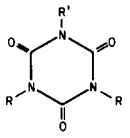
Chemistry of Isocyanurates. II (1a). Preparation of Unsymmetrically Trisubstituted Isocyanurates (1b)

Perry A. Argabright and Brian L. Phillips

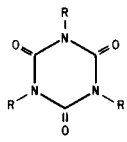
Denver Research Center, Marathon Oil Company

The synthesis of unsymmetrically trisubstituted isocyanurates (I) has been limited to two methods. The more commonly employed synthesis is the base-catalyzed

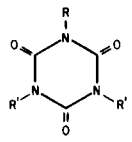


I

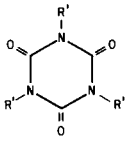
cotrimerization of two isocyanates (RNCO and R'NCO). As shown by Juenge and Francis (2), this technique suffers from low yields and an involved separation scheme to isolate I from the three other possible cotrimers (II, III, and IV).



II



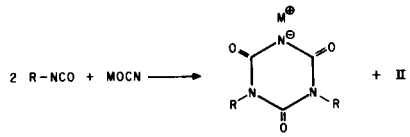
III



IV

Finally, the preparation of diethyl phenyl isocyanurate (I, R = C_2H_5, and R' = ϕ) in low yield from the sequential reaction of ethyl isocyanate and phenyl isocyanate with a trialkyltin alkoxide has been reported (3).

We wish to report a new and convenient synthetic route to I. As described in an earlier paper (4), organic isocyanates readily react with alkali metal cyanates (MOCN) in dipolar aprotic media (*e.g.*, dimethylformamide) to give the salt of the corresponding disubstituted isocyanuric acid (V) and trimer, II, as the singular by-product.



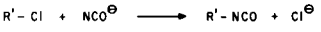
V

Subsequent reaction of V with the appropriate organic halide (R'X) in dimethylformamide (DMF) affords high yields of I.

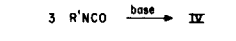
As summarized in Table I, this method is applicable to the preparation of a spectrum of unsymmetrically trisubstituted isocyanurates (I). For the most part, chlorides provide a good compromise between rate and availability. Only in the case of 2° halides did we find it necessary to use the bromide or iodide in order to attain reasonable rates. Attempts to utilize aryl halides have failed.

In some cases, high yields of I are obtained when the salt (V) synthesis is carried out in the presence of an organic halide.

As shown in Table II, for the phenyl isocyanate-KOCN system, excellent yields of I can be obtained when a reactive halide (*e.g.*, benzylic or allylic) is employed. It is worthy of note that the singular by-product is triphenyl isocyanurate (II, R = C_6H_5) arising from the base (V) catalyzed trimerization of phenyl isocyanate. The absence of cotrimers, III and IV, in the product mixtures argues strongly that the reaction of phenyl isocyanate with cyanate ion (NCO^-) is much faster than the reaction of R'Cl with NCO^- (5,6).



The *in situ* generation of R'NCO would manifest itself in the formation of III and IV *via* base catalyzed cotrimerization (2) and trimerization (6) of R'NCO respectively:

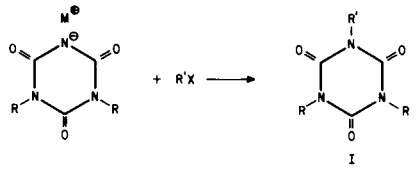


EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer Model 521 Spectrometer using potassium bromide discs for solids. Nuclear magnetic resonance spectra were obtained on a Varian A-60. Pertinent ir and nmr data for all of the products listed in Tables I and II are given in Table III. Melting points reported are uncor-

TABLE I

Preparation of Unsymmetrically Trisubstituted Isocyanurates (I) (a)

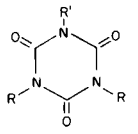


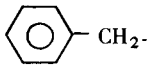
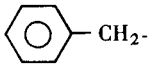
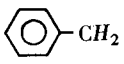
I

R	M	R′	X	Temp., °C	Time, Hours	Yield, %	M.p. (Sol.) (b) or b.p., °C	Formula		C	H	N
C_6H_5	Na	$C_6H_5CH_2$	Cl	100	3	100	246.5-247 (E)	$C_{22}H_{17}N_3O_3$	Calcd.,%	71.15	4.61	11.32
									Found,%	71.09	4.90	11.33
C_6H_5	Na	CH_2=$CHCH_2$	Cl	100	3	96	149.5-150 (E)	$C_{18}H_{15}N_3O_3$	Calcd.,%	67.28	4.71	13.08
									Found,%	67.20	4.87	13.38
C_6H_5	Ma	*n*-C_8H_{17}	Cl	100	3	80	119-119.5 (C)	$C_{23}H_{27}N_3O_3$	Calcd.%	70.20	6.92	10.68
									Found,%	70.06	7.04	10.64
C_6H_5	Na	*n*-C_8H_{17}	Br	100	3	100						
C_6H_5	Na	*sec*-C_4H_9	Cl	100	21	31	140.5-141.5 (E-W)	$C_{19}H_{19}N_3O_3$	Calcd.,%	67.64	5.68	12.46
									Found,%	67.70	5.59	12.82
C_6H_5	Na	*sec*-C_4H_9	Br	100	5	95						
C_6H_5	Na	$CH_3(CH_2)_5CHCH_3$	Br	100	5	68	100.5-102.5 (E-W)	$C_{23}H_{27}N_3O_3$	Calcd.,%	70.20	6.92	10.68
									Found,%	70.06	6.85	10.69
CH_2=$CHCH_2$	K	$C_6H_5CH_2$	Cl	100	3	92	68.5-69.5 (E)	$C_{16}H_{17}N_3O_3$	Calcd.,%	64.20	5.72	14.04
									Found,%	64.52	5.81	13.91
CH_2=$CHCH_2$	K	*n*-C_4H_9	Cl	100	5	97	100-103 (.05 mm.)	$C_{13}H_{19}N_3O_3$	Calcd.,%	58.85	7.22	15.84
									Found,%	59.00	7.39	15.88
CH_2=$CHCH_2$	K	CH_3	I	50	5	96	88 (.04 mm.)	$C_{10}H_{13}N_3O_3$	Calcd.,%	53.80	5.87	18.83
									Found,%	54.07	5.87	18.93

(a) Reactions carried out in DMF. (b) Crystallization solvent: E = ethanol, W = water, C = cyclohexane.

TABLE III

Spectral Data for 

R	R′	Type of Hydrogen	NMR (a) δ (b)	Relative Intensity	IR (c), cm^{-1}
	CH_2=CH-CH_2-	Aryl	7.43	10.1	1690, 1430 (d)
		CH_2=CH-	5.08-6.18	2.9	683, 753, 583
		CH_2-N	4.43	2.0	
	$CH_3CH_2CH_2CH_2$-	Aryl	7.43	10.0	2950, 2920,
		$CH_3CH_2CH_2$	0.90-1.52	7.2	2860, 1700, 1430 (d)
		CH_2N	3.87	2.0	750, 683, 585, 545
		Aryl	7.23-7.45	17.0	1690, 1425 (d)
		CH_2	5.03	2.0	750, 683, 582, 525
	$CH_3\overset{\vert}{C}HCH_2CH_3$	Aryl	7.35 (e)	11.2	1700, 1410 (d)
		CH_3CH_2	0.92	3.2	759 (d), 750
		CH_3CH	1.47	3.4	688
		CH_2	1.93	2.4	
		CHN	4.85	1.0	
	$CH_3(CH_2)_7$-	Aryl	7.48 (e)	10.7	1700, 1435 (d)
		CH_2N	3.92	2.0	750, 692
		$CH_3(CH_2)_6$	0.87-1.67	16.5	591
	CH_3-$\overset{\vert}{C}H(CH_2)_5CH_3$	Aryl	7.35 (e)	10.8	2950, 2920, 2850
		CHN	4.92	1.0	1700, 1500, 1420 (d)
		CH_3CHCH_2	1.93		
		CH_3CH	1.47	17.3	759 (d), 753, 693,
		$CH_3(CH_2)_4$	0.88-1.30		593
CH_2=CH-CH_2-	CH_3-	CH_2=CH	5.17-5.87	6.1	1680, 1460 (d)
		CH_2N	4.38	4.1	988, 925
		CH_3	3.20	3.0	757 (d)
CH_2=CH-CH_2-	$CH_3CH_2CH_2CH_2$-	CH_2=CH	5.18-5.82	6.5	2950, 2930, 2865
		CH_2=CH-CH_2	4.38	4.3	1690, 1455 (d)
		CH_2N	3.80	2.0	1375, 1315, 987
		$CH_3CH_2CH_2$	0.90-1.45	7.7	925, 758 (d)
CH_2=CH-CH_2-		Aryl	7.18-7.43	5.0	1685, 1450 (d)
		CH_2=CH	5.17-5.88		1358, 1313, 980,
			4.97	8.0	905, 760 (d), 750
		CH_2=CH-CH_2	4.38	4.0	693, 600

(a) Measured in d_6-dimethylsulfoxide with TMS as internal standard. (b) Measured at center of multiplet. (c) Only intense bands listed. (d) Characteristic of the isocyanurate ring; however, the longer wave length absorption may be obscured by aromatic substitution band. (e) Deuterochloroform employed as solvent.

rected. Elemental analyses were carried out by Huffman Laboratories, Inc., Wheatridge, Colorado.

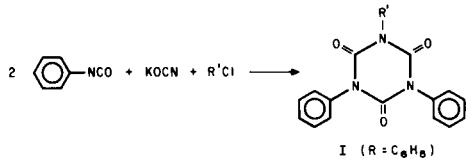
DMF was purified by stirring overnight with calcium hydride and was then distilled at reduced pressure through a packed column. A center cut was used for all experiments.

Sodium cyanate (Fairmount Chemical Co.) and potassium cyanate (Matheson, Coleman and Bell) were dried at 60° *in vacuo* and stored in desiccators.

The isocyanates and halides employed were all reagent grade chemicals and were used as received.

TABLE II

Direct Synthesis of some Diphenyl Isocyanurates (a)



R'	Conversion, % (b)	Selectivity, % (c)
CH_2=$CHCH_2$	93	92
$C_6H_5CH_2$	97	94
n-C_4H_9	95	49 (d)

(a) Reactions carried out at 75° in DMF' (b) Mole % of phenyl isocyanate reacted. (c) Mole % of reacted phenyl isocyanate that leads to I. (d) Low selectivity due to incomplete alkylation of intermediate, potassium diphenyl isocyanurate.

Sodium Diphenyl Isocyanurate.

A solution of 142.8 g. (1.20 moles) of phenyl isocyanate in 400 ml. of DMF was added dropwise in a nitrogen atmosphere to a stirred slurry of 42.9 g. (0.66 mole) of sodium cyanate in 800 ml. of DMF. The addition required about 1.5 hours during which the reaction exothermed to 35-40°. The reaction mixture was stirred at ambient temperature for an additional 1.5 hours, filtered, and the DMF distilled from the filtrate *in vacuo*. The resulting solid residue was triturated with distilled water, and the insoluble triphenyl isocyanurate (63.5 g.) removed by filtration. The filtrate was vacuum distilled to dryness, the residue triturated with acetone, filtered and dried to give 122.1 g. of a white solid. The nmr and ir spectra of this product showed it to be 75% sodium diphenyl isocyanurate and 25% residual solvents. A small sample was exhaustively dried and submitted for elemental analysis.

Anal. Calcd. for $C_{15}H_{10}N_3O_3Na$: N, 13.86; Na, 7.58. Found: N, 13.95; Na, 6.73.

Potassium Diallyl Isocyanurate

A slurry of 51.9 g. (0.64 mole) of potassium cyanate in 1 liter of DMF was heated to 75° under a nitrogen atmosphere. A solution of 99.7 g. (1.2 moles) of allyl isocyanate in 200 ml. of DMF was added over 3 hours followed by an additional reaction period of 1 hour. The reaction mixture was filtered at ambient temperature, and the filtrate vacuum distilled to an oily residue. This residue was stirred with distilled water, and the chloroform added to dissolve the insoluble oil which formed. The phases were separated, and 43.1 g. of an oil (predominantly triallyl isocyanurate) was recovered from the chloroform on evaporation of the solvent. The aqueous layer was evaporated to dryness *in vacuo* to give a solid residue which was triturated with acetone, filtered, and dried to give 82.1 g. of a white solid. The ir and nmr spectra of this product indicated it was the desired potassium diallyl isocyanurate containing 1.5% residual water. A thoroughly dried sample was submitted for elemental analysis.

Anal. Calcd. for $C_9H_{10}N_3O_3K$: N, 16.99; K, 15.81. Found: N, 17.04; K, 16.36.

Reaction of Disubstituted Isocyanurate Salts with Alkyl Halides (Table I).

A solution of 0.025 mole of the disubstituted isocyanurate salt and 0.028 mole of the halide in 100 ml. of DMF was maintained at the indicated temperature. The reaction mixture was vacuum distilled to dryness and the resulting residue triturated vigorously with water. The crude product (I) was obtained as an insoluble solid or in some cases as an immiscible oil. The products were purified by recrystallization or by distillation. Unreacted disubstituted isocyanurate, if present, was recovered on acidification of the aqueous phase.

Direct Synthesis of Diphenyl Alkyl Isocyanurates (Table II).

A slurry of 0.16 mole of potassium cyanate in 200 ml. of DMF was heated to 75° under a nitrogen atmosphere. A solution of 0.30 mole of phenyl isocyanate and 0.15 mole of alkyl chloride in 100 ml. of DMF was added dropwise over 1 hour. After stirring at 75° for an additional hour, the inorganic salts were removed, the filtrate vacuum stripped, and the residue triturated with water. The crude product was removed by filtration and analyzed by gas chromatography (7). The isolated product (I) was found to be contaminated with a small amount of triphenyl isocyanurate. In each case, the pure diphenyl alkyl isocyanurate was obtained by recrystallization. In the preparation of diphenyl n-butyl isocyanurate, considerable diphenyl isocyanurate was isolated by acidifying the water used to wash the reaction products.

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