The Isocyanurates. I. A Novel Method of Synthesizing Trialkyl Isocyanurates

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Some esters of isocyanuric acid are interesting as heat resistant resins1,2) because of their symmetrical triazine ring structure. Only a few of the isocyanurates have, however, been used as practical chemical intermediates. This is because of the methods of synthesizing them are not sufficiently economical for general use.

Hofmann first indicated that trimethyl isocyanurate had been prepared by the thermal isomerization of trimethyl cyanurate both without3) or with4) methyl iodide. The trimethyl cyanurate was synthesized from cyanuric chloride and methyl alcohol in the presence of alkali hydroxide. However, his method was applied only to the preparation of lower alkyl esters. Other classical preparative methods of isocyanurates were by the reaction of alkyl iodides with silver cyanurate5) and by that of potassium alkyl sulfate with potassium cyanate or potassium cyanurate.6) The trimerization of alkyl isocyanates to isocyanurates catalyzed by phosphines or tertiary amines7-9) has been used in laboratory techniques. Since, however, this method involves the treatment of poisonous and expensive isocyanates, it is not preferable to synthesizing many isocyanurates.

Although Kaiser and his co-workers reported10) that the reaction of alkali cyanates with alkyl halides in acetonitrile as a solvent under pressure afforded alkyl isocyanurates, the yield was generally very low and it was difficult to purify the products to an extent similar to that of the other known methods. Kaiser also reported that the syntheses of unsaturated carbamates from potassium cyanate and alkenyl halides in alcohols were accompanied by the formation of alkenyl isocyanurates as a by-product.11) De Pree reported that, in the syntheses of isocyanates from the reaction of alkyl halides with alkali cyanates catalyzed by tertiary amines, considerable amounts of isocyanurates were formed, along with isocyanates.12)

In the previous works of our laboratory,13-22) several aprotic solvents, such as dimethylformamide, dimethyl sulfoxide, dimethylacetamide, tetramethylene sulfoxide, tetramethyl urea, *N*-formyl morpholine, and *N*-formyl piperidine, were found to be powerful solvents for the nucleophilic displacement reaction of organic halides with metal cyanates and for the subsequent trimerization of isocyanates to isocyanurates.

Recently Frazier23) reported an improvement of the isocyanurates synthesis by means of the reaction of alkenyl halides with cyanuric acid in aqueous alkali in the presence of cuprous chloride. Tazuma and his co-worker patented24) a method of synthesizing isocyanurates from potassium cyanate and alkyl halides with tertiary amines in inert solvents. As an improvement of Frazier's method, Francis showed that the reaction of alkyl halides with alkali cyanurates proceeded smoothly in dimethylformamide as a reaction medium.25)

In the present paper, the reactions between alkyl halides and potassium cyanate in aprotic solvents, such as dimethylformamide and dimethyl sulfoxide, have been studied. The

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Table I. Yield and properties of isocyanurates

Substituent of isocyanurate	Yield %	B. p. °C/4 mmHg	n_D^{25}	Composion C H O N	Analysis, N % Found	Analysis, N % Calcd.
Trimethyl[a]	90	274[b]	—	$C_6H_9O_3N_3$	24.52	24.55
Triethyl[c]	88	106[d]	—	$C_9H_{15}O_3N_3$	19.70	19.71
Tri-*n*-propyl[e]	85	136[f]	1.4746	$C_{12}H_{21}O_3N_3$	16.40	16.46
Tri-*n*-butyl	85	162[g]	1.4720	$C_{15}H_{27}O_3N_3$	14.20	14.13
Tri-*n*-amyl	80	186[h]	1.4725	$C_{18}H_{33}O_3N_3$	12.45	12.39
Tri-*n*-hexyl	88	212[i]	1.4730	$C_{21}H_{39}O_3N_3$	11.08	11.01
Tri-*n*-heptyl	75	232[j]	1.4733	$C_{24}H_{45}O_3N_3$	9.94	9.92
Tri-*n*-octyl	73	257[k]	1.4730	$C_{27}H_{51}O_3N_3$	9.07	9.02
Tri-*n*-nonyl	70	281	1.4720	$C_{30}H_{57}O_3N_3$	8.41	8.28
Tri-*n*-decyl	68	300	1.4730[l]	$C_{33}H_{63}O_3N_3$	7.77	7.64
Tri-isobutyl[m]	70	145—147	—	$C_{15}H_{27}O_3N_3$	14.15	14.13
Tri-*s*-butyl	75	138—139	1.4600[n]	$C_{15}H_{27}O_3N_3$	14.25	14.13
Tri-isoamyl	70	176/3	1.4710[l]	$C_{18}H_{33}O_3N_3$	12.44	12.39
Tri-*s*-heptyl[o]	57	208	1.4750[l]	$C_{24}H_{45}O_3N_3$	10.04	9.92
Tri-isooctyl[p]	80	221/3	1.4762[l]	$C_{27}H_{51}O_3N_3$	9.14	9.02
Tri-isononyl[q]	75	244	1.4712[l]	$C_{30}H_{57}O_3N_3$	8.40	8.28
Tribenzyl[r]	83	382[s]	—	$C_{24}H_{21}O_3N_3$	10.49	10.52
Tris-(2-methoxyethyl)	55	194—195/6	1.4865[l]	$C_{12}H_{21}O_6N_3$	13.77	13.86
Tris-(2-ethoxyethyl)	51	193—194/3	1.4766[l]	$C_{15}H_{27}O_6N_3$	12.21	12.17
Tris-(2-butoxyethyl)	70	234	—	$C_{21}H_{39}O_6N_3$	9.83	9.78
Tris-(2-vinyloxyethyl)[t]	—	175—178[u]	—	$C_{15}H_{39}O_6N_3$	12.35	12.38

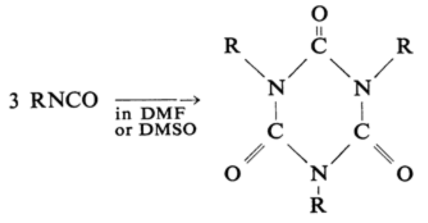
a) Melted at 177°C. b) Boiling point at ordinary pressure. c) M. p. 95°C. d) B. p. 276°C/760 mmHg. e) M. p. 24°C. f) B. p. 286°C/760 mmHg. g) B. p. 318°C/760 mmHg. h) B. p. 336°C/760 mmHg. i) 356°C/760 mmHg. j) B. p. 373°C/760 mmHg. k) B. p. 388°C/760 mmHg. l) n_D^{20}. m) M. p. 50—51°C. n) n_D^{15}. o) 1-Ethylpentyl-. p) 2-Ethylhexyl-. q) 3, 5, 5-Trimethylhexyl-. r) M. p. 157°C. s) Boiling point at ordinary pressure, slightly decomposed. t) M. p. 59°C. u) Partial polymerization was observed.

Table II. The influence of water content in the reaction mixtures

H_2O g.	$\frac{H_2O}{C_4H_9Br}$ mol./mol.	$\frac{H_2O}{DMF+KCNO}$ wt.%	Yield of raw urea g.	Yield of raw urea %	Yield of isocyanurate g.	Yield of isocyanurate %	Conversion of water %	Total yield %
0.0	0.0	—	trace	—	25	84.2	—	84.2
0.5	0.09	0.33	4.0	15.5	21	70.7	84	86.2
1.0	0.19	0.67	6.0	23.2	17	67.3	63	80.5
1.5	0.28	1.00	9.5	36.8	13	43.8	67	80.6
2.0	0.39	1.33	13	50.4	8.5	28.9	68	79.3
2.5	0.47	1.66	17	65.9	6	20.2	71	86.1
2.7	0.50	1.79	18	69.7	4	13.4	70	83.1
3.0	0.56	1.99	19.5	75.2	2	6.7	68	81.9

yield of the isocyanurates was generally good enough to be applied to the synthetic purpose, and the techniques of synthesis and the purification of the products were also easy. The reactions may be written as follows:

$$RX + KCNO \xrightarrow[\text{in DMF or DMSO}]{} RNCO + KX \quad (1)$$



(2)

As a side reaction, the formation of 1, 3-dialkyl ureas from moisture and alkyl isocyanates were observed as follows:

$$2\ RNCO + H_2O \xrightarrow[\text{in DMF or DMSO}]{} (RNH)_2CO + CO_2 \quad (3)$$

Although the rate of the reaction 3 of isocyanates with miosture was faster than that of the reaction 2, the formation of ureas was effectively avoided by drying the solvents and reactants before use. The condition of reactions 1 and 2 were moderate. The preferable conditions were a reaction temperature of 110—150°C and a molar ratio of the solvent to the halide of at least 2.5. The yields and the properties of isocyanurates are listed in Table I.

The trialkyl isocyanurates and tris-(2-alkoxyethyl) isocyanurates shown in Table I were relatively thermostable compounds, could be distilled under atmospheric pressure without decomposition, and were resistant to chemicals at ordinary temperatures. Tris-(2-vinyloxyethyl) isocyanurate was easily polymerized with a cationic catalyst such as boron trifluoride etherate in a hydrocarbon solvent, leading to a heat-stable polymer.

The urea formation was affected by the amount of water involved in the reaction mixture. The influence of water was observed in the reaction of *n*-butyl bromide with potassium cyanate. The results are listed in Table II.

To increase the yield of isocyanurate, it is extremely necessary to remove the water in the reaction mixture carefully. The total yield of tri-*n*-butyl isocyanurate and 1, 3-di-*n*-butyl urea was 80—87%.

Experimental(26)

1) **Materials.**—Alkyl halides were prepared from the corresponding alcohols by the usual method and were purified by fractional distillation. 2-Alkoxyethyl bromides were prepared by the reaction of alkyl cellosolves with phosphorus tribromide, and crude products were fractionally distilled to give pure samples. 2-Vinyloxyethyl chloride was obtained by the elimination distillation of bis-(2-chloroethyl)ether with sodium hydroxide. The raw product was dried over potassium carbonate and then fractionally distilled. A distillate which boiled at 109—110°C was collected.(27)

Potassium cyanate was prepared by a method of fusing analytical-grade anhydrous potassium carbonate and pure urea,(28) while the hard blocks of potassium cyanate were pulverized by a closed-type ball-mill in order to get them through a 40 mesh sieve. The fine potassium cyanate was then dried over phosphorus pentoxide in vacuo. The purity was determined by the use of a silver nitrate solution. There was a min. of 98% of potassium cyanate. If the blocks of potassium cyanate formed by the fusion method had dull surfaces, the potassium cyanate content was 70% (max.), indicating the presence of unreacted potassium carbonate.

Commercial dimethylformamide (DMF) or dimethyl sulfoxide (DMSO) was mixed with about 10% benzene and distilled to remove water as by the benzene-water azeotrope process. After most of the water had been removed, the aprotic solvent was dried over porous barium oxide overnight and then fractionally distilled under reduced pressure.(29-31) The pure DMF had a boiling point of 72—73°C/41 mmHg, while the pure DMSO boiled at 73—74°C/10 mmHg.

2) **Trimethyl Isocyanurate.**—In a 1 l. four-necked flask fitted with a reflux condenser, a thermometer, a stirrer and a dropping funnel, 105 g. (1.3 mol.) of potassium cyanate and 300 g. (4.0 mol.) of DMF were placed. The mixture was then heated to 130—134°C in an oil bath, and 142 g. (1 mol.) of methyl iodide was added from the dropping funnel over a period of about 1 hr. with stirring. The temperature was kept at 100—110°C for about 2 hr. From the reaction mixture, a precipitate of potassium iodide was then filtered off and washed with 50 ml. of acetone. After the solvents had been removed from the combined filtrate, the residue was recrystallized from aqueous ethanol to give trimethyl isocyanurate, m. p. 176—177°C.(32) (Yield, 51 g. (90%)).

3) **Triethyl Isocyanurate.**—A mixture of 47 g. (0.3 mol.) of ethyl iodide, 110 g. (1.3 mol.) of DMSO and 30 g. (0.37 mol.) of potassium cyanate was kept, with stirring, at 70—80°C for about 3 hr. (until no refluxing of ethyl iodide was observed in the condenser). The temperature was then raised to 135°C and maintained at that point for about 1 hr. After the reaction mixture had then been cooled, 50 ml. of ethanol was added for filtration. The filtrate yielded, on the evaporation of the solvents under reduced pressure and recrystallization from aqueous ethanol, triethyl isocyanurate, m. p. 94—95°C (Ref. 32 : 95°C).

4) **Tri-*n*-propyl Isocyanurate.**—*n*-Propyl bromide (124 g.) (1 mol.) was dropped into a mixture of 105 g. (1.3 mol.) of potassium cyanate and 250 ml. (3.6 mol.) of DMSO at 110°C with stirring. After all of the bromide had been added over a 1.5-hr. period, the reaction mixture was gradually heated to 130°C and the stirring was continued for an additional 2 hr. The reaction mixture was then poured into cold water, and the product was extracted with ether. The extract was washed, dried over anhydrous magnesium sulfate, and distilled.

5) **Tributyl Isocyanurates.**—To a mixture of 105 g. of potassium cyanate (1.3 mol.) and 200 g. (2.7 mol.) of DMF, 137 g. (1 mol.) of butyl bromide was added drop-by-drop at 135—140°C. The reaction time depended on the reactivity of the bromide, generally it took 1—3 hr. after addition of the bromide. The reaction mixture was then cooled, and a white precipitate of potassium bromide was filtered off and washed with small portions of ethyl methyl ketone. From the combined filtrated, tributyl isocyanurate was yielded by the evaporation of the solvents and by the fractional distillation of the residue.

6) **Tri-*s*-heptyl Isocyanurate.**—A mixture of 108 g. (1.35 mol.) of potassium cyanate, 179 g. (1 mol.) of 3-bromo-heptane and 250 g. (3.4 mol.) of DMF was heated to 140—145°C while being stirred in

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26) The boiling points and melting points are uncorrected.

27) L. H. Cretcher et al., *J. Am. Chem. Soc.*, **47**, 1175 (1925).

28) A. Scattergood, "Inorganic Syntheses," Vol. 2, 86 (1946).

29) D. P. Ames, and P. G. Sears, *J. Phys. Chem.*, **59**, 16 (1955).

30) P. G. Sears, E. D. Wilhorit and L. R. Dawson, ibid., **59**, 373 (1955).

31) A. B. Thomas and E. G. Rochow, *J. Am. Chem. Soc.*, **79**, 1843 (1957).

32) E. M. Smolin and L. Rapoport, "The Chemistry of Heterocyclic Compounds, *s*-Triazines and Derivatives," Interscience Publ., N. Y. (1959), p. 404.

an oil bath. As the reaction proceeded, the reaction temperature was seen to become lower as a result of the formation of heptenes as by-products. When most of the bromide had been added, the reaction temperature was lowered to about 100°C, the reaction was then continued for 3 hr. more. The reaction mixture was then cooled, poured into ice-cold water, and filtered after which the filtrate was extracted with ether. The ethereal solution was separated and dried over calcium chloride. After the ether had been removed, heptenes (13.5 g.) (20%), 3-bromo-heptane (3.5 g.) (2%) and crude tri-*s*-heptyl isocyanurate (73 g.) (57%) were obtained. Tri-*s*-heptyl isocyanurate was redistilled to give a pure sample. The above-mentioned precipitate, which had been separated from the water extract, was recrystallized from boiling water to give mono-potassium isocyanurate (about 1 g.).

7) **Tribenzyl Isocyanurate.**—To a suspension of 105 g. (1.3 mol.) of potassium cyanate in 250 ml. (3.2 mol.) of DMF, 126.6 g. (1 mol.) of benzyl cholride was added through a dropping funnel, the reaction mixture was then stirred at 140—145°C for 3 hr. The reaction mixture was then cooled and poured into cold water. The flocculated product was collected by filtration, crushed into small particles, and recrystallized from ethanol to give colorless needles. (The m.p. in Ref. 33 is 157°C, while that in Ref. 32 is 165°C.)

8) **Tri-higher Alkyl Isocyanurate.**—Two moles of potassium cyanate and 1 mol. of higher alkyl bromide were reacted in 300 g. (4 mol.) of DMF in a manner which has been described in Experiments 5). The temperature of the reaction mixture should be kept at 140—150°C for at least 3 hr. The mixture was then poured into cold water and extracted with benzene. After the extract had been dried with anhydrous magnesium sulfate and the solvents had been removed, the residue was distilled to yield pure tri-higher alkyl isocyanurate.

9) **Tris-(2-alkoxyethyl) Isocyanurates.**—A mixture of 200 g. (2.7 mol.) of DMF, 88 g. (1.1 mol.) of potassium cyanate and 153 g. (1 mol.) of 2-ethoxyethyl bromide was heated to 135—140°C while being stirred for 2 hr. After it had then been cooled, the reaction mixture was poured into cold water and extracted with benzene. The extract was washed with water, dried with anhydrous potassium carbonate, and distilled. Other tris-(2-alkoxyethyl) isocyanurates were prepared by a similar method from corresponding bromides.

10) **Tris-(2-vinyloxyethyl) Isocyanurate.**—Into a suspension of 249 g. (3 mol.) of potassium cyanate in 500 ml. (6.5 mol.) of DMF, 213 g. (2 mol.) of 2-vinyloxyethyl chloride (freshly distilled) was gradually stirred through a dropping funnel for about 2 hr. After half of the solvent had been removed under reduced nitrogen pressure, the reaction mixture was poured into brine and extracted with benzene. Under a nitrogen current, the solvent was carefully removed; the residue was then distilled to collect a 130—180°C/4 mmHg fraction. The distillate was recrystallized from ethanol to give pure tris-(2-vinyloxyethyl) isocyanurate as colorless needles. (Precaution should be taken against polymerization during the distillation.)

One gram of the tris-(2-vinyloxyethyl) isocyanurate was dissolved in 250 ml. of pure *n*-heptane by slightly warming it, yielding a clear solution. To this solution 0.1 g. of boron trifluoride etherate was added, and the mixture was stirred for about an hour. The resulting white precipitate was then filtered, washed with ether, and dried under reduced pressure to give poly-tris-(2-vinyloxyethyl) isocyanurate. The polymer did not show a weight loss on 1 hr.'s exposure to 200°C in a nitrogen stream and did not dissolve in ethanol, acetone or DMF.

11) **The Influence of Water in the Reaction System.**—In a 300-ml. flask, 41 g. (0.3 mol.) of *n*-butyl bromide, 40.5 g. (0.5 mol.) of potassium cyanate and 110 g. (1.5 mol.) of DMF were mixed; then a calculated quantity of water was added. After the temperature of the mixture had been raised to 130°C, the reaction mixture was stirred at 128—130°C for 3 hr. The solvent was then removed after the filtration of the potassium bromide. The residue was mixed with a 1/2 vol. of petroleum ether and cooled to −3°C. 1,3-Di-*n*-butyl urea was then separated as white crystals. Tri-*n*-butyl isocyanurate was obtained after the evaporation of the petroleum ether and weighed. The results are shown in Table II. The crude 1,3-*n*-butyl urea was recrystallized from a ligroin-methyl ethyl ketone mixture to form a pure sample melting at 74°C; this was identified by means of comparison with an authentic specimen.

Summary

Reactions of alkyl halides with potassium cyanate have been carried out in several aprotic solvents. Dimethylformamide and dimethyl sulfoxide have been proved to play a superior role as aprotic solvents in the displacement reaction and also in the subsequent trimerization of the isocyanates. Several trialkyl isocyanurates have been obtained in yields better than those of the other known methods.

From 2-alkoxyethyl halides and 2-vinyloxyethyl chloride respectively, tris-(2-alkoxyethyl) isocyanurates and tris-(2-vinyloxyethyl) isocyanurate have been synthesized.

The presence of water in the reaction mixture results in the formation of 1,3-dialkyl ureas, consequently decreasing the yield of isocyanurates.

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[33] N. A. Lange, "Handbook of Chemistry," Handbook Publishers, Inc. Sandusky, Ohio, Ninth Edition, (1956), p. 426.