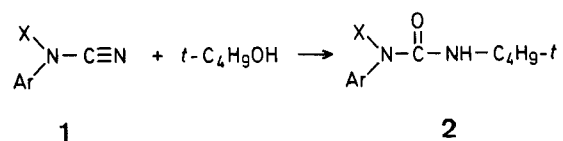


A New Procedure for the Preparation of Substituted Ureas, Acylureas, and Sulfonylureas*

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In continuation of our studies on Ritter-type and related reactions^{1,2,3} we have now submitted *N*-acyl-*N*-aryl-, *N*-alkoxycarbonyl-*N*-aryl-, and *N*-aryl-*N*-sulfonylcyanamides **1** to the reaction with *t*-butyl alcohol in the presence of boron trifluoride etherate. The corresponding *N,N*-disubstituted-*N'*-*t*-butylureas **2** were obtained, generally in high yields.



The structures of compounds **2** were established by comparison of the physical characteristics and by comparison of the I.R. spectrum of a sample of **2** (Ar = C₆H₅, X = H) prepared by this method with that of a sample prepared by the classical process⁴.

The cyanamides are prepared by reaction of cyanogen bromide—obtained *in situ* from bromine and potassium cyanide in water—with amines or anilines. These cyanamides are transformed readily to the *N,N*-substituted cyanamides **1** by the Schotten-Baumann method.

From these acylated and sulfonylated cyanamides we have prepared some previously unknown acyl- and sulfonylureas of the type **2** with one unsubstituted position on the two nitrogen atoms.

The melting points were measured on a Kofler apparatus and are not corrected. The purity of the obtained compounds has been verified by thin layer chromatography. The elemental analyses were carried out by Madame Huot of the microanalysis service of the Faculté des Sciences de Reims and gave results corresponding to the theoretical values within $\pm 0.2\%$. The I.R. spectra were recorded using a double beam Perkin Elmer 521 spectrometer.

The previously known compounds are indicated by the presence of a reference number. The scope of the reactions are indicated by the following tables and examples of the experimental procedure.

2,3-Dimethylphenyl Cyanamide:

Bromine (27.3 ml, 0.5 mol) and water (160 ml) are put into a three-necked flask. The bromine mixture is stirred mechanically and potassium cyanide (34.6 g, 0.5 mol) in water (320 ml) is added from a dropping funnel, the temperature of mixture being kept below 10° by external cooling. At the end of the addition the mixture becomes colourless. With continued stirring at 10° 2,3-dimethylaniline (121 g, 1 mol) is added from a dropping funnel. After 3 h, the oily droplets begin to solidify. The product is filtered, washed with water, dried, and recrystallised from benzene: yield: 65.5 g (90%); m.p. 124°.

C ₉ H ₁₀ N ₂	calc.	C 73.94	H 6.89	N 19.16
(146.1)	found	73.95	7.01	19.24























N-(2-Nitrobenzenesulfonyl)-*N*-(2,3-dimethylphenyl) Cyanamide (**1**): 2,3-Dimethylphenyl cyanamide (5.84 g, 40 mmol) is dissolved in 2.5 *N* aqueous potassium hydroxide (20 ml). With magnetic stirring 2-nitrobenzenesulfonyl chloride (9.74 g, 44 mmol) dissolved

in acetone (20 ml) is added to the mixture with cooling. Stirring is continued for 3 h, acetone is removed under reduced pressure, and the product is crystallised from acetone/ethanol; yield: 10.6 g (80%); m.p. 156°.

$C_{15}H_{13}N_3O_4S$	calc.	C 54.37	H 3.95	N 12.68
(331.2)	found	54.24	3.97	12.71

All products listed in Table 1 were prepared analogously.

Table 1. Preparation of *N,N*-Disubstituted Cyanamides **1**

Ar	X	M.P. (recryst. from)	Yield (%) ^a
	C_2H_5O-CO-	b.p. 165°/16 torr ⁶	77
	 $-CO-$	126° (ethanol) ⁵	51
	H_3C-SO_2-	oil	
	 $-SO_2-$	145° (ethyl acetate)	74
	 $-SO_2-$	87° (ethanol) ⁵	78
	 $-CO-$	127° (ethanol) ⁷	60
	 $-CO-$	121° (ethanol)	73
	 $-SO_2-$	120° (ethanol/diisopropyl ether)	73
	 $-SO_2-$	100° (ethanol)	84
	 $-SO_2-$	122° (ethanol)	81
	 $-CO-$	60° (ethanol)	51
	 $-SO_2-$	120° (ethanol)	90
	 $-SO_2-$	120° (ethanol/diisopropyl ether)	73
	C_2H_5O-CO-	60° (ethyl acetate)	67
	 $-CO-$	98° (ethanol)	65
	 $-CO-$	130° (ethanol)	86
	 $-OCH_2-CO-$	156° (ethyl acetate)	64
	H_3C-SO_2-	100° (ethanol)	45
	 $-SO_2-$	156° (ethanol/acetone)	80
	 $-SO_2-$	123° (ethyl acetate)	92
	 $-SO_2-$	167° (ethyl acetate)	57
	 $-SO_2-$	103° (ethanol)	82

^a Yield based on Ar-NH-C≡N.






















***N*-(2-Nitrobenzenesulfonyl)-*N*-(2,3-dimethylphenyl)-*N'*-*t*-butylurea (**2**):**

To a stirred mixture of *N*-(2-nitrobenzenesulfonyl)-*N*-(2,3-dimethylphenyl) cyanamide (3.31 g 10 mmol) and *t*-butyl alcohol (13 ml) is added boron trifluoride etherate followed by dioxan (10 ml). The mixture is allowed to stand at room temperature overnight and is then heated at 60° for 1 h. After being allowed to cool, water (50 ml) is added to the mixture. The solid product is filtered off and recrystallised from ethanol; yield: 3.1 g (77%); m.p. 140°.

$C_{16}H_{23}N_3O_5S$	calc.	C 56.28	H 5.72	N 10.36
(405.2)	found	56.40	5.75	10.28

All products listed in Table 2 were prepared analogously.

Table 2. Preparation of *N,N*-Disubstituted-*N'*-*t*-butylureas **2**

Ar	X	M.p. (recryst. from)	Yield (%) ^a
H		168° (methanol/water or ethyl acetate ⁴)	40
		185° (ethanol/water)	37
	 $-CO-$	142° (ethanol/water)	79
	 $-CO-$	120° (diisopropyl ether)	61
	C_2H_5O-CO-	63° (petroleum ether)	40
	 $-CO-$	118° (ethanol/water)	51
	 $-SO_2-$	193° (acetone/water)	81
	 $-SO_2-$	155° (ethanol)	68
	 $-SO_2-$	128° (diisopropyl ether)	72
	 $-SO_2-$	132° (ethanol)	68
	 $-SO_2-$	148° (ethanol)	65
	 $-CO-$	125° (ethanol)	47
	 $-SO_2-$	130° (ethanol)	84
	 $-SO_2-$	173° (ethyl acetate)	83
	 $-SO_2-$	140° (ethanol)	77
	 $-SO_2-$	182° (ethyl acetate)	64
	 $-SO_2-$	165° (acetone)	69
	 $-SO_2-$	125° (ethanol)	83

^a Yield based on **1**.

***N*-Ethoxycarbonyl-*N*-(2,3-dimethylphenyl)-urea (**3**):**

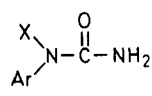
A mixture of *N*-(2,3-dimethylphenyl)-*N*-ethoxycarbonyl cyanamide (2.18 g, 10 mmol), ethanol (10 ml) and concentrated hydro-

chloric acid (5 ml) is heated under reflux for 30 min. The mixture is then cooled, the solid product filtered off, and recrystallised from ethanol; yield: 1.9 g (80%); m.p. 185°.



$C_{12}H_{16}N_2O_3$ calc. C 61.00 H 6.82 N 11.86
(236.1) found 60.94 6.92 11.97

The products listed in Table 3 were prepared analogously.

Table 3. Preparation of *N,N*-Disubstituted Ureas **3**



3

Ar	X	M.p. (recryst. from)	Yield (%) ^a
	C_2H_5O-CO-	150° (ethanol/water) ⁸	90
	H_3C-SO_2-	174° (ethanol)	60
	C_2H_5O-CO-	185° (ethanol/water)	80
	H_3C-SO_2-	162° (ethanol/ diisopropyl ether)	60

^a Yield based on **1**.

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* A request of a patent has been registered: PV 7.340 527 on 14/11/1973.

¹ J. Anatol, *C. R. Acad. Sci. Paris* **235**, 249 (1952); *Thèse Doctorat ès Sciences Physiques*, Paris, 1953.

² D. Giraud-Clenet, J. Anatol, *C. R. Acad. Sci. Paris, Sér. C* **262**, 244 (1966).

³ J. Anatol, A. Medete, *Synthesis* **1971**, 538.

⁴ R. N. Lacey, *J. Chem. Soc.* **1960**, 1633.

⁵ F. Kurzer, *J. Chem. Soc.* **1949**, 3029.

⁶ J. R. Scott, J. B. Cohen, *J. Chem. Soc.* **121**, 2034 (1922).

⁷ L. Hunter, H. A. Rees, *J. Chem. Soc.* **1945**, 617.

⁸ H. Biltz, *Ber. dtsch. chem. Ges.* **56**, 359 (1917).