SYNTHESIS OF Δ^3-DIHYDROTHIAPYRAN-1,1-DIOXIDES AND THEIR RAMBERG-BÄCKLUND CONVERSION TO CYCLOPENTADIENES.

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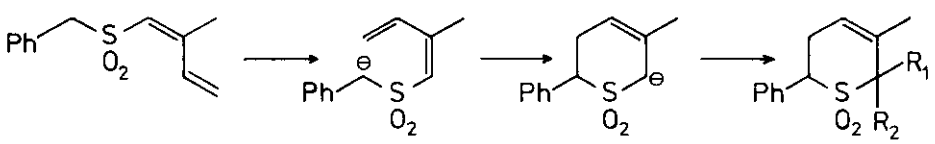
Abstract - Treatment of Z-sulfone 1 with n-BuLi gives complete conversion to the cyclized anion 3. The anion 3 is protonated to 4. Reaction of 3 with hexachloroethane leads to a mixture of 4, 5 and 6. Ramberg-Bäcklund rearrangement of 5 with one equivalent of n-BuLi affords 6 and 7. The same reaction with 6 gives 8.

During a synthetic study directed to conjugated isoprenoid polyenes[1], we have come across the facile base-promoted ringclosure of sulfone 1[2] to the substituted Δ^3-dihydrothiapyran-1,1-dioxides 4, 5 and 6 (Scheme 1). The cyclization appears to be general for sulfones carrying a hydrogen at the α-position and a Z-butadienyl moiety at the α'-position[2]. It allows the simultaneous introduction of substituents at the positions 3 and 6 of the thiapyran ring, while position 2 may be either left unsubstituted or be substituted by chlorine.

The Ramberg-Bäcklund desulfurization of the chlorosulfones 5 and 6 leads to the cyclopentadienes 7 and 8 (Schemes 2 and 3), respectively. The monochlorocyclopentadienyl derivative 7 may be considered as a cyclopentenone precursor. The overall reaction constitutes a cyclopentadiene synthesis starting from an acyclic sulfone.

Scheme 1



1 2 3

4: $R_1 = R_2 = H$

5: $R_1 = R_2 = Cl$

6: $R_1 = H$; $R_2 = Cl$

Treatment of 1 with one equivalent of lithium diisopropyl amide (LDA) in THF at -78°C leads to the anion 2, that enters in an intramolecular 1,4-addition to give the cyclized anion 3 (Scheme 1). When the reaction mixture is acidified at this stage with gaseous HCl, the dark-red colour of 3 disappears at once and 3-methyl-6-phenyl-Δ^3-dihydrothiapyran-1,1-dioxide (4) is formed quantitatively. Evaporation of the solvent and chromatographic purification[3] of the non-volatile fraction of the reaction mixture affords 4 as a colourless crystalline compound (mp 117-118°C). ^{1}H NMR ($CDCl_3$, TMS, δ=0): 7.57-7.31 (phenyl, m); 5.80-5.60 (C4-H, m); 4.25-4.05 (C6-H, q); 3.90-2.65 (C2-H and C5-H, m); 1.83 (C3-Me, d, J 0.5 Hz).

When the cold THF solution of anion 3 is added to a fivefold molar excess of hexachloroethane (HCE) in THF at -78°C, the dark-red colour of 3 fades away upon warming to room temperature. Evaporation of the solvent and the unconverted HCE gives a mixture consisting of the thiapyran-1,1-dioxides 4, 5 and 6 (1:1:1) in 58% yield. Low pressure liquid chromatography gave in the order of elution:

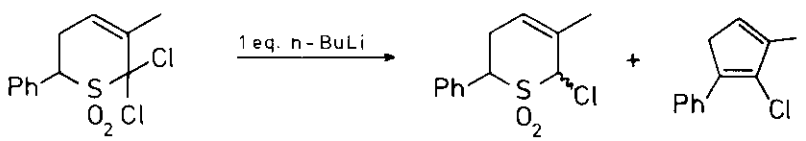
2,2-dichloro-3-methyl-6-phenyl-Δ^3-dihydrothiapyran-1,1-dioxide (5), mp 140-141°C). ^{1}H NMR ($CDCl_3$): 7.67-7.37 (phenyl, m); 5.78-5.63 (C4-H, m); 5.00-4.80 (C6-H, q, X-part of ABX); 3.52-2.61 (C5-H, m, AB-part of ABX); 2.16 (C3-Me, m). IR ($CHCl_3$): 3040, 3020, 1450 (C-H), 1600 (weak, C=C), 1490, 1385 (phenyl), 1350 and 1160 cm^{-1} (SO_2). Analysis: Calcd for $C_{12}H_{12}SO_2Cl_2$: C, 49.49; H, 4.16; S, 11.01; Cl, 24.35. Found: C, 49.33; H, 4.14; S, 10.98; Cl, 24.56.

2-Chloro-3-methyl-6-phenyl-Δ^3-dihydrothiapyran-1,1-dioxide (6), mp 127-128°C. ^{1}H NMR ($CDCl_3$): 7.56-7.33 (phenyl, m); 5.86-5.69 (C4-H, m); 4.85 (C2-H, s); 4.68-4.47 (C6-H, q, X-part of ABX); 3.48-2.57 (C5-H, m, AB-part of ABX); 1.98 (C3-Me, m). IR ($CHCl_3$): 3040 (C-H), 1600 (weak, C=C), 1495, 1385 (phenyl), 1330, 1150 and 1130 cm^{-1} (SO_2). Analysis: Calcd for $C_{12}H_{13}SO_2Cl$: C, 56.14; H, 5.10; S, 12.49; Cl, 13.81. Found: C, 56.23; H, 5.15; S, 12.52; Cl, 13.92.

Only one stereoisomer is observed. We have not been able to establish the relative configurations at the asymmetric centers.

Compound 4, already described above.

Scheme 2



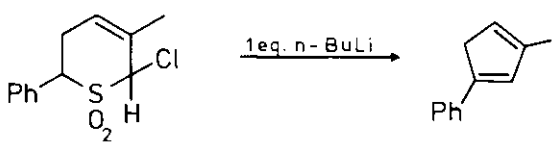
5 6 7

Reaction of the dichlorosulfone 5 with one equivalent of n-BuLi in THF at -78°C, followed by warming to room temperature, leads to a 1:1 mixture of 6 and 7 after neutralization with dilute acid. Chromatographic separation[3] afforded the monochlorosulfone 6 (34% yield) and 1-phenyl-2-chloro-3-methylcyclopentadiene (7, 26% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$): 7.81-7.64 (phenyl, m); 7.55-7.14 (phenyl, m); 6.11 (C4-H, m); 3.34 (C5-H, m); 2.03 (C3-Me, m). IR ($CHCl_3$): 2930, 1710, 1600, 1490, 1445 and 1375 cm^{-1}. UV_{max}^{EtOH}: 217 (7972); 297 (11568). Analysis: Calcd for $C_{12}H_{11}Cl$: C, 75.59; H, 5.82; Cl, 18.59. Found: C, 75.92; H, 6.31; Cl, 17.42. The compound is slightly unstable since the chlorine content, found by combustion analysis, gradually lowers upon standing.

The stereochemical configurations of the monochlorosulfones 6, prepared following Schemes 1 and 2 are identical according to ^{1}H NMR.

We assume that the observations must be explained by two competitive reactions of comparable velocity: i) the halogen/metal exchange of 5 with n-BuLi to 6 and ii) the Ramberg-Bäcklund rearrangement of 5 to give the lithium salt of 7, which is reprotonated regiospecifically at the C5-position[4].

Scheme 3



6 8

Since the monochlorosulfone 6 gives a smooth Ramberg-Bäcklund reaction with one equivalent of n-BuLi in THF at -78°C, converting one half of 6 into the lithium salt of 8 (Scheme 3), one would expect that two equivalents of base should result in complete conversion of 5 and 6 into the corresponding cyclopentadienes 7 and 8. However, we have been unable thus far to find the correct reaction conditions for this conversion[5].

Starting from 6, 1-phenyl-3-methyl-cyclopentadiene (8), mp 59-62°C, is obtained in 30% yield upon chromatographic separation[3] of the neutralized reaction mixture[6]. ^{1}H NMR ($CDCl_3$): 7.62-7.16 (phenyl, m); 6.76 (C2-H, broad s); 6.02 (C4-H, m); 3.35 (C5-H, m); 2.04 (C3-Me, m). IR ($CHCl_3$): 2920, 1595, 1485, 1445 and 1380 cm^{-1}.

UV_{max}^{EtOH}: 219 (8074); 304 (11650). Analysis: Calcd for $C_{12}H_{12}$: C, 92.26; H, 7.74. Found: C, 92.17; H, 7.87. The configuration of the recovered sulfone (28%) is identical to that of the starting sulfone 6.

Preliminary experiments with the mono- and dichlorinated thiapyran-1,1-dioxides, derived from prenyl-Z-2-methyl-1,3-butadienyl sulfone[7], showed an identical behaviour upon treatment with base.

REFERENCES AND NOTES

1. J.J. Burger, T.B.R.A. Chen, E.R. de Waard and H.O. Huisman, Tetrahedron, in press.
2. J.J. Burger, T.B.R.A. Chen, E.R. de Waard and H.O. Huisman, Tetrahedron, 1980, 36, 723.
3. The separations were performed on prepacked columns (Merck, Lobar, LiChroprep Si 60) using varying proportions of EtOAc and P.A. as an eluens at 2 atm pressure.
4. No double bond isomers of 7 were observed under the reaction circumstances.
5. Treatment with more than one equivalent of n-BuLi caused appreciable polymerization.
6. No isomers of 8 were observed. Purification of 8 by sublimation caused double bond isomerization of the initially formed cyclopentadiene.
7. J.J. Burger, T.B.R.A. Chen, E.R. de Waard and H.O. Huisman, Tetrahedron, in press.

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