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# ADDITION OF CHLOROSULPHONYL ISOCYANATE TO TETRASUBSTITUTED CYCLOPENTADIENES; A FACILE ROUTE FOR THE SYNTHESIS OF AZEPINES

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Abstract - The β-lactams 2, 2a obtained by the cycloaddition of chlorosulphonyl isocyanate to the dienes 1, 1a give the azepinones 5, 5a through the sulphonate esters 4, 4a. The sulphonate ester 6 obtained from 4, when treated with sodium hydride gives the dihydroazepine 8.

Chlorosulphonyl isocyanate (CSI)[1] is very reactive towards a variety of olefins[2]. Tetraphenylcyclopentadiene 1 and 7,9-diphenyl-8H-cyclopenta(a)-acenaphthylene 1a could react with CSI by many pathways. We wish to report a facile route for the synthesis of azepines through the sulphonate esters 4, 4a.

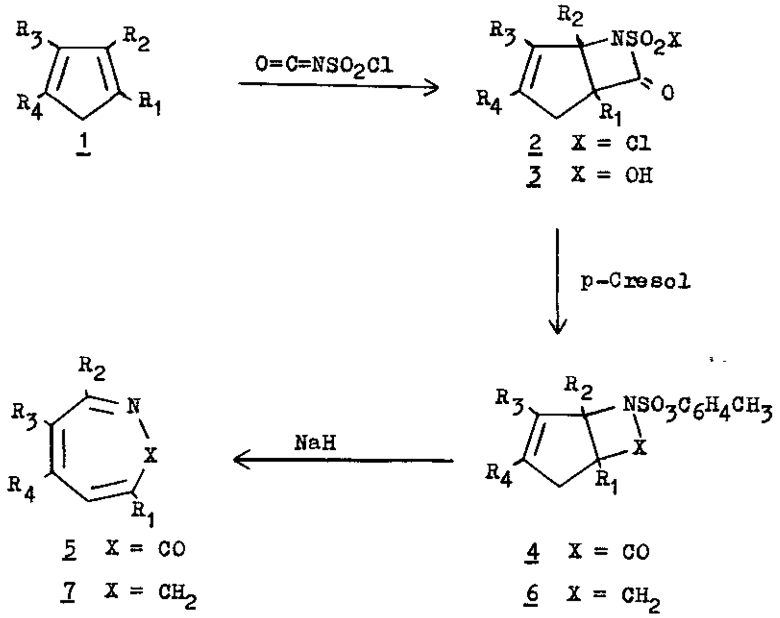
CSI rapidly reacted with tetraphenylcyclopentadiene in anhydrous ether to give the sulphonyl chloride 2, exhibited in its ir spectrum β-lactam carbonyl at 1755 $cm^{-1}$. The $^1$Hnmr spectrum of 2 showed the presence of allylic protons as a singlet at $\delta$ 4.24 in addition to a multiplet at $\delta$ 6.9-7.2 for the aromatic protons. The sulphonyl chloride 2 reacted with water to give the sulphonic acid 3 as a yellow stable solid. The ir spectrum of 3 exhibited the lactam carbonyl at 1725 $cm^{-1}$ and the shift in the lactam $\nu_{C=O}$ could be due to intramolecular hydrogen bonding between lactam >C=O and $SO_3H$ group. The $^1$Hnmr spectrum of 3 displayed sharp singlet at $\delta$ 4.53 for the allylic protons, a broad singlet at $\delta$ 5.65-5.75, which disappeared on adding $D_2O$ and the aromatic protons appeared as a multiplet at $\delta$ 6.8-7.2. 3 regenerated 1 when treated with ethanolic KOH. The equivalence of the allylic protons in $^1$Hnmr and the higher $\nu_{C=O}$ in ir lend support for the (2+2) mode of addition. Addition of CSI to indene has been reported to give similar β-lactam[3].

2 was converted to the p-toluenesulphonate ester 4 by reacting with p-cresol. The $^1$Hnmr spectrum of 4 displayed the allylic protons as a singlet at $\delta$ 4.31 and

another singlet at $\delta$2.23 for the methyl protons with aromatic protons at $\delta$ 6.9-7.2. Treatment of 4 with NaH in dry THF gave a product (mp 52°C, 40%) which in $^{1}$Hnmr showed only the aromatic protons as a multiplet at $\delta$ 7.0-7.4 and the ir spectrum showed the presence of $\nu_{C=O}$ at 1700 cm$^{-1}$ and $\nu_{C=N}$ at 1600 cm$^{-1}$. The compound was identified as 3,5,6,7-tetraphenyl-2H-azepin-2-one 5.

Reduction of 4 with $LiAlH_4$ in THF gave a colourless liquid 6, whose $^{1}$Hnmr spectrum showed a three-proton singlet at $\delta$ 2.08 and a two-proton singlet at $\delta$3.40. The allylic protons appeared as a singlet at $\delta$ 4.33. Treatment of 4 with NaH afforded 7 (mp 48°C, 30%) which in its $^{1}$Hnmr displayed a two-proton singlet at $\delta$ 4.02 in addition to the aromatic protons at $\delta$ 6.8-7.4.

The potentiality of the above synthetic route for the construction of azepinones was further explored with the sulphonyl chloride 2a derived from CSI and 1a. The sulphonate ester 4a was obtained by the reaction of p-cresol with 2a. Treatment of 4a with NaH in dry THF gave the azepinone 5a. The reaction sequence is summarised in the following scheme.



1, 2, 3, 4, 5, 6, 7 $R_1 = R_2 = R_3 = R_4 = Ph$

1a, 2a, 4a, 5a $R_1 = R_4 = Ph$, $R_2$ & $R_3$ =

## EXPERIMENTAL

All melting points are uncorrected. Ir spectra were recorded on Beckmann Ir-20 spectrophotometer with either KBr or $CHCl_3$ and $^1$Hnmr were obtained in $CCl_4$ using Perkin-Elmer R-32 (90 MHz) spectrophotometer. Chemical shifts are reported in δ units downfield from internal $Me_4Si$ and mass spectra were obtained at 70 ev.

### Recommended general procedure for the addition of CSI to the dienes

To a stirred solution of the diene (0.01 mol) in dry ether (40 ml) a solution of CSI (0.01 mol) in dry ether (10 ml) was added during 15 min. The reaction mixture was left overnight and removal of ether afforded the sulphonyl chloride.

### Reaction of CSI with 1 and 1a

Addition of CSI (1.41 g) to the diene 1 (3.70 g) gave the sulphonyl chloride 2 (4.09 g, 80%). Ir: νmax 3010, 2950, 1755, 1495, 1450, 1350 & 1170 $cm^{-1}$; $^1$Hnmr: 4.24 (S, 2H), 6.9-7.2 (m, 20 H); mass spectrum: m/z 511 ($M^+$), 513 $(M+2)^+$. Anal. calcd. for $C_{30}H_{22}Cl\ NO_3S$: C, 70.39; H, 4.30; N, 2.74. Found: C, 70.50; H, 4.24; N, 2.65%.

Addition of CSI (1.41 g to the diene 1a afforded 2a (3.38 g, 72%). Ir: νmax 3000, 2950, 1755, 1480, 1440, 1340 & 1150 $cm^{-1}$; $^1$Hnmr: 4.31 (S, 2H), 7.0-7.6 (m, 16 H); mass spectrum: m/z 483 ($M^+$), 485 $(M+2)^+$. Anal. calcd. for $C_{28}H_{18}Cl\ NO_3S$: C, 69.50; H, 3.72; N, 2.89. Found: C, 69.38; H, 3.70; N, 2.85%.

### Hydrolysis of 2 to the sulphonic acid 3

A mixture of 2 (5.11 g, 0.01 mol) when stirred with water (20 ml) afforded a bright yellow solid 3 (4.44 g, 90%), mp 198°C (ethanol). Ir νmax: 3400, 3250, 3030, 1725, 1490, 1450, 1380, 1180 $cm^{-1}$; $^1$Hnmr: 4.53 (S, 2H), 5.65-5.75(S, 1H) 6.8-7.2 (m, 20H); mass spectrum: m/z 493 ($M^+$). Anal. calcd. for $C_{30}H_{23}NO_4S$: C, 73.03; H, 4.66; N, 2.84. Found: C, 73.01; H, 4.69; N, 2.82%.

### General procedure for the formation of sulphonate esters

A mixture of the sulphonyl chloride (0.01 mol) and p-cresol (0.011 mol) in dry benzene (50 ml) was refluxed with few drops of concentrated $H_2SO_4$ for 5 h. The reaction mixture was poured onto ice (200 g) and extracted with ether (2 x 50 ml). The combined ether layer was washed with water and with dilute NaOH (20 ml, 3N). The ether layer was dried ($Na_2SO_4$) and evaporated to give the sulphonate ester. The sulphonate ester 4 and 4a were purified by distillation at low pressure.

### Reaction of the sulphonyl chloride 2 and 2a with p- cresol

Reaction of p-cresol (10.8 ml) with 2 (5.11 g) gave an viscous oil which on purification by distillation (58°C/20 mm) afforded 4 (4.49 g, 77%). Ir: $\nu_{max}$ 3000, 1755, 1600, 1330 & 1170 $cm^{-1}$; $^1$Hnmr: 2.23 (S, 3H), 4.31 (S, 2H), 6.9-7.2 (m, 24 H); mass spectrum: m/z 583 $(M)^+$. Anal. calcd. for $C_{37}H_{29}NO_4S$: C, 76.16; H, 4.97; N, 2.40. Found: C, 76.11; H, 4.95; N, 2.41%.

Reaction of p-cresol (10.8 ml) with 2a (4.83 g) afforded 4a (71°C/20 mm; 3.83 g, 69%). Ir: $\nu_{max}$ 3010, 1755, 1590, 1330 & 1160 $cm^{-1}$; $^1$Hnmr: 2.30 (S, 3H), 4.42 (S, 2H), 7.0-7.3 (m, 20 H); mass spectrum: m/z 555 $(M^+)$. Anal. calcd. for $C_{35}H_{25}NO_4S$: C, 75.68; H, 4.50; N, 2.52. Found: C, 75.76; H, 4.51; N, 2.53%.

### General procedure for the reaction of the sulphonate esters with NaH

To a stirred suspension of sodium hydride (0.025 mol) in anhydrous THF (50 ml) a solution of the sulphonate ester (0.02 mol) in THF (20 ml) was added in a dropwise manner during a period of 30 min under nitrogen atmosphere. The reaction mixture was stirred for 2.5 h at room temperature, then refluxed for 30 min, poured onto ice (250 g) and extracted with ether (2 x 30 ml). The combined ether layer washed with water, dried ($K_2CO_3$) and evaporated.

### Reaction of the sulphonate ester 4 and 4a with NaH

Reaction of the sulphonate ester 4 (11.66 g) with NaH (0.60 g) in THF gave the azepinone 5 (3.30 g, 40%) mp 52°C (Petrol). Ir: $\nu_{max}$ 3010, 1700, 1600, 1450 $cm^{-1}$; $^1$Hnmr: 7.0-7.4 (m); mass spectrum: m/z 411 $(M^+)$. Anal. calcd. for $C_{30}H_{21}NO$: C, 87.59; H, 5.11; N, 3.41. Found: C, 87.85; H, 5.05; N, 3.34%.

Sulphonyl ester 4a (11.10 g) under similar condition gave 5a (3.60 g, 45%) mp 57°C (Petrol). Ir: $\nu_{max}$ 3000, 1690, 1600, 1450, 1380 $cm^{-1}$; $^1$Hnmr: 7.1-7.6 (m); mass spectrum: m/z 383 $(M^+)$. Anal. calcd. for $C_{28}H_{17}NO$: C, 87.73; H, 4.44; N, 3.66. Found: C, 87.8; H, 4.24; N, 3.55%.

### $LiAlH_4$ reduction of 4

A mixture of 4 (5.83 g, 0.01 mol) and $LiAlH_4$ (0.38 g, 0.01 mol) in anhydrous THF (50 ml) was stirred at room temperature for 1.5 h and then refluxed over water bath for 2 h. Unreacted $LiAlH_4$ was decomposed by adding ethyl acetate (5 ml). The reaction mixture was poured onto ice (250 g) and extracted with ether (2 x 40ml). Removal of ether afforded 6 (50°C/19 mm) (2.56 g, 45%). Ir: $\nu_{max}$ 3030, 1580, 1450, 1420, 1330, 1200, 1170 $cm^{-1}$; $^1$Hnmr: 2.08 (S, 3H), 3.40 (S, 2H), 4.33 (S, 2H), 7.1-7.8 (m, 24 H); mass spectrum: m/z 569 ($M^+$). Anal. calcd. for $C_{37}H_{31}NO_3S$: C, 78.03; H, 5.45; N, 2.46. Found: C, 78.09; H, 5.49; N, 2.45%.

### Reaction of 6 with NaH

Reaction of the sulphonate ester 6 (5.69 g, 0.01 mol) with NaH (0.36 g, 0.015 mol) in dry THF (50 ml) after usual work-up afforded the dihydroazepine 7 (1.16 g, 30%) mp 48°C (Petrol). Ir: $\nu$max 3020, 1600, 1580, 1450 $cm^{-1}$. $^1$Hnmr: 4.02 (S, 2H), 6.8-7.4 (m, 21 H); mass spectrum: m/z 397 ($M^+$). Anal. calcd. for $C_{30}H_{23}N$; C, 90.68; H, 5.79; N, 3.53. Found: C, 93.15; H, 5.98; N, 3.58%.

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