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**PROCEDURE FOR LARGE-SCALE PREPARATIONS  
OF OLIGOETHYLENE GLYCOL TOLUENESULPHONATES\***Ivan STIBOR<sup>a</sup>, Oldřich KOCIÁN<sup>b</sup>, Petr HOLÝ<sup>a</sup> and Jiří ZÁVADA<sup>a</sup><sup>a</sup> *Institute of Organic Chemistry and Biochemistry,  
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Phase transfer catalysis allows a synthesis of oligoethylene glycol di-*p*-toluenesulphonates *IVa–e* and *V* from the corresponding diols *Ia–e* and *II*, respectively, in yields  $\geq 95\%$ . A preferential tosylation of primary hydroxyl groups in the diols *IIIa* and *IIIb* can be also accomplished almost quantitatively under the phase-transfer conditions.

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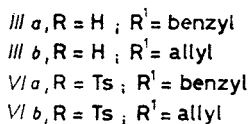
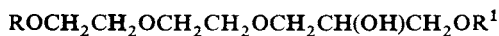
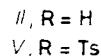
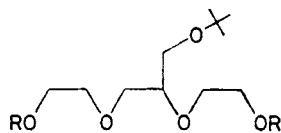
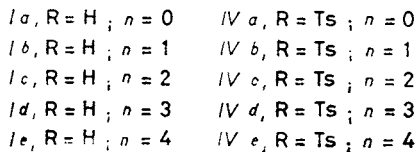
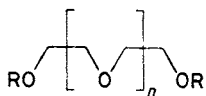
Oligoethylene glycol toluenesulphonates constitute versatile building blocks for synthesis of crown ethers, cryptands, and their open-chain analogues. Preparations on large scale are often required owing to increasing importance of the multisite ligands both in industry and research<sup>1,2</sup>.

The established tosylation procedure utilizing pyridine as a condensing agent<sup>3</sup> is *a priori* inconvenient for large-scale preparations. Moreover, the procedure does not work well when primary alcohols are involved, proclivity of primary toluenesulphonates to a rapid ( $S_N2$ ) decomposition<sup>4</sup> with pyridine being the impending factor. Accordingly, only mediocre yields of oligoethylene glycol toluenesulphonates by this procedure have been obtained<sup>5</sup>. Looking for a more effectual solution of the practical problem, we examined reaction of a series of unsubstituted and alkoxy-methyl-substituted oligoethylene glycols with *p*-toluenesulphonyl chloride and sodium hydroxide under phase-transfer conditions. Successful application of phase-transfer catalysis in sulphonylation reactions has been already reported<sup>6,7</sup>.

We now report that with aid of phase-transfer catalysis excellent yields of di-*p*-toluenesulphonates *IVa–e* and *V* from the parent diols *Ia–e* and *II*, respectively, can be obtained. At the same time we report that a highly selective synthesis of the mono-*p*-toluenesulphonates *VIa* and *VIb* from the  $\omega$ -alkoxymethyl-substituted diols *IIIa* and *IIIb*, respectively, can be also accomplished in high yields under the phase-transfer conditions. The alkoxy-methyl-substituted *p*-toluenesulphonates are useful for synthesis of functionalized crowns.

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\* Part V in the series Chemistry of Multidentate Ligands; Part IV: Collect. Czech. Chem. Commun. 50, 1184 (1985).



For compound *VII* see  
 formula *V* with one Ts group  
 only, R = H or Ts.

## EXPERIMENTAL

Analytical samples were dried *in vacuo* (6.5 Pa) at ambient temperature. Melting points were determined on a Kofler block and are uncorrected. Unsubstituted oligoethylene glycols *Ia–e* were commercial samples (Aldrich 99%). Alkoxyethyl-substituted glycols *II*, *IIIa*, and *IIIb* were prepared by the known procedures<sup>8,9</sup>.

### Unsubstituted Oligoethylene Glycol Di-*p*-toluenesulphonates *IVa–e*

A solution of *p*-toluenesulphonyl chloride (630 g; 3.3 mol) in dichloromethane (750 ml) was slowly added (30 min) under stirring and cooling (ice-bath) to a mixture of an appropriate diol *Ia–e* (1.5 mol), 30% aqueous sodium hydroxide (1.125 ml), dichloromethane (1.500 ml), and triethylbenzylammonium chloride (13.5 g). At ambient temperature stirring was continued until *p*-toluenesulphonyl chloride disappeared (4–6 h; monitored by thin-layer chromatography on Silufol UV 254 with CH<sub>2</sub>Cl<sub>2</sub> as eluent). Thereafter the mixture was poured into water (500 ml), the organic layer was separated, washed with water (3 × 750 ml), dried (MgSO<sub>4</sub>) and solvent was taken down on rotatory evaporator. Purity of the crude product was checked by a flash chromatography (silicagel; 20 : 1 : 1 mixture of benzene, dioxane, and ethylacetate) and it was found to be better than 95%. Yields and melting points are summarized in Table I.

### 4-Tert-butyloxymethyl-3,6-dioxaoctane-1,8-diol Mono- and Di-*p*-toluenesulphonates (*VII* and *V*)

The title compounds were prepared from diol *II* (23.8 g; 0.1 mol) and *p*-toluenesulphonyl chloride (42 g; 0.22 mol) under analogous conditions as described above for the compounds *IVa–e*, except for a prolonged reaction time (72 h at ambient temperature). Flash chromatography

(silicagel; elution with a benzene-dioxane-ethyl acetate mixture in 20 : 1 : 1—5 : 1 : 1 gradient) of the crude product afforded 48 g (88%) of the diester *V* and 3.5 g (7%) of the monoester *VII*. Yields, elemental analyses, and spectral data are summarized in Tables II and III.

1-Alkoxyethyl-9-*p*-toluenesulphonyloxy-4,7-dioxanonane-2-ols (*VIa*, *VIb*)

The title compounds were prepared analogously from diols *IIIa* and *IIIb* by treatment with an equimolar amount (10% excess) of *p*-toluenesulphonyl chloride. After stirring for 15 min at 0—5°C the mixture was worked-up as described above. According to flash chromatography

TABLE I

Tosylation of unsubstituted glycols: Melting points and yields

Product	Starting glycol	M.p., °C	Yield, %
<i>IVa</i>	<i>Ia</i>	125—126 <sup>a</sup> (ref. <sup>4</sup> 126—127)	93 (85 <sup>a</sup> )
<i>IVb</i>	<i>Ib</i>	98 <sup>a</sup> (ref. <sup>5</sup> 98)	95 (84 <sup>a</sup> )
<i>IVc</i>	<i>Ic</i>	78 <sup>a</sup> (ref. <sup>5</sup> 78)	95 (85 <sup>a</sup> )
<i>IVd</i>	<i>Id</i>	— <sup>b</sup>	95
<i>IVe</i>	<i>Ie</i>	— <sup>c</sup>	95

<sup>a</sup> After crystallization from ethanol. <sup>b</sup> Oil; *cf.* ref.<sup>5</sup>. <sup>c</sup> Oil; not described in literature. For C<sub>24</sub>H<sub>34</sub>.O<sub>10</sub>S<sub>2</sub> (546.7) calculated: 52.72% C, 6.27% H; found: 52.48% C, 6.17% H. Spectral data are in Table III.

TABLE II

Tosylation of alkoxyethyl-substituted glycols: Yields and elemental analyses

Product	Starting glycol	Yield %	Formula (mol. weight)	Calculated/found	
				% C	% H
<i>V</i>	<i>II</i>	88	C <sub>25</sub> H <sub>36</sub> O <sub>9</sub> S <sub>2</sub> (544.7)	55.13 55.40	6.66 6.72
<i>VIa</i>	<i>IIIa</i>	89	C <sub>21</sub> H <sub>28</sub> O <sub>7</sub> S (424.5)	59.42 59.58	6.64 6.50
<i>VIb</i>	<i>IIIb</i>	92	C <sub>17</sub> H <sub>26</sub> O <sub>7</sub> S (374.5)	54.52 54.52	7.00 6.82
<i>VII</i>	<i>II</i>	7 <sup>a</sup>	C <sub>18</sub> H <sub>30</sub> O <sub>7</sub> S (390.5)	55.37 55.52	7.74 7.68

<sup>a</sup> As a by-product in preparation of *V*.

TABLE III  
Spectral data of new *p*-toluenesulphonates

Compound	<sup>1</sup> H NMR: $\delta$ (assignment)	Mass spectra: $m/z$ (rel. intensity, %)
<i>IVe</i>	2.42 s, 6 H (CH <sub>3</sub> ); 3.60 m, 16 H (CH <sub>2</sub> O); 4.08 m, 4 H (CH <sub>2</sub> OTs); 7.25, 7.40, 7.75, 7.90 4 H (AB, H arom.)	91(100); 63(61); 199(29); 158(26); 65(26); 107(16); 243(2)
<i>V</i>	1.52 m, 9 H (CH <sub>3</sub> ); 2.43 s, 3 H (CH <sub>3</sub> -Ar); 3.2-3.85 m, 9 H (CH <sub>2</sub> -O, CH-O); 4.00-4.25 m, 4 H (CH <sub>2</sub> OTs); 7.22, 7.56, 7.70, 7.84 4 H (AB, H arom.)	91(100); 65(45); 87(25); 155(13); 100(8); 172(6); 107(6); 199(3)
<i>VIa</i>	2.40 s, 3 H (CH <sub>3</sub> ); 3.40-3.85 m, 11 H (CH <sub>2</sub> O, CH-O); 4.00-4.20 m, 2 H (CH <sub>2</sub> OTs); 4.53 s, 2 H (C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> -O); 7.28, 7.53, 7.70, 7.85 4 H (AB, Ts); 7.28 bs, 5 H (H arom.)	91(100); 65(23); 155(10); 105(7); 199(6); 172(2); 303(1)
<i>VIb</i>	2.40 s, 3 H (CH <sub>3</sub> ); 3.40-3.80 m, 11 H (CH <sub>2</sub> O, CH-O); 3.90-4.30 m, 4 H (CH <sub>2</sub> OTs, CH <sub>2</sub> -CH=); 5.00-6.20 m, 3 H (CH <sub>2</sub> =CH-); 7.25, 7.40, 7.70, 7.85 4 H (AB, H arom.)	91(100); 199(96); 155(91); 65(24); 58(14); 303(10); 59(10); 57(10)
<i>VII</i>	1.20 m, 9 H (CH <sub>3</sub> ); 2.42 s, 3 H (CH <sub>3</sub> ); 3.3-3.9 m, 11 H (CH <sub>2</sub> -O, CH-O); 3.95-4.3 m, 2 H (CH <sub>2</sub> OTs); 7.22, 7.46, 7.68, 7.92 4 H (AB, H arom.)	57(100); 91(66); 65(23); 87(18); 155(15); 101(6); 199(5)

(silicagel; benzene-dioxane-ethyl acetate 10 : 1 : 1), purity of the crude product was better than 95%. Yields, elemental analyses, and spectral data are summarized in Tables II and III.

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