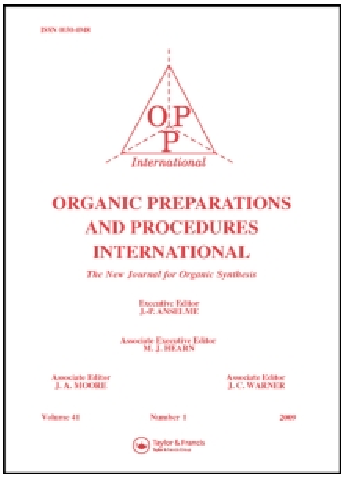

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

PHASE TRANSFER CATALYZED N-ALKYLATION OF *sym*-N,N'-DIARYLUREAS

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To cite this Article Kalkote, U. R. , Choudhary, A. R. and Ayyangar, N. R.(1992) 'PHASE TRANSFER CATALYZED N-ALKYLATION OF *sym*-N,N'-DIARYLUREAS', Organic Preparations and Procedures International, 24: 1, 83 — 87
To link to this Article: DOI: 10.1080/00304949209356709
URL: http://dx.doi.org/10.1080/00304949209356709

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PHASE TRANSFER CATALYZED N-ALKYLATION OF *sym*-N,N'-DIARYLUREAS[†]

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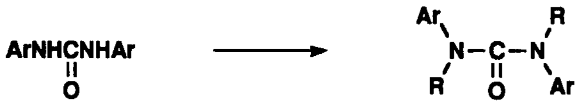
sym-N,N'-Diethyldiphenylurea (Centralite I) is used commercially as stabilizer for a number of explosives.[1] Recently a non-phosgene route involving the N-ethylation of *sym*-N,N'-diphenylurea (DPU) using phase-transfer catalyst (PTC) has been reported.[2] As an extension of our work on the N-alkylation of benzanilides[3] and aminoanthraquinones,[4] we now describe the alkylation of diarylureas (DAU, **1a-d**) in the presence of base and phase-transfer catalysts.

Alkylation of DAU with diethyl sulfate, in presence of triethylbutylammonium bromide (TEBuAB), was studied using different alkalis. The results are summarized in Table 1. The use of a mixture of powdered sodium hydroxide and potassium carbonate as alkali proved to be ideal. Alkylation of **1a** with diethyl sulfate in the presence of a mixture of powdered sodium hydroxide and



1

a) Ar = C_6H_5
b) Ar = 2-ClC_6H_4
c) Ar = 3-MeC_6H_4
d) Ar = 4-$MeOC_6H_4$

2

a) Ar = C_6H_5, R = Me
c) Ar = C_6H_5, R = n-C_3H_7
e) Ar = C_6H_5, R = $PhCH_2$
g) Ar = 2-ClC_6H_4, R = Et
e) Ar = 3-MeC_6H_4, R = Et
k) Ar = 4-$MeOC_6H_4$, R = Et

b) Ar = C_6H_5, R = Et
d) Ar = C_6H_5, R = n-C_4H_9
f) Ar = 2-ClC_6H_4, R = Me
h) Ar = 3-MeC_6H_4, R = Me
j) Ar = 4-MeC_6H_4 R = Me

potassium carbonate was carried out using different PTC. The results are presented in Table 2. The use of tetrabutylammonium hydrogen sulfate (TBuAHS), tetrapropylammonium hydrogen sulfate

TABLE 1. Ethylation of **1a** Using Different Alkali[a]

Alkali	Time (hrs)	Yield (%)
1. 50% NaOH (5.0 mol)	7	78
2. Powdered NaOH (5.0 mol)	4	85
3. Powdered NaOH (5.0 mol)+ Powdered K_2CO_3 (1.0 mol)	4	93
4. Powdered NAOH (5.0 mol)+ Powdered NA_2CO_3 (1.0 mol)	4	89

a) In all reactions PTC used is triethylbutylammonium bromide. Ethylating agent used is diethyl sulfate 2..2 mol/1 mol of substrate and the reaction temperature is toluene at reflux.

TABLE 2: Ethylation of **1a** Using Different PTC

PTC	Time (hrs)	Yield (%)	PTC	Time (hrs)	Yield (%)
	6	36	TBUAB	4	95
TEBuAB	4	93	TBUAC	4	95
TEBAC	4	92	TBUAHS	3	97
TEBuAHS	3	96	TPABR	4	92
TBuAI	5	90	TPAHS	3	95

In all reactions base used is a mixture of powdered NaOH(5.0 mol) and potassium carbonate (1.0 mol) per mol of substrate and 2.20 mol of diethylsulfate as ethylating agent. The temperature of all reactions is toluene at reflux.

(TPAHS) and triethylbutylammonium hydrogen sulfate (TEBuAHS) gave better results than triethylbutylammonium bromide (TEBuAB), triethylbenzylammonium chloride (TEBAC), tetrabutylammonium iodide (TBuAI), tetrapropylammonium bromide (TPAB), tetrabutylammonium bromide (TBuAB) and tetrabutylammonium chloride (TBuAC). TEBuAHS was chosen as PTC catalyst because it is less expensive (Table 3).

TABLE 3. Alkylation of Diarylureas (**1a-d**) to N,N-Dialkyldiarylureas (**2a-k**).

Urea	Alkylating Agent	Time (hrs)	Product	Yield (%)	mp. (°C)	lit. (°C)
1a	Me_2SO_4	3	**2a**	92	122	121[5]
1a	Et_2SO_4	3	**2b**	93	73	74[6]
1a	$n-C_3H_7Br$	4	**2c**	91	39	—
1a	$n-C_4H_9Br$	4	**2d**	89	85	85[5]
1a	$PHCH_2Cl$	4	**2e**	94	89	89[7]
1b	Me_2SO_4	3	**2f**	92	91	—
1b	Et_2SO_4	4	**2g**	95	83	—
1c	Me_2SO_4	3	**2h**	96	45	—
1c	Et_2SO_4	4	**2i**	90	62	—
1d	Me_2SO_4	3	**2j**	95	87	87[8]
1d	Et_2SO_4	4	**2k**	93	56	—

Temperature of all reaction is toluene at reflux and PTC used is (TEBuAB); alkylating agent used is 2.2 mol/1.0 mol of substrate.

EXPERIMENTAL SECTION

All the melting points are uncorrected. Infrared spectra were recorded on Perkin Elmer 137B as a Nujol mulls. ^1H NMR were recorded on Brucker W.H. 90 spectrometer using THS as internal standard in ppm downfield from TMS. Mass spectra were determined on CEC-21-110 B mass spectrometer. The purity of the compounds were checked by TLC. All the substrates (**1a-d**) were prepared by following the standard procedures.[8-10]

General Procedure for the Preparation of Dialkyldiarylureas

(**1a-1c**).- In a four-necked round bottom flask equipped with mechanical stirrer, condenser and thermometer pocket were placed diphenylurea (**1a-d**, 0.5 mol), toluene (1000 mL), powdered sodium hydroxide (100 g, 2.5 mol), anhydrous potassium carbonate (69 g, 0.5 mol) and triethylbutylammonium bromide (2.38 g, 0.01 mol). The mixture was heated to reflux with mechanical stirring for 1 hr (a slimy mass separated from the reaction mixture). The alkylating agent (alkyl sulfatea/alkyl halides, 1.1 mol) was added to the reaction mixture over period of 1 hr and stirred at reflux temperature for 3-4 hrs, the progress of reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was cooled to room temperature and filtered. The toluene filtrate was washed with 1N

HCl (3 x 100 mL) followed by water (2 x 250 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave products **2a-k** in 89-96% yield (Table 3). The spectral and analytical data for the new compounds are as follows.

sym-N,N'-Dipropyldiphenylurea (2c), mp. 39-40°, 91% yield. IR (Nujol): 1670, 1605, 1500, 1462, 1405, 1390, 1148, 762 and 705 cm^{-1}. ^{1}H NMR (CCl$_4$): δ 0.73-1.10 (t, 6H, J = 7Hz), 1.23-1.80 (m, 4H), 3.20-3.57 (t, 4H, J = 7Hz), 6.27-7.00 (m, 10 H, ArH). MS: m/e (rel. int. %): 296 (M$^+$, 80), 267 (16), 253 (16), 212 (6.2), 182 (27), 163 (100), 134 (53), 120 (98), 106 (74), 93 (56), 77 (62).

Anal. Calcd for $C_{19}H_{24}N_2O$: C, 77.02; H, 8.10; N, 9.64. Found: C, 76.78; H, 8.36; N, 9.38

sym-N,N'-Dimethyl-di-(_o_-chlorophenyl)urea (2f), mp. 91°, 92% yield. IR (Nujol): 1640, 1590, 1485, 1360, 1130, 1060, 790, 760, 730 and 670 cm^{-1}. ^{1}H NMR (CCl$_4$): δ 3.17 (s, 6H), 6.90-7.37 (m, 8H, ArH); MS: m/e (rel. int. %): 312 (M$^+$, 2), 310 (8), 308 (12), 274 (36), 272 (70), 181 (15), 170 (75), 168 (100), 155 (19), 153 (49), 142 (24), 140 (62), 127 (32), 125 (32), 125 (32), 111 (42), 79 (28).

Anal. Calcd. for $C_{15}H_{14}Cl_2N_2O$: C, 58-06; H, 4.51; N, 9.03. Found: C, 58.02; H, 4.79; N, 8.74

sym-N,N'-Diethyl-di-(_o_-chlorophenyl)urea (2g), mp. 83°; 95% yield. IR (Nujol) : 1660, 1610, 1495, 1440, 1395, 1200, 1110, 1030 and 720 cm^{-1}. ^{1}H NMR (CCl$_4$): δ 0.90 -1.27 (t, 6H, J = 7Hz), 3.10-3.57 (q, 4H, J = 7Hz), 6.13-6.73 (m, BH, ArH); MS: m/e (rel. int. %): 340 (M$^+$, 14), 338 (61), 336 (70), 300 (100), 274 (43), 230 (46), 209 (62), 198 (29), 182 (100), 154 (100), 140 (73), 101 (70), 99 (21).

Anal. Calcd. for $C_{17}H_{18}Cl_2N_2O$: C, 60.35; H, 5.32; N, 8.28. Found: C, 60.15; H, 5.55; N, 8.44

sym-N,N'-Dimethyl-di-(_m_-tolyl)urea (2h), mp. 45°; 96% yield. IR (Nujol) : 1665, 1615, 1500, 1355, 1280, 1210, 1135, 815, 800, 770 and 710 cm^{-1}. ^{1}H NMR (CCl$_4$): δ 2.13 (s, 6H), 3.06 (s, 6H), 6.33-6.93 (m, 8H, ArH); MS: m/e (rel. int. %) 268 (M$^+$, 100), 211 (12), 161 (6), 148 (90), 133 (5), 120 (12), 91 (11).

Anal. Calcd. for $C_{17}H_{20}N_2O$: C, 76.12; H, 7.46; N, 10.44. Found: C, 76.30; H, 7.71; N, 10.18

sym-N,N'-Diethyl-di-(_o_-tolyl)urea (2i), mp. 62°; 90% yield. IR (Nujol): 1665, 1595, 1490, 1310, 1280, 1085, 770, 740, 710 and 685 cm H NMR (CCl$_4$): δ 0.87-1.27 (t, 6H, J = 7Hz), 2-17 (s, 6H), 3.13-3.60 (q, 4H, J = 7Hz), 6.30-6.87 (m, 8H); MS: m/e (rel. int. %): 296 (M$^+$, 98), 281 (8), 267 (24), 224 (10), 210 (28), 181 (13), 17844), 163 (44), 162100), 149 (18), 135 (98), 120 (28), 106 (41), 91 (80).

Anal. Calcd. for $C_{29}H\,_{24}N_2O$: C, 77.02; H, 8.10; N, 9.46. Found: C, 77.07; H, 8.36; N, 9.50

sym-N,N'-Diethyl-di-(_p_-methoxyphenyl)urea (2k), mp. 56°; 93% yield. IR (Nujol): 1645, 1510, 1445, 1395, 1295, 1250, 1040, 830, 775 and 600 cm^{-1}. ^{1}H NMR (CCl$_4$): δ 0.87-1.23 (t, 6H, J = 7Hz), 3.10-3.47 (q, 4H, J = 7Hz), 3.83 (s, 6H), 6.77 (s, 8H, ArH); MS: m/e (rel. int. %) 328 (M$^+$, 100), 313 (12), 296 (9), 205 (17), 194 (3), 178 (61), 150 (38), 135 (42), 122 (38), 106 (20).

Anal. Cacld. for $C_{19}H_{24}N_2O_3$: C, 69.51; H, 7.31; N, 8.53. Found: C, 69.50; H, 7.32; N, 8.42

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THE RESOLUTION OF RACEMIC AMINES BY THE FORMATION OF DIASTEREOMERIC AMIDES WITH AMINO ACIDS

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Racemic primary amines (**1a** and **1b**) were needed as intermediates and it was necessary to separate them into their enantiomers on gram scales in good yields and high optical purity. Although there are many acidic resolving agents available,[1] we found that the yields and purities were not satisfactory. We investigated the use of the amino acids, CBz-L-phenylalanine, CBz-L-valine and *t*-Boc-L-valine as chiral auxiliaries. In each case, the amide diastereomers obtained after coupling provided only a small degree of separation on TLC.[2] However, when the N-*t*-butoxycarbonyl group was