

PHOSPHOROUS IN ORGANIC CHEMISTRY. PART II¹: A NEW
METHOD OF PREPARING N-N' DISUBSTITUTED ARYL UREAS
USING PHENYL N'-PHENYLPHOSPHORAMIDOAZIDATE REAGENT.

by

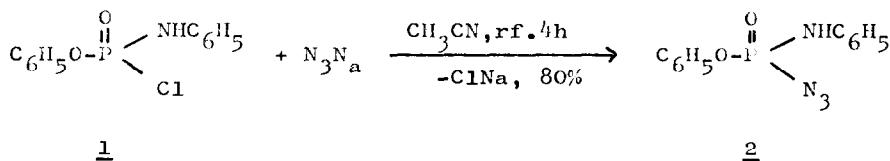
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Summary: N-N' Disubstituted ureas were obtained from carboxylic acids, amines and phenyl N-phenylphosphoramidoazidate in good yields. This procedure constitutes an adequate modified Curtius reaction.

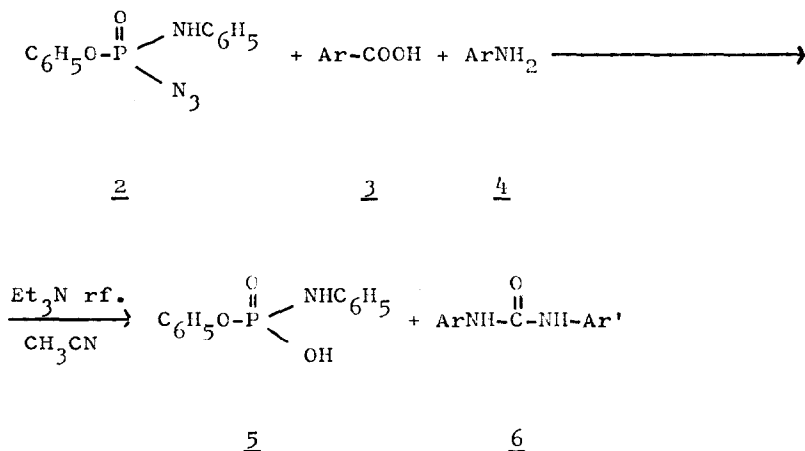
Phosphorazidates of type 2 are well known and used recently, specially for urethane, carboxamide and peptide synthesis^{2,3}. These procedures are known as modified Curtius reactions.

We wish to report a new reagent of type 2 and its application in the synthesis of N-N'disubstituted ureas, substances which are of a great interest, basically for the preparation of carbodiimides^{4,5} and of a great variety of heterocycles⁶. Particularly, the N-N'disubstituted aryl ureas are of interest because of their antimicrobial activity⁷.

Phenyl N-phenylphosphoramidoazidate 2 is a white solid conveniently prepared by treatment of phenyl N-phenylphosphoramidochloridate 1 with sodium azide in acetonitrile, and can be stored without precautions, as it does not show any sensitivity to dry or moist air at room temperature for several months, in contrast to other related organophosphorous reagents as, for example, diethylphosphorazidate⁸.

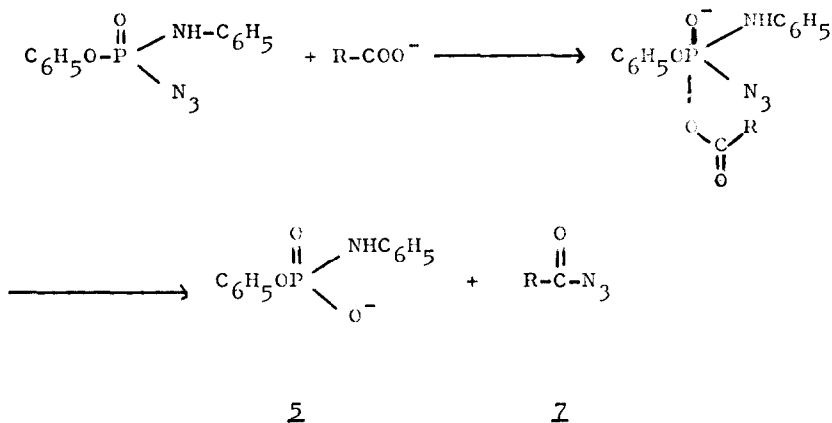


Equivalent amounts of aromatic carboxylic acid 3, primary aryl amine 4 and the title reagent 2 in acetonitrile at reflux lead to excellent yields of the corresponding N-N'disubstituted ureas 6; the results are summarized in the Table.



The phosphoramidic acid 5 is reconverted into the phosphoramidochloridate 1 by treatment with phosphorous pentachloride and this reconverted into reagent 2.

As expected, the reaction is not efficient in benzene. In acetonitrile, good results are obtained, possibly due to the highly dielectric constant, which increases the rate of nucleophilic attack if the carboxylate ion on phosphorus as the following scheme shows:



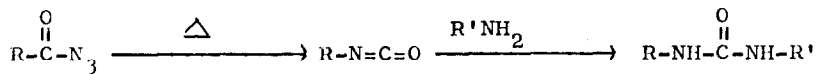


Table- N-N'diaryl ureas from carboxylic acids 3, arylamines 4 and the little reagent 2.

	Carboxylic Acid	Amine	Reaction solvent	time (h)	Yield (%)	m.p(°C) (lit.m.p)
1	C ₆ H ₅ COOH	C ₆ H ₅ NH ₂	CH ₃ CN	1.5	94	233-234 (235)6
2a	p-ClC ₆ H ₄ COOH	C ₆ H ₅ NH ₂	CH ₃ CN	1.5	90	234-238 (237-238)8
2b			C ₆ H ₅	2	38	
3a	C ₆ H ₅ COOH	C ₅ H ₄ NNH ₂	CH ₃ CN	1.5	80	183-185 (185-186)8
3b			C ₆ H ₆	2	40	
4	O-ClC ₆ H ₄ COOH	O-Cl-C ₆ H ₄ NH ₂	CH ₃ CN	1.5	87	234-236 (235-236)6

Experimental procedures:

Phenyl N-phenylphosphoramidoazidate 2

A mixture of phenyl N-phenylphosphoramidochloridate 1 (13.35 g, 0.5 moles), sodium azide (4 g, 0.615 moles) in acetonitrile (50 ml) is stirred under reflux for 4h. The mixture is cooled down to 0°C and the precipitate is filtered off. Evaporation of the solvent gives a crude oil, which is treated with water (15 ml) and the precipitate filtered off, to give phenyl N-phenylphosphoramidoazidate 2 (12.8 g, 93%), m.p. 50-52.3°C recrystallized from dichloromethane-n-hexane to yield (11 g, 80%) with m.p. 52-52.5°C.

C ₁₂ H ₁₄ N ₄ O ₂ P	cal.	C 52.56	H 4.04	N 20.40
(274.2)	found	52.33	4.06	20.38

I.R.(Cl₂CH₂) $\nu_{\text{cm}^{-1}}$: 3470(ν-NH-), 2300(-N₃), 1600(C-H arom.)

N.M.R.(Cl₃CH) $\delta_{\text{p.p.m.}}$: 7.12(S, 5H, arom.), 7.10(S, 5H, arom.)

Reaction of triphenylphosphine with the reagent 2.

Triphenylphosphine (0.6 g, 2.3 mmol) is added to a solution of phenylphosphoramidoazidate 2 (0.69 g, 2.5 mmol) in dichloromethane (10 ml), and the mixture is stirred at room temperature for 3 h. Evaporation of the solvent gives phenyl N-phenylphosphoramidotriphenylphosphazene (1.06 g, 90.7%), m-p-195-200°C, recrystallized from benzene m-p. 201-202°C.

Preparation of N-N'disubstituted aryl ureas 6.

Phenyl N-phenylphosphoramidoazidate 2 (0.69g, 2.5 mmol) is added to a solution of carboxylic acid (2.5 mmol) in acetonitrile (10 ml), and the mixture heated under reflux for 1.5 h. Evaporation of the solvent yields an oil, which is treated with water (15 ml). The resulting precipitate is filtered off and washed with water. Recrystallization from a suitable solvent gives the corresponding N,N'disubstituted urea which is characterized through its m.p. and i.r. and n.m.r. spectra.

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