Tetrahedron Letters No.38, pp. 3309-3312, 1970. Pergamon Press. Printed in Great Britain.

PHENYL ISONITRILE FROM THE ACTION OF ALKYLLITHIUMS ON ETHYL N-PHENYLFORMIMIDATE. ADDITION OF ORGANOLITHIUMS TO ISONITRILES

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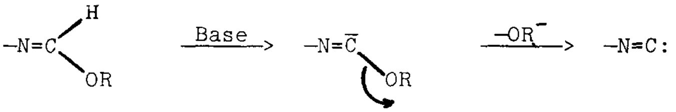
(Received in USA 2 July 1970; received in UK for publication 14 July 1970)

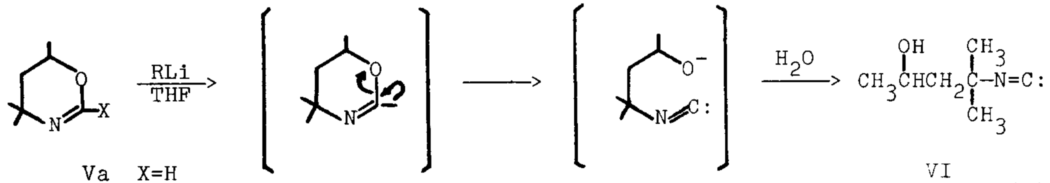
Our quest for a successful synthesis of diphenylamino isonitrile ($Ph_2N—N=C:$)[1] led us to consider the base induced α-elimination of the elements of ROH from formimidate derivatives as a potentially general route to the isonitrile function (eq. 1).[2] The recent reports of Meyers and Adickes[3] and of Walborsky and Niznik[4] prompts us to communicate our own results at this time.



(1)

In order to determine the feasibility of this route, the action of *n*-butyllithium on ethyl N-phenylformimidate(I) was investigated. Treatment of an ethereal solution of I with three equivalents of *n*-butyllithium in *n*-hexane (22%) gave two liquids in addition to recovered starting material. The unpleasant smelling volatile product (20%) had a sharp strong absorption at 2130 cm^{-1} and was identified as phenyl isonitrile(II) by comparison of its infrared spectrum with that of an authentic sample. The major product (46%) was isolated as a colorless liquid, bp. 112-113°/1.2 mm., identified as N-(5-nonyl)aniline(III)[5] n_D^{16} 1.5146, by its boiling point and by comparison of its infrared spectrum, refractive index and glc retention time with those of an authentic sample.[5] Control experiments showed that *n*-butyllithium gave a 30% yield of III with phenyl isonitrile while no III could be isolated from the reaction of *n*-butyllithium with N-phenyl pentaldimine(IV). These results are in agreement with those of Meyers and Adickes[3] and of Walborsky and Niznik.[4]

The former authors reported the formation of hydroxy isonitrile(IV) from oxazine Va, a cyclic formimidate, with n-butyllithium (Vb also gave the same result) in tetrahydrofuran; addition to the >C=N bond was observed with ether as the solvent at -78°.

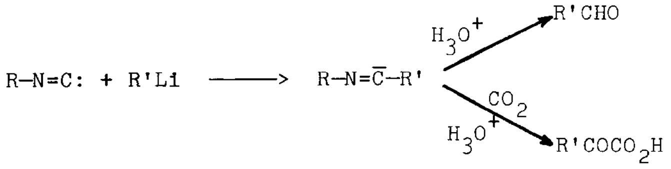


Va X=H
X=Br

VI

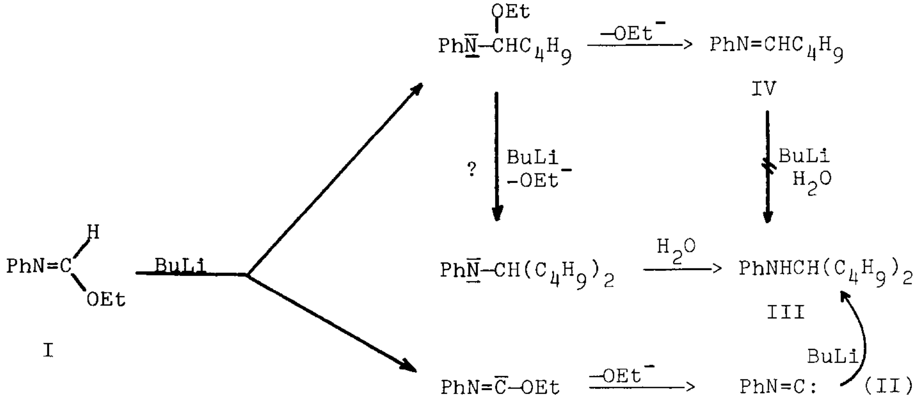
(Eq.(2)

Almost simultaneously, Walborsky and Niznik[4] reported the addition of lithium alkyls to the isonitrile group to give the aldimine anions which could be hydrolyzed to the corresponding aldehydes or converted to the α-keto acids by addition of carbon dioxide followed by hydrolysis.



(3)

Our own results can be rationalized as depicted in equation 4. Our inability to identify III from the reaction of IV with n-butyllithium makes the high yield of III from I and n-butyllithium difficult to explain except as shown below.



I

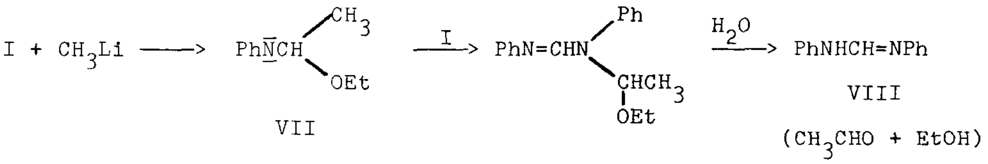
IV

III

(II)

(4)

With methyllithium I gave, in addition to 30% yield of phenyl isonitrile, a colorless solid, mp. 136-138°, in 25% yield (based on formimidate). It was identified as N,N'-diphenylformamidine(VIII) by a mixture mp. and by comparison of its infrared spectrum with that of an authentic sample. The formation of VIII may be viewed as occurring by the reaction of the initial addition product (VII) with unreacted I as shown in equation 5.



$$\mathrm{I} + \mathrm{CH_3Li} \longrightarrow \mathrm{Ph\bar{N}CH(CH_3)(OEt)}\ (\mathrm{VII}) \xrightarrow{\mathrm{I}} \mathrm{PhN{=}CHN(Ph)(CH(OEt)CH_3)} \xrightarrow{H_2O} \mathrm{PhNHCH{=}NPh}\ (\mathrm{VIII})\ (\mathrm{CH_3CHO + EtOH}) \qquad (5)$$

Exploratory attempts to make this approach a useful isonitrile synthesis were not rewarding. With triphenylmethyllithium, only traces (<10%) of phenyl isonitrile could be detected by IR and a large amount of the starting formimidate was recovered. The reaction of aniline with triethyl orthothioformate gave ∿ 10% of phenyl isonitrile directly, ethyl mercaptan and unreacted starting material; in addition, a compound which may be ethyl N-phenylthioformimidate was isolated but its structure was not investigated further.

$$\mathrm{PhNH_2} + \mathrm{HC(SEt)_3} \longrightarrow \mathrm{PhN{=}C{:}} + \mathrm{C_2H_5SH} + \mathrm{PhN{=}CHSEt} \qquad (6)$$

The action of alkyllithiums, though evidently giving only moderate yields of phenyl isonitrile with ethyl N-phenylformimidate, appears to be a promising route to symmetrically branched anilines of type $\mathrm{PhNHCHR_2}$.[6]

Acknowledgment. Partial support of this work by the Alfred P. Sloan Foundation is hereby acknowledged.

REFERENCES

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(1) N. Koga and J.-P. Anselme, Tetrahedron, 26, 1909 (1970).

(2) This expectation was based on the fact that the most generally useful isonitrile syntheses [I. Ugi et al., Angew. Chem. International Ed., 4, 472 (1965)] involve an α-elimination of HX as the ultimate step of the reaction. In a brief report, Hagedorn, Lichtel and Winkelman [Angew. Chem., International Ed., 4, 702 (1965)] reported without experimental data the formation of benzalamino isonitrile (PhCH=N–N=C:) from treatment of PhCH=N–N=CHOR with triphenylmethyl sodium.

(3) A. I. Meyers and H. W. Adickes, Tetrahedron Letters, 5151 (1969).

(4) H. M. Walborsky and G. E. Niznik, J. Am. Chem. Soc., 91, 7778 (1969).

(5) This previously unreported compound gave correct elemental analysis. An authentic sample, bp. 124-125°/2 mm., n_D^{16} 1.5145, was prepared by the alkylation of aniline with 5-bromononane.

(6) The reaction seems to be a general one (at least for simple alkyl- and aryllithium compounds) as shown by the formation of N-benzhydrylaniline in 97% from the addition of three equivalents of phenyllithium to I.