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A Facile and High-yielding Preparation of 1-Aryl-3,3-dialkylureas†

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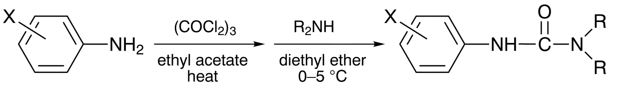
A convenient procedure for the preparation of 1-aryl-3,3-dialkylureas using bis(trichoromethyl) carbonate ('triphosgene') is described.

Owing to their good potentials in serving as highly effective and low toxicity herbicides and pesticides, many efforts have been devoted in the past to the synthesis of various 1-aryl-3,3-dialkylurea compounds.[1–4] As shown in the literature, one of the most commonly used synthetic methods is that adapted by Boehmer[4] utilizing the reaction of isocyanates with amines, where, however, a rather lengthy preparation of the corresponding isocyanates, including highly toxic, corrosive, and volatile reagents, is involved. There are other methods used in recent years for preparing this type of compound, such as sequential transamination of urea with anilines and dialkylamines,[1] mixing of amines with *N*-arylureas, alkyl *N*-arylcarbamates, thiocarbamic acid salts,[2] *etc.*[3] The applicabilities of these methods may sometimes be limited, however, due either to the relatively low overall yield, inconvenient experimental conditions, or unavailability of the starting materials. Here, we wish to report a facile method for the preparation of 1-aryl-3,3-dialkylureas, which provides high product yields and can also be carried out under mild conditions.

The synthesis of ureas using this new method is depicted in the following Scheme 1.

The use of bis(trichloromethyl) carbonate ('triphosgene') as a relatively safe substitute for phosgene in the preparations of a variety of compounds including chloroformate esters, carbamoyl chlorides, isocyanates and isocyanides, *etc.*, was pioneered by Eckert and Forster in 1987.[6] Soon after, Cotarca *et al.*[5] reported a kinetic and mechanistic investigation on the two-step formation of the symmetrical ureas by reactions of triphosgene with aromatic amines, implying that the preparation of the unsymmetrical ureas may be possible because the second step of the reaction was found to be much slower.[5] In the present preparation, since care had been taken to promptly manipulate the intermediate products of the first step and due also to the easy separation of the undesired symmetrical urea by-product owing to its poor solubility under the reaction conditions, the yields of final products (1-aryl-3,3-dialkylureas) were near quantitative.



1 (R = Me) *or* **2** (R ≠ Me)

	X		X		X	R
1a	4-MeO	**g**	4-MeCO	**2a**	4-Me	Et
b	4-Me	**h**	4-NO$_2$	**b**	4-Me	Pr^i
c	H	**i**	2-Me	**c**	4-Me	CH$_2$Ph
d	4-Cl	**j**	2-Cl			
e	4-Br	**k**	3-Br			
f	4-I					

Scheme 1

During the preparation, the intermediate compounds formed upon mixing triphosgene with anilines were allowed to further react with dialkylamines without purification. Both steps of the reaction proceeded very smoothly and the yields of the isolated final products were high. In the preparations of the type **2** ureas, sometimes dialkylamine hydrochlorides may precipitate out from the solution, but they can be readily removed upon washing with water. Obviously the method presented here is very simple and can promise high product yields for many ureas derivatives of similar structure. In addition, owing to the low volatility of triphosgene, only usual safety precautions are necessary during synthesis.

Table 1 Yields, melting points and recrystallization conditions of 1-aryl-3,3-dialkylureas

		Mp/°C		
Compound	Yield (%)	Obs.	Lit.	Recrystallization solvent
1a	95	130–131	129–130[a]	ethyl acetate–light petroleum[e]
1b	95	151–152	148–149[a]	ethyl acetate–light petroleum[e]
1c	92	130–130.5	130–131[a]	ethyl acetate–light petroleum[e]
1d	96	173.5–174.5	173.5–175.5[a]	ethyl acetate
1e	93	169.5–170.5	170–171[b]	ethyl acetate
1f	92	186–187		ethyl acetate
1g	96	137–138		ethyl acetate
1h	95	219–220	220–221[c]	acetonitrile
1i	95	142–143	141–142[b]	ethyl acetate–light petroleum[e]
1j	90	94–95	94–95[b]	ethyl acetate
1k	92	150.5–151	150.5–151.5[b]	ethyl acetate
2a	83	69–70	69.5–70.5[d]	ether–*n*-hexane
2b	85	143–144	145–146[d]	acetone
2c	86	171–171.5	172.5–173.5[d]	acetone

[a] Ref. 7(*a*). [b] Ref. 7(*b*). [c] Ref. 7(*c*). [d] Ref. 7(*d*). [e] Bp 30–60 °C.

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By the method described herein (see also Experimental), fourteen 1-aryl-3,3-dialkylureas (**1a**–**k**, **2a**–**c**) were synthesized and relevant data are shown in Table 1, where **f** and **g** are reported for the first time.

In summary, we present a convenient method for the preparation of 1-aryl-3,3-dialkylureas. The most advantageous features of the synthetic procedure are: (*i*) the starting materials are readily available and less toxic, (*ii*) the reaction is rapid and the reaction conditions are mild, (*iii*) the reaction is very clean and the product work-up is very easy, and (*iv*) the product yield is usually very high. Using this method, preparation of variously substituted 1-aryl-3,3-dialkylureas are expected to be no longer a challenging obstacle in ordinary laboratories.

Experimental

Mps (uncorrected) were measured on a Yanaco apparatus; ^1H NMR spectra were recorded on a JEOL-90Q NMR spectrometer, using Me_4Si as internal standard; elemental analyses were performed on a PE-240 elementary analyzer. Common reagents, anilines and dialkylamines were commercial products. Triphosgene was prepared according to the literature method.[6] Ethyl acetate was dried and distilled from P_2O_5 before use.

General Procedure for the Preparation of Compounds **1** *and* **2** [*Taking* 3,3-*Dimethyl*-1-(4-*tolyl*)*urea* **1b** *as an Example*].—To a solution containing 0.6 g (2 mmol) triphosgene dissolved in 20 ml dry ethyl acetate was added 0.6 g (5.6 mmol) *p*-toluidine (dissolved in 15 ml dry ethyl acetate) dropwise under stirring at room temperature. The mixture was warmed to dissolve the precipitates and was kept refluxing for an additional 15 min. After cooling to room temperature, the solution mixture was rota-evaporated, then 30 ml anhydrous ether was added and the insolubles were filtered off. To the filtrate was added dropwise a 30% aqueous dimethylamine solution (containing 1.0 g amine) with stirring at 0–5 °C. The resulting crystals were filtered off and were washed with cold water and ether consecutively. Recrystallization from ethyl acetate–light petroleum (bp. 30–60 °C) gave colorless needles, yield 95%.

3,3-*Dimethyl*-1-(4-*iodophenyl*)*urea* **1f**.—Mp 186–187 °C; δ_H [$(CD_3)_2SO$] 2.98 (6 H, s), 7.43 (4 H, t) (Found: C, 37.39; H, 3.98; N, 9.55. $C_9H_{11}IN_2O$. requires C, 37.26; H, 3.88; N, 9.66%).

1-(4-*Acetylphenyl*)-3,3-*dimethylurea* **1g**.—Mp 137–138 °C; δ_H [$(CD_3)_2SO$] 2.50 (3 H, s), 2.99 (6 H, s), 7.77 (4 H, t) (Found: C, 64.17; H, 6.76; N, 13.79. $C_{11}H_{14}N_2O_2$. requires C, 64.06; H, 6.82; N, 13.68%).

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