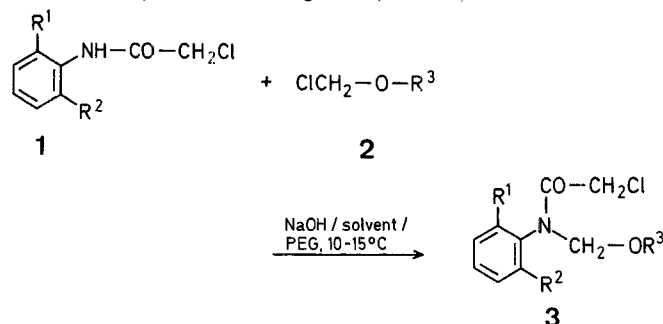
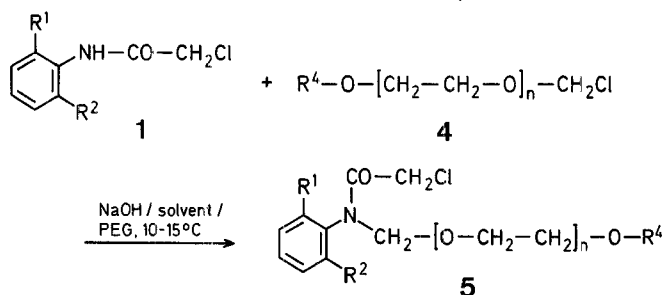


Now we report a promising new method for the preparation of *N*-alkoxymethyl derivatives **3** using the phase-transfer technique in the presence of polyethylene glycols (PEG) as neutral, open-chain ligands. It is interesting to mention that, in contrast to *C*-methoxymethylation under phase transfer-catalysed (PTC) conditions with benzyltriethylammonium chloride (TEBA) as catalyst where dimer formation was reported<sup>3</sup>, *N*-alkoxymethylation proceeds smoothly under mild conditions and so the formation of alkoxymethyl derivatives **3** was observed in yields exceeding 90% (Table 1).



By the same method, some *N*-alkoxyethoxymethyl derivatives **5** of acylanilines were also accessible (Table 2). As in some previous cases<sup>6,7,8,9,10</sup>, in all experiments presented, polyethylene glycols (PEG) of different average relative molecular mass  $\bar{M}$ , inexpensive and also on an industrial scale accessible compounds, served as phase-transfer catalysts.



The corresponding alkoxymethyl chlorides **2** and alkoxyethoxymethyl chlorides **4** were prepared in accordance with the Wedekind method<sup>11</sup>, with the modification that a rapid stream of gaseous hydrogen chloride was passed through the moderately stirred mixture of paraformaldehyde and alcohol, respectively, glycol monoether.

***N*-Butoxymethyl-*N*-chloroacetyl-2,6-diethylaniline (3d); Typical Procedure:**

2,6-Diethylchloroacetylaniline (6.77 g, 0.030 mol) in benzene (30 ml), PEG-400 (2.40 g, 0.006 mol), and 52% aqueous sodium hydroxide (4.80 g in 4.34 ml water) are placed in a flask, equipped with a magnetic stirrer. *n*-Butoxymethyl chloride (5.52 g, 0.045 mol) in benzene (6 ml) is added dropwise over a period of 15 min at a temperature of 15 °C. After addition, the mixture is stirred for 2 h at the same temperature, diluted with water (3 × 36 ml), the solvent is removed under reduced pressure and the residue digested with petroleum ether (b. p. 40–70 °C; 44 ml) in order to remove unreacted **1**. The mixture is cooled, filtered and the filtrate washed with water (3 × 18 ml). The solvent is removed under reduced pressure. The product is a pale yellow liquid; yield: 8.19 g (88%); purity: 94.8% (G.L.C., 3% OV 17 on silica gel at 250 °C; F.I.D.).

$C_{17}H_{26}ClNO_2$	calc.	Cl 11.37
(311.8)	found	10.9

***N*-Methoxyethoxymethyl-*N*-chloroacetyl-2,6-dimethylaniline (5a); Typical Procedure:**

2,6-Dimethyl-*N*-chloroacetylaniline (19.77 g, 0.1 mol) in benzene (100 ml), PEG-400 (8.0 g, 0.02 mol), and 52% aqueous sodium hydroxide (16.0 g in 14.8 ml water) are placed in a flask equipped with a mechan-

### Preparation of Alkoxymethyl and Alkoxyethoxymethyl Derivatives of Acylanilines using Polyethylene Glycols as Phase Transfer Catalysts

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*N*-Alkoxyalkyl derivatives **3** of acylanilines **1** are compounds of considerable interest because of the biological activity many of them exhibit<sup>1</sup>. Hitherto in the case of *N*-alkoxymethyl derivatives the only path described was that proceeding over the Schiff base which is not easily accessible<sup>2</sup>.

Table 1. *N*-Alkoxyethylation of Acylanilines<sup>4,5</sup> 1

Product <sup>a</sup> No.	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Yield [%] <sup>b</sup>	m.p. [°C] or n <sub>D</sub> <sup>20</sup> or b.p. [°C]/torr	Molecular formula or Lit. data	I.R. (film) [cm <sup>-1</sup> ]	
							$\nu_{C=O}$	$\nu_{C-O-C}$
3a	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	93	38–40°	40–41° <sup>13</sup> ; 152–153.5°/0.1 <sup>13</sup>	1700	1070
3b	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	87	1.5196	— <sup>c</sup>	1700	1110
3c	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	67	1.5184	— <sup>c</sup>	1700	1070
3d	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	88	1.5149	— <sup>c</sup>	1700	1110
3e	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub>	85	1.5112	— <sup>c</sup>	1700	1090
3f	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	CH(CH <sub>3</sub> )OCH <sub>3</sub>	61	1.5180; 154–155°/0.07	C <sub>16</sub> H <sub>24</sub> ClNO <sub>3</sub> (313.8) <sup>d</sup>	1690	1060
3g	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	CH(CH <sub>3</sub> )OCH <sub>3</sub>	69	1.5170; 151–156°/0.05–0.07	C <sub>17</sub> H <sub>26</sub> ClNO <sub>3</sub> (327.9) <sup>e</sup>	1690	1060
3h	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	95	1.5272; 134°/0.4	— <sup>c</sup>	1690	1090
3i	CH <sub>3</sub>	CH <sub>3</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub>	87	1.5111	— <sup>c</sup>	1700	1070

<sup>a</sup> Molar ratio of 1 : 2 : NaOH : PEG-400 = 1 : 1.5 : 5 : 0.2; reaction time 2 h at 15 °C.

<sup>b</sup> Yield of isolated product; purity: ≤95% by G.L.C. and Cl analysis. Purity sufficient for practical application as herbicides<sup>7</sup>, e.g., 3a, 3d, 3h, 3i.

<sup>c</sup> Cl Analysis ±0.52% by destruction of organic material in ethylene glycol/KOH followed by potentiometric titration of chloride ion<sup>14</sup>.

<sup>d</sup> calc. C 61.24 H 7.71 N 4.46

found 61.06 7.82 4.64

<sup>e</sup> calc. C 62.28 H 7.99 N 4.27

found 61.65 7.82 4.36

Table 2. *N*-Alkoxyethoxymethylation of Acylanilines 1

Product <sup>a</sup> No.	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	n	Yield [%] <sup>b</sup>	b.p. [°C]/ torr (n <sub>D</sub> <sup>20</sup> )	Molecular formula <sup>c</sup>	I.R. (film) [cm <sup>-1</sup> ]		<sup>1</sup> H-N.M.R. (CDCl <sub>3</sub> ) δ [ppm]
								$\nu_{C=O}$	$\nu_{C-O-C}$	
5a	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	1	79	152–153°/0.1 (1.5271)	C <sub>14</sub> H <sub>20</sub> ClNO <sub>3</sub> (285.6)	1690	1100	2.20 (s, 6H); 3.27 (s, 3H); 3.4–4.0 (m, 4H); 3.67 (s, 2H); 5.02 (s, 2H); 6.9–7.3 (m, 3H)
5b	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	1	73	155–158°/0.1 (1.5252)	C <sub>15</sub> H <sub>22</sub> ClNO <sub>3</sub> (299.8)	1690	1100	1.23 (t, 3H, <i>J</i> = 8 Hz); 2.23 (s, 3H); 2.56 (q, 2H, <i>J</i> = 8 Hz); 3.4–4.0 (m, 4H); 3.68 (s, 2H); 5.04 (s, 2H); 6.9–7.5 (m, 3H)
5c	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	1	73	155–159°/ 0.07–0.1 (1.5201)	C <sub>16</sub> H <sub>24</sub> ClNO <sub>3</sub> (313.8)	1690	1100	1.24 (t, 6H, <i>J</i> = 8 Hz); 2.58 (q, 4H, <i>J</i> = 8 Hz); 3.30 (s, 3H); 3.4–4.0 (m, 4H); 3.68 (s, 2H); 5.04 (s, 2H); 7.0–7.5 (m, 3H)
5d	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	1	73	162–165°/0.1 (1.5232)	C <sub>16</sub> H <sub>24</sub> ClNO <sub>3</sub> (313.8)	1690	1100	1.17 (t, 3H, <i>J</i> = 6 Hz); 1.23 (t, 3H, <i>J</i> = 8 Hz); 2.24 (s, 3H); 2.57 (q, 2H, <i>J</i> = 8 Hz); 3.53 (q, 2H, <i>J</i> = 6 Hz); 3.4–4.1 (m, 4H); 3.69 (s, 2H); 5.05 (s, 2H); 7.0–7.5 (m, 3H)
5e	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	1	90	165–166°/0.1 (1.5183)	C <sub>17</sub> H <sub>26</sub> ClNO <sub>3</sub> (327.9)	1690	1100	1.17 (t, 3H, <i>J</i> = 6 Hz); 1.23 (t, 6H, <i>J</i> = 8 Hz); 2.57 (q, 4H, <i>J</i> = 8 Hz); 3.53 (q, 2H, <i>J</i> = 6 Hz); 3.69 (s, 2H); 5.05 (s, 2H); 3.4–4.1 (m, 4H); 7.0–7.6 (m, 3H)
5f	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	2	70	188–191°/ 0.07–0.1 (1.5135)	C <sub>18</sub> H <sub>28</sub> ClNO <sub>4</sub> (357.9)	1700	1120	1.17 (t, 3H, <i>J</i> = 6 Hz); 1.24 (t, 3H, <i>J</i> = 8 Hz); 2.26 (s, 3H); 2.56 (q, 2H, <i>J</i> = 8 Hz); 3.52 (q, 2H, <i>J</i> = 6 Hz); 3.4–4.1 (m, 8H); 3.68 (s, 2H); 5.06 (s, 2H); 7.0–7.5 (m, 3H)
5g	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	2	74	202–203°/0.15 (1.5125)	C <sub>19</sub> H <sub>30</sub> ClNO <sub>4</sub> (371.9)			1.18 (t, 3H, <i>J</i> = 6 Hz); 1.24 (t, 6H, <i>J</i> = 8 Hz); 2.58 (q, 4H, <i>J</i> = 8 Hz); 3.57 (q, 2H, <i>J</i> = 6 Hz); 3.4–4.1 (m, 8H); 3.68 (s, 2H); 5.06 (s, 2H); 7.1–7.5 (m, 3H)

<sup>a</sup> Molar ratio of 1 : 2 : NaOH : PEG-400 = 1 : 1.5 : 4 : 0.2; reaction time: 2 h at 15 °C.

<sup>b</sup> Yield of distilled product.

<sup>c</sup> Satisfactory microanalyses obtained: C ±0.30, H ±0.24, N ±0.14.

ical stirrer. Methoxyethoxymethyl chloride (18.69 g, 0.115 mol) in benzene (20 ml) is added dropwise over a period of 15 min at a temperature of 15 °C. After the addition, the mixture is stirred for 2 h at the same temperature and then diluted with water (120 ml). The organic layer is separated and washed with water (3 × 60 ml). The solvent is removed under reduced pressure and the residue digested with petroleum ether (b.p. 40–70 °C; 110 ml) in order to remove unreacted 1. The mixture is cooled, filtered, and filtrate washed with water (3 × 60 ml). The solvent is removed under reduced pressure and the residue

distilled in vacuo in a stream of dry hydrogen. The distilled product is a pale yellow liquid; yield: 22.5 g (79%); n<sub>D</sub><sup>20</sup>: 1.5271; b.p. 152–153 °C/0.1 torr.

C <sub>14</sub> H <sub>20</sub> ClNO <sub>3</sub> (285.8)	calc.	C 58.84	H 7.05	H 4.90
	found	58.82	6.81	5.01

#### *n*-Butoxymethyl Chloride; Typical Procedure:

*n*-Butanol (311.32 g, 4.2 mol) and 95% paraformaldehyde (132.75 g, 4.2 mol) are placed in a flask equipped with mechanical stirrer. The mix-

ture is cooled in an ice bath and dry hydrogen chloride is bubbled through it with gentle mixing. The stream of hydrogen chloride is maintained so that the temperature of the reaction mixture is 15–20 °C. After 3.25 h, the reaction is completed and the water layer separated. The crude product (a slightly opalescent liquid) is dried with calcium chloride and fractionated in a stream of dry hydrogen over a column (10 cm length) filled with Braunschweig spirals. The distilled product is a colourless liquid; yield: 386.73 g (75%); b.p. 132 °C/760 torr;  $n_D^{20}$ : 1.4183; Ref.<sup>12</sup>, b.p. 134 °C/760 torr; Ref.<sup>12</sup>,  $n_D^{20}$ : 1.4208.

C <sub>5</sub> H <sub>11</sub> ClO	calc.	Cl 28.92
(122.5)	found	28.3

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