

DISSOLVING METAL REDUCTION WITH CROWN ETHER
----- REDUCTIVE DECYANATION¹⁾

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Summary: Toluene radical anion generated from potassium metal/dicyclohexano-18-crown-6/toluene system has been proved to be highly effective for reductive decyanation reaction of primary, secondary and tertiary cyanides.

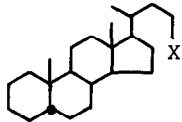


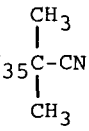
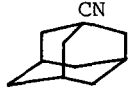
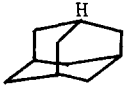
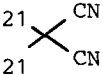
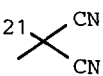
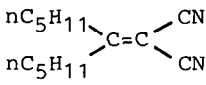
We recently reported a highly effective method for reductive defluorination of primary, secondary and tertiary alkyl fluorides to the corresponding hydrocarbons with potassium metal/dicyclohexano-18-crown-6/toluene system²⁾. The active species is believed to be a toluene radical anion generated by one electron transfer to toluene from the initially liberated potassium anion by complexation of potassium metal with dicyclohexano-18-crown-6³⁾. Taking accounts of the unusual efficiency observed in defluorination, the availability in organic synthesis of this uncommon species as well as potassium anions liberated in diglyme, tetrahydrofuran or ether has been widely examined, choosing O-sulfonates⁴⁾, sulfonamides⁴⁾, olefins^{5,6)}, dithioacetals⁵⁾, acetylenes⁵⁾, sulfides⁶⁾, sulfoxides⁶⁾ and sulfones⁶⁾ as substrates.

We now report an efficient method for reductive removal of nitrile groups of primary, secondary and tertiary alkyl cyanides to the corresponding hydrocarbons. Alkyl cyanides were chosen as substrates because a nitrile group is counted as one of the pseudo-halogens⁷⁻¹⁴⁾, and thus should behave like halides on exposure to the present reducing systems.

A typical experimental procedure is as follows¹⁵⁾: A lump (ca. 1 cm³) of potassium metal was added to a mixture of nonadecanonitrile (0.5 mmol) and dicyclohexano-18-crown-6 (1 mmol) in toluene (20 ml). The mixture was stirred under nitrogen at ambient temperature overnight, followed by quenching with isopropanol or water. Isolation of the product was carried out by usual work-up and column chromatography over silica gel.

Table 1

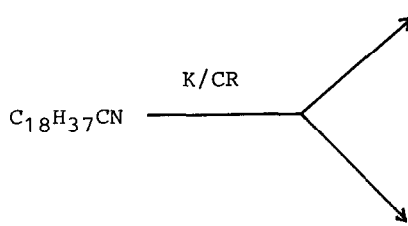
REDUCTIVE DECYANATION of NITRILES with
K/DICYCLOHEXANO-18-CROWN-6/TOLUENE

Entry	Nitriles	Product	Yield %
1	$nC_{18}H_{37}CN$	$nC_{18}H_{38}$	95.7
2	$nC_{12}H_{25}CN$	$nC_{12}H_{26}$	82.9
3	 (X=CN) (X=H)		95.3
4	$nC_{12}H_{25}$  $nC_{12}H_{25}$	$nC_{25}H_{52}$	93.5
5	$nC_{17}H_{35}$ 	$nC_{19}H_{40}$	quant
6	$nC_{17}H_{35}$ 	$nC_{17}H_{35}CH(CH_3)_2$	83.0
7			quant (GLC)
8	$(nC_{10}H_{21})_3CCN$	$(nC_{10}H_{21})_3CH$	93.5
9	$nC_{10}H_{21}$  $nC_{10}H_{21}$	$nC_{21}H_{44}$	72.3
10	$nC_{10}H_{21}$ 	(starting material recovd.)	
11	nC_5H_{11}  nC_5H_{11}	(starting material recovd.)	

As is shown in Table 1, decyanation of simple alkyl cyanides proceeded smoothly to afford the corresponding hydrocarbons in high isolation yields. The exceptions are the mono-alkyl derivative of malononitrile (entry 10), which retains an acidic alpha hydrogen susceptible to metalation, and the alkyldene derivative of malononitrile (entry 11) with rather strong C-CN bond.

Scheme 1

TOLUENE vs. THF-H⁺ as SOLVENT for K/CROWN ETHER REDUCTION*

	solvent	
	toluene	THF-H ⁺
$C_{18}H_{37}CN$ 	96 %	34-35 %
	--	37-46 %

* Nonadecanonitrile (0.75 mmol) was treated with excess potassium metal and dicyclohexano-18-crown-6 (1.5 mmol) in toluene (30 ml) or in tetrahydrofuran (30 ml) containing isopropanol (0.75 ml) under nitrogen at ambient temperature overnight.

It should be noted that a remarkable solvent effect was observed in the K/dicyclohexano-18-crown-6 reduction of a nitrile as is shown in Scheme 1. With toluene as solvent, cleavage of C-CN bond occurred selectively to yield the hydrocarbon in 96 % yield. On the other hand, with tetrahydrofuran containing isopropanol, reduction of CN group took place yielding the primary amine (37-46 %) in addition to the expected hydrocarbon (34-35 %).

Carbon-carbon bond forming reaction at the alpha position of nitrile in combination with subsequent decyanation will lead to a versatile method for the construction of rather complex molecules. Synthetic works along this line are now in progress.

Acknowledgement

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References and Notes

- 1) This work was presented in part at the 105th Annual Meeting of Pharmaceutical Society of Japan (AMPSJ), Kanazawa, April, 1985, (Abstracts of papers, p636).
- 2) T. Ohsawa, T. Takagaki, A. Haneda and T. Oishi, Tetrahedron Lett., 2583 (1981); T. Ohsawa and T. Oishi, J. Inclusion Phenomena, **2**, 185 (1984).
- 3) Reviews on alkali metal anion chemistry: J.L. Dye, Angew. Chem. Int. Ed. Engl., **18**, 587 (1979); J.M. Lehn, Pure Appl. Chem., **52**, 2303 (1980). Application studies of alkali metal anion for organic syntheses are limited. See A.G.M. Barrett, P.A. Prokopiou and D.H.R. Barton, J. C. S. Perkin Trans. I, 1510 (1981), and references cited therein; D.J. Mathre and W.G. Guida, Tetrahedron Lett., 4773 (1980).
- 4) T. Ohsawa, T. Takagaki, F. Ikehara, Y. Takahashi and T. Oishi, Chem. Pharm. Bull., **30**, 3178 (1982).
- 5) T. Ohsawa, A. Takeda, I. Watanabe, K. Masuda, J. Uzawa and T. Oishi, 103rd AMPSJ, Tokyo, April, 1983 (Abstracts of papers, p175.).
- 6) T. Ohsawa, T. Takagaki, M. Oguchi, Y. Takahashi, T. Oishi and J. Uzawa, 102nd AMPSJ, Ohsaka, April, 1982 (Abstracts of papers, p459).
- 7) As for the published methods of reduction of nitriles, see references 8-14).
- 8) D.H.R. Barton and W.D. Ollis (ed.) "Comprehensive Organic Chemistry ---The Synthesis and Reactions of Organic Compounds", **2**, p549, Pergamon Press, Oxford, 1979.
- 9) L.A. Walter and S.M. McElvain, J. Am. Chem. Soc., **56**, 1614 (1934).
- 10) P.G. Arapacos, J. Am. Chem. Soc., **89**, 6794 (1967).
- 11) C. Fabre and Z. Welvart, Bull. Soc. Chim. Fr., **1965**, 2620.
- 12) K. Tomioka, K. Koga and S. Yamada, Chem. Pharm. Bull., **25**, 2681 (1977) and the references cited therein.
- 13) A. Debal, T. Cuvigny and M. Larcheveque, Synthesis, 391 (1976) and the references cited therein.
- 14) D. Savioa, E. Tagliavini, C. Trombini and A. Umani-Ronchi, J. Org. Chem., **45**, 3227 (1980).
- 15) As for the apparatus and the procedures, see reference 2) and 4).

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