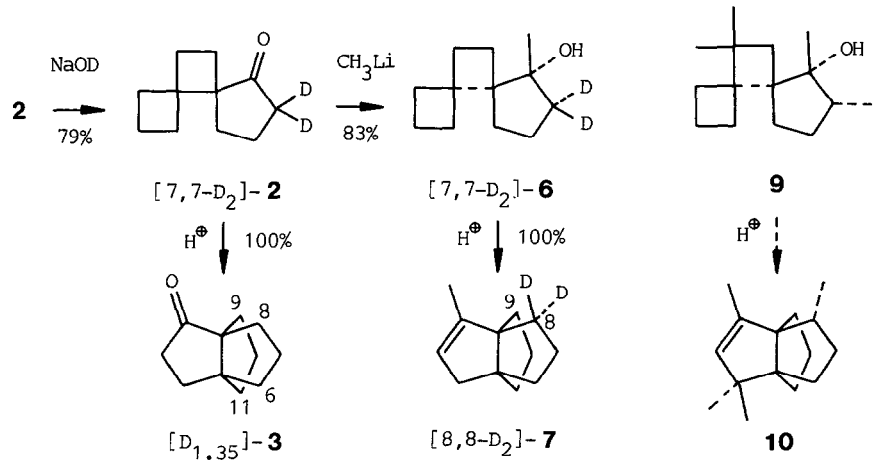
Summary: The dispiro[3.0.4.2]undecanes **2** and **6** undergo cascade rearrangements yielding the [3.3.3]propellanes **3** and **7**, respectively. The rearrangement of **6** proceeds regiospecifically and renders **9** a promising candidate for a direct conversion to (±)modhephene **10**.

Within studies on the synthesis of cyclopentanoic sesquiterpenes via rearrangement routes we recently described[2)] the synthesis and rearrangement of dispiro[3.0.3.3]undecanes **4** and **8** yielding the [3.3.3]propellanes **3** and **7**, respectively. We now report the synthesis and rearrangement of dispiro[3.0.4.2]undecanes **2** and **6** and their deuterated analogues [7,7-D_2]-**2** and [7,7-D_2]-**6**. Based on the regiochemistry of the rearrangement of [7,7-D_2]-**6** we consider that dispiro[3.0.4.2]-undecane **9** will rearrange directly to (±)modhephene **10**[3)].



Dispiro[3.0.4.2]undecanes **2**, **6**, [7,7-D_2]-**2** and [7,7-D_2]-**6** were prepared as follows: cyclobutylidenation of ketone **5**[4)] yielded olefin **1**[5)] which was epoxidized with m-chloroperbenzoic acid and subsequently rearranged in situ with boron trifluoride etherate to give the desired **2**[5)]. [7,7-D_2]-**2**[5)] [3% D_1, 97% D_2 (MS)] was obtained by treatment of **2** with sodium deuteroxide, and addition of methyllithium to **2** and [7,7-D_2]-**2** finally gave **6**[5)] and [7,7-D_2]-**6**[5)] [3% D_1, 97% D_2 (MS)], respectively.

When 0.30 molar solutions of **2** and [7,7-D_2]-**2** in benzene were heated with equivalent amounts (w/w) of Nafion-H[6)] for 39h at +70°C, quantitative conversions to the [3.3.3]propellanes **3**[2)] and [$D_{1.35}$]-**3** [19% D_0, 31% D_1, 31% D_2, 14% D_3 (MS)], respectively, were observed. Inspection of the ^{13}C-NMR spectrum of [$D_{1.35}$]-**3** revealed, however, that the rearrangement of [7,7-D_2]-**2** - and hence of **2** - had proceeded nonregiospecifically as most of the remaining deuterium had ended up either at C-6,11 (δ= 37.66, s and m) or C-8,9 (δ= 40.95, s and m) of [$D_{1.35}$]-**3**. We therefore turned towards the rearrangements of **6** and [7,7-D_2]-**6**.



This time, heating of 0.43 molar solutions in benzene with 0.17 equivalents (w/w) of Nafion-H[6] resulted within 2h at +70°C in quantitative conversions to the [3.3.3]propellanes **7**[2] and [8,8-D_2]-**7**[5], respectively. No loss of deuterium could be detected in the case of [8,8-D_2]-**7** [4% D_1, 96% D_2 (MS)], and in the ^{13}C-NMR spectrum all resonance lines except that of C-8,9 [δ = 37.60 (s), 36.90 (quint, J = 19.5 Hz)] were free of any concomitant splitting due to the presence of mono- or dideuterated carbon atoms. Together with the fact that the resonance line of C-8,9 had lost approximately 50% of its intensity compared with undeuterated **7**, this clearly indicates that the rearrangement of [7,7-D_2]-**6** - and hence of **6** - had proceeded regiospecifically initiated by an exclusive 1,2-shift of that cyclobutane bond having an antiperiplanar alignment with the leaving hydroxyl group.

We therefore expect that the still unknown dispiro[3.0.4.2]undecane **9** will undergo cascade rearrangement leading directly to (±)modhephene **10**. Other approaches to this unique naturally occuring sesquiterpene are based on totally different strategies[3].

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References and notes

1) Polyspiranes, 15, Cascade Rearrangements, 10; for communications 14 and 9 see M.Giersig, D.Wehle, L.Fitjer, N.Schormann and W.Clegg, **Chem. Ber.** 121 (1988), in press.

2) L.Fitjer, A.Kanschik and M.Majewski, **Tetrahedron Lett. 26**, 5277 (1985).

3) Reviews: L.A.Paquette, **Top. Curr. Chem. 79**, 41 (1979); **119**, 1 (1984); L.A.Paquette and A.M.Doherty, **Polyquinane Chemistry**, Springer-Verlag, Berlin Heidelberg 1987.

4) B.M.Trost, D.E.Keeley, H.C.Arndt and M.J.Bogdanowicz, **J. Am. Chem. Soc. 99**, 3088 (1977).

5) All new compounds (**1**, **2**, **6**) gave correct elemental analyses. IR, ^1H-NMR, ^{13}C-NMR and mass spectroscopic data are consistent with the given structures. Deuterated compounds ([7,7-D_2]-**2**, [$D_{1.35}$]-**3**, [7,7-D_2]-**6**, [8,8-D_2]-**7**) were analyzed by ^{13}C-NMR and mass spectroscopy. ^{13}C-NMR data are as follows: **1** (20 MHz, $CDCl_3$): δ = 16.32, 18.18, 23.98, 29.05, 29.71, 32.80, 33.84, 50.01, 129.36, 136.44; **2** (50.3 MHz, $CDCl_3$): δ = 15.32, 19.47, 24.44, 31.11, 31.37, 32.29, 32.95, 37.95, 48.44, 56.05, 220.94; [7,7-D_2]-**2** (50.3 MHz, C_6D_6): δ = 15.75, 19.44, 24.95, 31.27, 31.73, 32.62, 32.94, 37.09 (quint, J = 19.8 Hz), 48.53, 55.61, 218.04; [$D_{1.35}$]-**3** (50.3 MHz, C_6D_6): δ = 26.28, 26.38, 26.48 (C-7,10), 31.57 (C-4), 37.36 (C-3), 37.66 (C-6,11; s and m), 40.95 (C-8,9; s and m), 58.83 (C-5), 65.93 (C-1), 220.13 (C-2); **6** (50.3 MHz, $CDCl_3$): δ = 16.49, 18.63, 23.71, 26.93, 32.04, 32.18, 32.99, 33.13, 39.94, 47.15, 54.74, 82.66; [7,7-D_2]-**6** (50.3 MHz, $CDCl_3$): δ = 16.50, 18.41, 23.66, 26.90, 32.03, 32.18, 32.98, 33.13, 39.17 (quint, J = 19.6 Hz), 47.12, 54.75, 82.58; [8,8-D_2]-**7** (50.3 MHz, $CDCl_3$): δ = 13.83 (CH_3), 25.70, 25.90 (C-7, C-10), 36.90 (quint, J = 19.5 Hz, C-8), 37.60 (C-9), 41.73 (C-6,11), 47.37 (C-4), 60.20 (C-5), 69.91 (C-1), 121.99 (C-3), 144.11 (C-2). All assignments are based on ^{13}C-^{13}C-connectivity studies.

6) Review: G.A.Olah, **Synthesis 1986**, 513.

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