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A SYNTHESIS OF 1,6-DIOXASPIRO[4.5]DEC-3-ENES.

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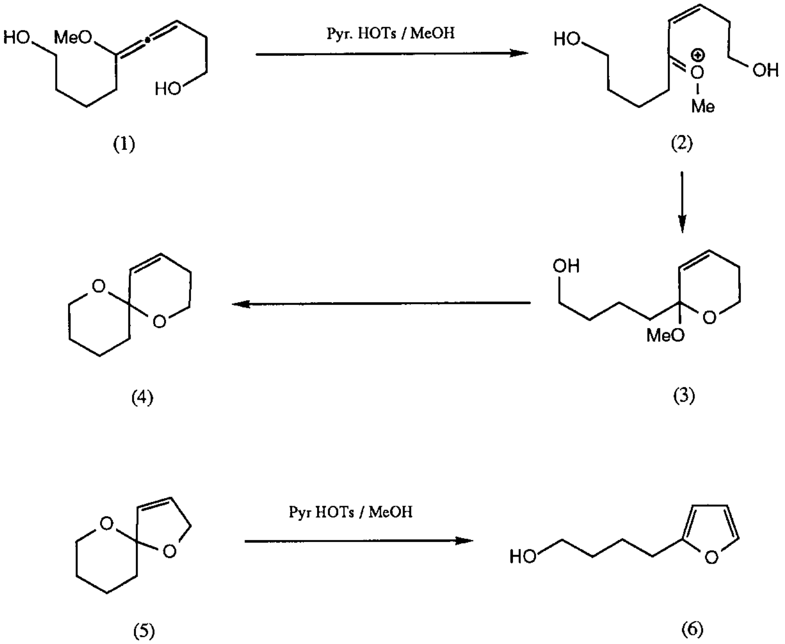
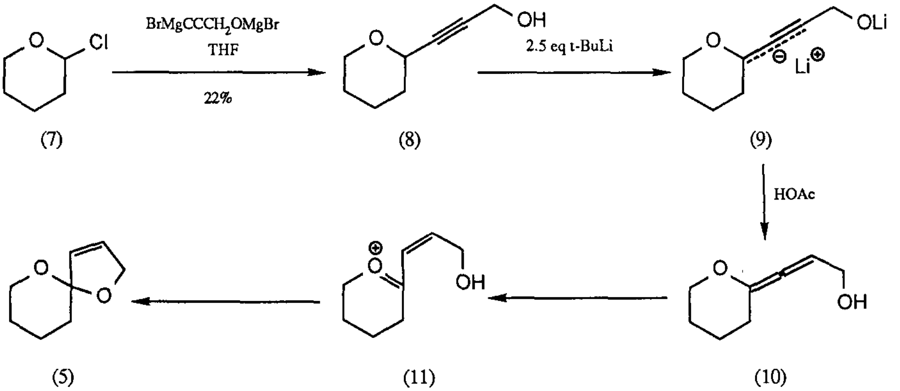
Summary: Base-catalysed rearrangement of a 2-alkynyl-tetrahydropyran generates an allenol ether intermediate which undergoes acid-catalysed cyclisation to the 1,6-dioxaspiro[4.5]dec-3-ene system.

We recently described a synthesis of the 1,7-dioxaspiro[5.5]undec-4-ene system (**4**)[1] which made strategic use of the stereoselective protonation[2] of the 1,3-dialkylalkoxyallene (**1**) (Scheme 1). The oxonium ion (**2**) underwent rapid tandem cyclisation to give the spiroacetal (**4**) in 60% yield. Critical to the success of this approach were the mild conditions used in the cyclisation which permitted isolation of the acid-sensitive spiroacetal. We now report a synthesis of the 1,6-dioxaspiro[4.5]dec-3-ene system (**5**) which is more challenging because it readily undergoes aromatisation to the furan (**6**) under the conditions previously used to generate the analogous spiroacetal (**4**).



Scheme 1

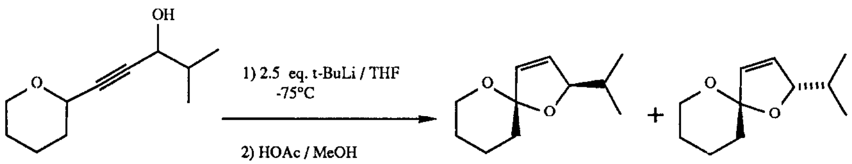
The procedure outlined in Scheme 2 for the synthesis of the hypersensitive parent 1,6-dioxaspiro[4.5]dec-3-ene (**5**) was designed to achieve the spirocyclisation in essentially one step under very mild conditions. Consequently the crucial allenol ether functionality was appended to the pre-formed pyran ring of intermediate (**10**). The intermediate (**10**) was generated *in situ* by protonation of the dianion (**9**) generated from the readily available 2-alkynyl-tetrahydropyran (**8**) by reaction with 2 equivalents of t-BuLi[3]. Although the unstable allenol ether intermediate could be isolated by quenching the reaction mixture with aqueous $NaHCO_3$ followed by normal extractive work-up, better overall yields of the desired spiroacetal were obtained by reaction of the dianion (**9**) with an excess of acetic acid at -60°C as described in the following experimental procedure.



Scheme 2

To a solution of alkyne (**8**) (0.65 g, 4.6 mmol) in THF (50 ml) at -70°C was added dropwise t-butyllithium (9 ml, 1.4 M solution in pentane, 13 mmol). After stirring for a further 1 h at -65°C the reaction was quenched by the addition of acetic acid (1 g) in MeOH (5 ml) and allowed to warm to -40°C over 1 h. The mixture was then poured into saturated aqueous $NaHCO_3$ (50 ml), dried over Na_2SO_4, and chromatographed on basic alumina (40% ether /hexane-100% ether) to afford the spiroacetal (**5**) as a colourless volatile oil which decomposes on attempted kugelrohr distillation.

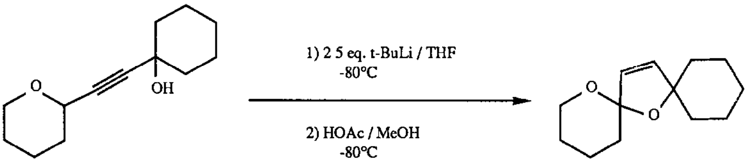
The procedure outlined in Scheme 2 can also be applied to substituted 1,6-dioxaspiro[4.5]dec-3-enes. For example treatment of (**12**) with t-BuLi followed by acetic acid as described gave a 75% yield of a 2:1 mixture of the isomeric spiroacetals (**13**) and (**14**) which were easily separated by column chromatography on silica gel eluting with ether-hexane. However best results were obtained in the cyclisation of the tertiary alcohol (**15**) where elimination to a furan is blocked. The cyclohexane ring has two effects: it somewhat destabilises the allenyl form of the dianion leading to less regioselective protonation [24% recovered alkyne (**15**)] but it also directs protonation of the allenol ether intermediate to give entirely *cis*-alkene. The yield of spiroacetal (**16**) was 99% based on recovered starting alkyne.



(12) (13) 2:1 (14)

Prepared in 76% yield from the Li salt of (17) and isobutanal.

50% [75% based on recovered (12)]

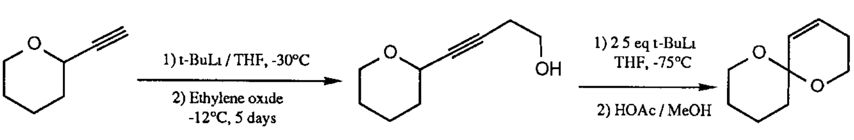


(15) (16)

M.p. 36.5-37 5°C (hexane)
Prepared in 86% yield from the Li salt of (17) and cyclohexanone

75% [99% based on recovered (15)]

The approach outlined herein can also be applied to the synthesis of the homologous 1,7-dioxaspiro[5.5]undec-4-ene ring system (**4**) as shown in Scheme 3.



(17) (18) (4)

Scheme 3

In conclusion we have exploited the extremely easy and stereoselective protonation of both cyclic and acyclic allenol ethers to generate oxonium ion intermediates which cyclise to the novel 1,6-dioxaspiro[4.5]dec-3-ene system and the better known 1,7-dioxaspiro[5.5]undecane system[1].

Acknowledgements. We thank Smith, Kline and French Ltd. for generous financial support.

References and Notes.

1. R. Whitby and P. Kocieński, *J. Chem. Soc., Chem. Commun.*, in press.

2. J. C. Clinet and G. Linstrumelle, *Tetrahedron Lett.*, 1978, 1137; F. Derguini and G. Linstrumelle, *ibid.*, 1984, **25**, 5763.

3. M. Stahle and M. Schlosser, *Angew. Chem. Int. Ed. Engl.*, 1979, **18**, 875.

4. Spectral data for selected compounds. The IR spectra were recorded as films and the ^{1}H- and ^{13}C-NMR data were recorded in $CDCl_3$ at 360 and 90.5 MHz respectively.

(**5**) IR : 2950, 2875, 1627, 1470, 1375, 1220, 1090, 1080, 1030, 985, 902 and 715 cm^{-1}; δ_H : 1.5-1.9 (6 H, m), 3.75 (1 H, dm, J 11 Hz), 3.98 (1 H, dt, J 3, J' 11 Hz), 4.58 (1 H, dt, J 13.5, J' 2 Hz), 4.74 (1 H, ddd, J 13.5, J'3, J"1.5 Hz), 5.77 (1 H, dt, J 6, J' 2.5 Hz), 6.145 (1 H, dt, J 6, J' 1.5 Hz). δ_C : 19.65 (t), 25.11 (t), 34.09 (t), 62.83 (t), 73.84 (t), 110.10 (s), 130.07 (d), 130.46 (d), m/z 140 (M$^+$, 24%), 122 (7), 119 (7), 111 (6), 107 (12), 94 (82), 85 (42), 81 (100), 57 (49).

(**13**) IR : 2960, 2880, 1625, 1468, 1368, 1212, 1075, 1025, 1005, 903, 822, 811 and 725 cm^{-1}; δ_H : 0.90 (3 H, d, J 6.6 Hz), 0.98 (3 H, d, J 6.6 Hz), 1.5-1.95 (7 H, m), 3.69 (1 H, dm, J 11.4 Hz), 4.00 (1 H, dt, J 3, J' 11.4 Hz), 4.46 (1 H, ddd, J 6.5, J' 2, J" 1.2 Hz), 5.73 (1 H, dd, J 6, J' 2 Hz), 6.04 (1 H, dd, J 6, J' 1.2 Hz). δ_C : 18.39 (q), 18.92 (q), 19.93 (t), 25.33 (t), 33.88 (d), 34.58 (t), 62.51 (t), 91.12 (d), 109.49 (s), 131.01 (d), 132.13 (d); m/z 182 (M$^+$, 27%), 167 (40), 149 (37), 139 (22), 123 (80), 121 (54), 109 (25), 107 (29), 81 (32), 55 (34), 43 (96).

(**14**) IR : 2960, 2880, 1625, 1468, 1368, 1211, 1072, 1022, 1002, 900, 818, 780 and 715 cm^{-1}; δ_H : 0.875 (3 H, d, J 6.6 Hz), 0.925 (3 H, d, J 6.6 Hz), 1.5-2 (7 H, m), 3.7 (1 H, dm, J 11.3 Hz), 3.995 (1 H, dt, J 3, J' 11.4 Hz), 4.71 (1 H, ddd, J 5.4, J' 2.4, J" 1.2 Hz), 5.79 (1 H, dd, J 6, J' 2.4 Hz), 6.035 (1 H, dd, J 6, J' 1.2 H). δ_C : 18.08 (q), 18.27 (q), 19.79 (t), 25.44 (t), 32.65 (d), 34.77 (t), 63.11 (t), 90.03 (d), 109.61 (s), 131.18 (d), 132.57 (d).

(**16**) IR : 2940, 2860, 1675, 1440, 1375, 1220, 1195, 1095, 1075, 1000, 910 and 745 cm^{-1}; δ_H : 1.35 (1 H, m), 1.5-1.8 (14 H, m), 1.95 (1 H, m), 3.68 (1 H, br d, J 11.5 Hz), 4.03 (1H, dt, J 3, J' 11.5 Hz), 5.69 (1 H, d, J 5.4 Hz), 6.11 (1 H, d, J 5.4 Hz). δ_C: 19.68 (t), 23.25 (t) 23.42 (t), 25.33 (t), 25.46 (t), 35.71 (t), 37.50 (t), 38.68 (t), 62.35 (t), 89.09 (s), 108.65 (s), 129.12 (d), 137.99 (d); m/z 208 (M$^+$, 27%), 190 (16), 165 (20), 163 (17), 153 (20), 151 (44), 150 (39), 137 (37), 135 (47), 114 (76), 107 (70), 95 (47), 94 (40), 55 (69).

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