Preparation of Phenyl Cyanate and Its Utilization for the Synthesis of α,β-Unsaturated Nitriles

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$$C_6H_5{-}OH + \underset{\mathbf{1}}{Br{-}CN} + (C_2H_5)_3N \xrightarrow{n\text{-pentane/ether}} \underset{\mathbf{2}}{C_6H_5{-}O{-}C{\equiv}N} + (C_2H_5)_3N\cdot HBr$$

The preparation of α,β-unsaturated nitriles is of considerable importance in synthetic methodology[1,2]. The procedure commonly employed entails a reaction of the appropriate organometallic substrate with cyanogen chloride[3] or with reagents derived from cyanogen chloride[2,4]. In view of the toxicity hazards associated with handling gaseous cyanogen chloride, we searched for a less volatile reagent embodying an electrophilic cyano moiety whose preparation does not require the use of cyanogen chloride. Phenyl cyanate (**2**) admirably satisfies these requirements in that it is a liquid at room temperature and thus may be conveniently transferred by means of a syringe. Also, its preparation involves the readily available cyanogen bromide (**1**) which is a solid.

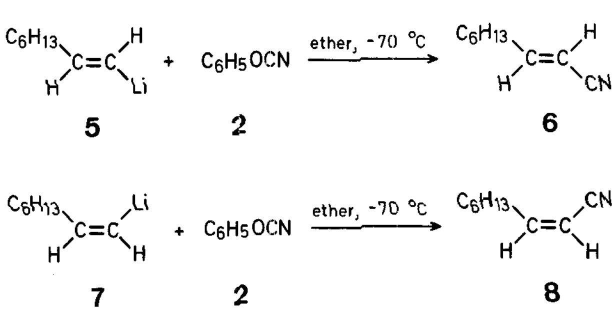
It was previously reported that treatment of a mixture of phenol and cyanogen bromide in acetone solvent with triethylamine affords the desired phenyl cyanate in only modest yield[5]. The competing von Braun degradation, in which part of the cyanogen bromide is consumed by reacting with triethylamine to produce the side-product diethylcyanamide, leaves behind unreacted phenol. This in turn serves as a cyclotrimerization catalyst converting large amounts of the phenyl cyanate into triphenyl cyanurate upon distillation or storage[5]. However, we have now found that changing the reaction medium from acetone to a mixture of *n*-pentane/ether greatly surpresses the von Braun degradation and affords the phenyl cyanate in better than 80% yield and contaminated with less than 2% of diethylcyanamide and less than 4% of phenol.

To determine the synthetic utility of the reagent, a number of lithium acetylenides **3a-g** in ether solvent were treated with 1.1 equiv of phenyl cyanate. The results obtained revealed that acetylenides containing hydrocarbon substituents **3a-e** or alkoxy substituents at the propargylic position **3f-g** reacted readily at −70 °C to produce the corresponding 2-alkynenitriles **4a-g** in high yields.

$$\underset{\mathbf{3a\text{-}g}}{R^1{-}C{\equiv}CLi} + \underset{\mathbf{2}}{C_6H_5OCN} \longrightarrow \underset{\mathbf{4a\text{-}g}}{R^1{-}C{\equiv}C{-}CN}$$

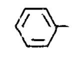
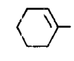
A summary of the yields of various 2-alkynenitriles obtained in the present work is given in the Table.

Finally, we briefly examined the cyanation of the (*E*)- and (*Z*)-1-lithio-1-octenes. The reagents were obtained by reacting the (*E*)- and (*Z*)-1-iodo-1-octenes with 2 equiv. of *t*-butyllithium[9]. Treatment of the (*E*)-vinyllithium compound **5** with phenyl cyanate (**2**) at −70 °C afforded an 80% isolated yield of isomerically pure (*E*)-2-nonenenitrile (**6**).



Interestingly, under similar experimental conditions, cyanation of the (*Z*)-isomer **7** produced the (*Z*)-nitrile **8** in only 48% yield. Fortunately, this problem could be circum-

Table. 2-Alkynenitriles **4** from Lithium Acetylenides **3** and Phenyl Cyanate (**2**)

Product	R^1	Yield[a] [%]	b.p./torr or m.p.	n_D^{23}	Molecular formula[b] or Lit. Data
4a	$n\text{-}C_6H_{13}$	94	59–60 °C/1.5	1.4536	$C_9H_{13}N$ (135.2)
4b		92	66–67 °C/2	1.4910	n_D^{11}: 1.4947[6]
4c	$t\text{-}C_4H_9$	87	63–64 °C/50	1.4303	n_D^{22}: 1.431[7]
4d		95	80 °C/3; 38–39 °C	—	m.p. 37 °C[8]
4e		94	60 °C/1	1.5415	C_9H_9N (131.2)[c]
4f	$Thp{-}O{-}\underset{\displaystyle CH_3}{\underset{\vert}{C}}H{-}$	76	60 °C/0.5	1.4715	$C_{10}H_{13}NO_2$ (179.2)
4g	$(C_2H_5O)_2CH{-}$	70	61–63 °C/5	1.4354	$C_8H_{11}NO_2$ (153.2)[d]

[a] Yield of isolated product.

[b] The microanalyses were in satisfactory agreement with the calculated values (C ±0.12, H ±0.12, N ±0.16).

[c] M.S.: $m/e = 131.0731$ (calc. 131.0736, M^+).

[d] M.S.: $m/e = 152.0742$ (calc. 152.0710, $M^+ - 1$).

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vented by adding the vinyllithium reagent, which was maintained at 0 °C, to an ethereal solution of phenyl cyanate at −70 °C. This slight modification gave the (*Z*)-alkenenitrile **8** in 80% yield.

Phenyl Cyanate (2):

Into a dry 500-ml three-necked flask equipped with a mechanical stirrer, thermometer and a rubber septum are placed *n*-pentane (200 ml) and anhydrous ether (80 ml). The solvent mixture is cooled in an ice bath, then it is treated with phenol (37.6 g, 0.400 mol) and cyanogen bromide (44.6 g, 0.420 mol). While vigorously stirring, triethylamine (42.6 g, 0.420 mol) is added dropwise via a syringe at a rate such as to prevent the temperature of the reaction mixture from rising above 30 °C. The resultant white slurry is stirred vigorously for an additional 1 h at 0 °C (ice bath), then the precipitated triethylamine hydrobromide is filtered on a Büchner funnel. The solid is washed with *n*-pentane (4 × 100 ml) and the combined filtrates are distilled to give **2**; yield: 40.6 g (80%); b.p. 60 °C/4 torr; n_D^{21}: 1.5064; d^{25}: 1.05. The reagent is stored at −20 °C.

I.R. (CCl_4): $\nu = 2250$ cm^{-1} ($C \equiv N$).

^{1}H-N.M.R. (neat): $\delta = 6.83$ ppm (m, 5 H_{arom}).

3-Cyclohexyl-2-propynenitrile (4b):

Into a dry flask kept under a static pressure of nitrogen are placed anhydrous ether (5 ml) and cyclohexylacetylene (2.16 g, 20.0 mmol). This solution is cooled to −70 °C (Dry Ice/acetone bath), and a hexane solution (8.3 ml) of *n*-butyllithium (20.3 mol) is added at a rate such that the reaction temperature could be maintained below −40 °C. Then, by means of a syringe, phenyl cyanate (**2**; 2.62 g, 22.0 mmol) is added at such a rate as to prevent the reaction from exotherming above −60 °C. After stirring for an additional 30 min, the resultant solution is brought to −40 °C, stirred for 15 min, and then allowed to come to room temperature before being poured into 6 molar sodium hydroxide solution (40 ml). After shaking well, the phases are separated and the aqueous layer is extracted with ether. The combined extracts are washed twice with 6 molar sodium hydroxide, four times with a saturated solution of sodium chloride, and dried with anhydrous magnesium sulfate. The solvents are removed and the residue distilled through a short path column to give the desired nitrile **4b**; yield: 2.44 g (92%); b.p. 66–67 °C/2 torr; n_D^{23}: 1.4910.

I.R. (neat): $\nu = 2320$ ($C \equiv C$); 2290 cm^{-1} ($C \equiv N$).

^{1}H-N.M.R. (neat): $\delta = 2.40$ (m, 1 H, $\underline{C}\underline{H}$—$C \equiv C$); 1.32 ppm (m, 10 H, cyclohexyl-$C\underline{H}_2$).

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