Dimethyl Carbonate as a Methylating Agent. The Selective Mono-C-methylation of Alkyl Aryl Sulfones

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At 180–210 °C, z-methylene sulfones (both benzyl aryl and alkyl aryl sulfones, RCH₂SO₂Ar: R = Ph, p-CI₂CH₃, p-MeC₆H₄, and R = Me, Ar = Ph, p-CI₂CH₃, p-MeC₆H₄) react with dimethyl carbonate to yield the corresponding mono-C-methyl derivatives [RCH₂(CH₃)SO₂Ar] in a selectivity >99%, at conversions of 76–99% (isolated yields: 97–92%).

<table>
<thead>
<tr>
<th>R</th>
<th>Ar</th>
<th>T/°C</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>Ph</td>
<td>180</td>
<td>78</td>
</tr>
<tr>
<td>3b</td>
<td>p-CI₂CH₃</td>
<td>180</td>
<td>76</td>
</tr>
<tr>
<td>3c</td>
<td>p-MeC₆H₄</td>
<td>180</td>
<td>92</td>
</tr>
<tr>
<td>3g</td>
<td>Ph</td>
<td>180</td>
<td>80</td>
</tr>
<tr>
<td>3h</td>
<td>p-CI₂CH₃</td>
<td>180</td>
<td>81</td>
</tr>
<tr>
<td>3d</td>
<td>Ph</td>
<td>200</td>
<td>85</td>
</tr>
<tr>
<td>3e</td>
<td>p-CI₂CH₃</td>
<td>200</td>
<td>77</td>
</tr>
<tr>
<td>3f</td>
<td>p-MeC₆H₄</td>
<td>210</td>
<td>76</td>
</tr>
</tbody>
</table>

A major influence on reactivity arises from the different ary1 and alkyl groups directly bound to the methane reacting group: thus benzyl aryl sulfones (ArCH₂SO₂Ar*: 2a–c, g–h) are efficiently mono-methylated at 180 °C while alkyl aryl sulfones (MeCH₂SO₂Ar: 2d–f) do not, and actually require a more elevated reaction temperature of 200–210 °C for the reaction to go to completion. Such a behaviour seems to be clearly related to the stabilization of aryl sulfonyl carbanions [ArSO₂CHAr* formed during the reactions] induced by the resonance with the adjacent Ar* group.

The methylation of the sulfones 2a–h follows, in all likelihood, the mechanistic pattern reported for aryl- and aralkyloxyacetic acid derivatives. Accordingly, the monomethyl selectivity is explicable through the occurrence of two consecutive nucleophilic displacements (Scheme 1): (i) a methoxycarbonylation of the initially formed sulfonyle carbanion [ArSO₂CHR] (B₃ mechanism) followed by (ii) a methylation of the resulting intermediate [ArSO₂CH(CO₂Me)Ar] (iVA mechanism) yielding the methyl derivative [ArSO₂CH(CO₂Me)Ar] (5); B₄ mechanism). Finally, compound 5 undergoes a de-methoxycarbonylation reaction to the final product [ArSO₂CH(Me)R].

**Scheme 1** Suggested mechanism for the mono-C-methylation of alkyl aryl sulfones with dimethyl carbonate

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Both intermediates 4 and 5 are detected during the reaction of DMC with sulfones 3a–h (maximum amount of 10–30%, by GC; structures assigned by GC–MS).

Also, methyl aryl sulfones (ArSO₂CH₃) react with DMC as in Scheme 1: the formation of methoxy carbonylated compounds (ArSO₂CH₂CO₂Me) as intermediates, allows the homologation of the methyl group to an isopropyl one. Thus, PhSO₂Me yields PhSO₂CHMe₂ and PhSO₂C(CO₂Me)Me₂ (6) (12 and 81%, respectively; 14 h at 180 °C; conversion 93%). Likewise, PhCH₂SO₂Me affords PhCH(Me)SO₂CHMe₂ and PhCH(Me)SO₂C(CO₂Me)(Me₂) (7) (14 and 50%, respectively; 21.5 h at 180 °C; conversion 98%). Compounds 6 and 7 have been isolated in 63 and 34% yields, respectively (characterized by ¹H and ¹³C NMR spectra).

¹H NMR and GC–MS spectra are given in the full text for all products.

The synthesis here discussed has both synthetic advantages and remarkable environmental benefits: (i) it affords selectively only mono-methyl derivatives; (ii) it uses an intrinsically safe methylating agent (DMC) in place of the toxic methyl chloride (or dimethyl sulfate); (iii) it gives neither organic nor inorganic by-products (alkylation procedures using alkyl halides cannot avoid the formation of stoichiometric amounts of inorganic salts to be disposed of); (iv) it does not require additional solvents. Moreover, the procedure discloses intriguing perspectives of the chemistry of sulfonyl carbamions since it shows that these anionic moieties can actually be generated also in the presence of very mild bases.

Techniques used: ¹H and ¹³C NMR, GC and GC–MS

References: 24

Table 1: Yields, reaction temperature and times, purification for products 3a–h

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