Tetrahedron Letters,Vol.24,No.43,pp 4671-4674,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain © 1983 Pergamon Press Ltd.

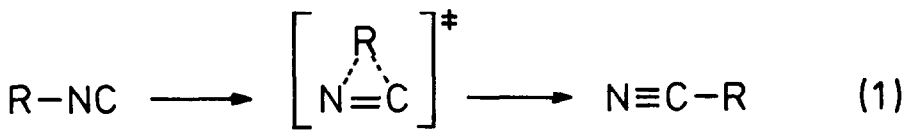
A FREE RADICAL CHAIN MECHANISM FOR THE ISONITRILE - NITRILE REARRANGEMENT IN SOLUTION AND ITS INHIBITION.[1)]

Michael Meier and Christoph Rüchardt*

Chemisches Laboratorium der Universität Freiburg, Albertstr. 21
D-7800 Freiburg, GERMANY

Abstract: A large fraction of the isonitrile-nitrile rearrangement of t-alkyl isonitriles in solution follows a free radical chain mechanism of the addition-elimination type.

The isonitrile-nitrile rearrangement[2)] of simple alkyl isonitriles is considered to be a typical example for an exothermic[3)] irreversible intramolecular thermal rearrangement via a cyclic transition state.



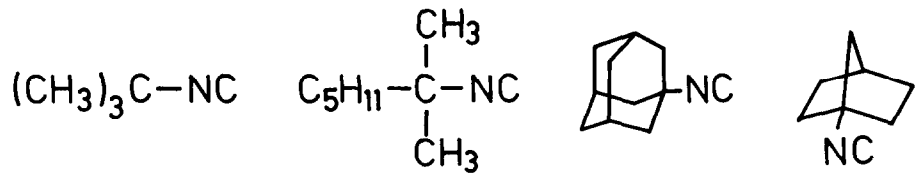
(1)

This conclusion was drawn mainly from gas phase kinetics[2,4)], from quantum chemical calculation[5)] and from the observed high percentage of retention of optical activity when optically active 2-butyl isonitrile[6)] was rearranged in the gas phase. When this type of rearrangement was performed in the liquid phase[7)], retention or racemisation of the migrating group was found as a function of concentration[7b)] and structure[7b)]. In addition, unexpected low activation entropies between -10 and -39 cal/degr·mol were reported for t-butyl (1)[8,9)], 1-adamantyl (2)[8,9)] and 1-norbornyl isonitrile (3)[9)] in solution kinetics. $\Delta S^{\ddagger}$ was in part influenced by the concentration[9)]. In some cases[8,9)], hydrocarbons RH were found as side products e.g. up to 40 % adamantane when 2 was isomerized in diglyme solution[8)].
Because several publications about free radical additions to isonitriles have become known in recent years[1,2b,10)], we suspected that at higher isonitrile concentrations a free radical chain mechanism (2) and (3)[11)] was competing with the synchronous pathway.

$$R\text{-}NC + R^{\cdot} \longrightarrow R\text{-}N=\dot{C}\text{-}R \qquad (2)$$

$$R\text{-}N=\dot{C}\text{-}R \longrightarrow R^{\cdot} + NC\text{-}R \qquad (3)$$

A similar reaction sequence was proposed previously for explaining the products when di-t-butylperoxide was decomposed in t-butylisonitrile[12].
In context with our interest in migration aptitudes of bridgehead groups in 1.2-rearrangements[13], we therefore began a quantitative investigation of the products and of the kinetics of the rearrangement of the isonitriles 1 - 4 in n-alkane solution in the presence of free radical inhibitors (see table).



1 2 3 4

From the first column in the table it is seen, that the yields of nitrile are almost quantitative for the isonitriles 2 - 4. The lower yield for the 1 rearrangement, may be due to analytical problems with the more volatile compounds. Only minor amounts of hydrocarbon RH have been detected (see footnote i of the table). The last column of the table shows, that the inhibited reactions occur at a temperatureof 50°C higher than when no inhibitor is present. Therefore the uninhibited reaction must proceed mainly by the free radical chain mechanism (2) and (3). $\Delta G^{\neq}$(250°C) of the inhibited reaction is identical for the isonitriles 1 - 4 , which supports the pyramidal geometry of the migrating carbon at the transition state of the concerted process (1) [2,4] as proposed by theory[5]. The entropies of activation $\Delta S^{\neq} \sim 0$ are also in agreement with this mechanism. The activation parameters for the rearrangement of 1 are probably less accurate due to a systematic error in the analytical procedure. From the data in the table a rate constant $k_1 = 0.59 \cdot 10^{-5} s^{-1}$ is extrapolated for 1 at 200°C which is slower than the gas phase value $k_1 = 1.34 \cdot 10^{-5} s^{-1}$ of ref. 4d) for this temperature. This discrepancy as well as the negative $\Delta S^{\neq}$ value[8] of this reaction may be an indication, that even in the more dilute gas phase the radical chain reaction (2) and (3) is a competing process. When the rates of isomerisation of 3 and 4 in the gas phase were measured by differential scanning calorimetry (DSC)[14], activation parameters in very close agreement with those in the table were obtained without adding an inhibitor[1].

Table : Isonitrile - nitrile rearrangement of $\underline{1}$ - $\underline{4}$ in 0.06 - 0.1 M solutions inhibited by 3-cyanopyridine or 1.1-diphenylethylene

RNC	% RCN [T°C]	$\Delta G^{\neq}$[250°C] $\pm \sigma$[a] [kcal·mol^{-1}]	$\Delta H^{\neq}$ $\pm \sigma$[a]	$\Delta S^{\neq}$ $\pm \sigma$[a] [e.u.]	n[b] ΔT[c]	T[°C] ($\tau_{1/2}$=1h)[d]
$\underline{1}$[e]	75-80[f,g]	39.0[f,g]	43.3	8.1	6	238
	(200-250)	(0.5)	(0.4)	(0.7)	210-252	(183)[d]
$\underline{2}$[h]	83-93[f,g,i]	39.2[f]	38.7	-1.0	5	240
	(210-250)	(0.5)	(0.3)	(0.6)	210-252	-
$\underline{3}$[h]	100[f]	39.0[f]	39.4	0.8	5	236
	(240)	(1.1)	(0.7)	(1.5)	210-250	(180)[d,k]
$\underline{4}$[h]	100[f]	38.8[f]	39.4	1.1	5	234
	(235)	(0.5)	(0.3)	(0.6)	210-251	(175)[d]

a) σ = standard deviation; the kinetics were followed by GC analysis of the isonitrile concentration.
b) number of kinetic runs.
c) temperature range of kinetic runs.
d) T($\tau_{1/2}$= 1h) for the non inhibited reaction is given in brackets[9] in °C at ca. c = 6 · 10^{-2} mol/l.
e) in dodecane.
f) inhibitor: 1.1-diphenylethylene in c = 0.1 mol/l.
g) inhibitor: 3-cyanopyridine in c = 0.16 mol/l.
h) in hexadecane.
i) in addition 6-7% 2-methyloctane and corresponding alkenes were analyzed.
k) for $c_o \sim 6 \cdot 10^{-4}$ mol/l.

Work is in progress to perform an analogous analysis for other isonitriles and to test our conclusions by stereochemical tests. It is hoped that this analysis will aid in making the isonitrile - nitrile rearrangement more useful for synthetic work[2].

Acknowledgement: The authors are grateful to Dr.I.Mergelsberg for some preliminary experiments, to Drs. H.-D.Beckhaus and H.Langhals for advice and discussions and to the "Fonds der Chemischen Industrie" for financial support.

References:

1. Taken from the diploma thesis of M.Meier, Universität Freiburg 1983.
2. For reviews see a) I.K.Ugi, Isonitrile Chemistry, Academic Press New York-London, 1971; b) H.M.Walborsky and M.P.Periasamy in The Chemistry of the Nitrile and Isonitrile Group (Z.Rappoport and S.Patai editors) (preprint).
3. a) M.H.Baghal-Veyjoodee, J.L.Collister and H.O.Pritchard, Can.J.Chem. 55, 2634 (1977); b) S.W.Benson, J.Chem.Educ. 42, 502 (1965)
4. a) K.M.Maloney and B.S.Rabinovitch, J.Phys.Chem. 73, 1652 (1969);
   b) J.L.Collister and H.O.Pritchard, Can.J.Chem. 54, 2380 (1976);
   c) D.L.Bunker and W.L.Hase, J.Chem.Phys. 59, 4621 (1973);
   d) J.Casanova, N.D.Werner and R.E.Schuster, J.Org.Chem. 31, 3473 (1966) and references cited in these papers.
5. a) G.W.Van Dine and R.Hoffmann, J.Amer.Chem.Soc. 90, 3227 (1968);
   b) M.J.S.Dewar and M.C.Kohn, ibid. 94, 2704 (1972);
   c) D.H.Liskow, C.F.Bender and H.F.Schaefer, ibid. 94, 5178 (1972);
   d) P.Saxe, Y.Yamaguchi, P.Pulay and H.F.Schaefer, ibid. 102, 3718 (1980).
6. 87 % but apparently not complete retention in the migrating 2-butyl- group is reported in ref. 4d).
7. a) R.W.Horobin, N.R.Khan, J.McKenna and B.G.Hutley,Tetrahedron Lett. 1966, 5087; b) M.Shibasaki, T.Sato, N.Ohashi, S.Terashima and S.Yamada, Chem. Pharm.Bull. 21, 1868 (1973) and previous papers in this series.
8. T.Sasaki, S.Eguchi and T.Katada, J.Org.Chem. 39, 1239 (1974).
9. G.Range, Dissertation Universität Freiburg 1979.
10. a) D.H.R.Barton, G.Bringmann, G.Lamotte, W.B.Motherwell, R.S.H.Motherwell and A.E.A.Porter, J.C.S.Perkin I, 1980, 2657; D.H.R.Barton and W.B. Motherwell in Organic Synthesis Today and Tomorrow (B.M.Trost and C.R. Hutchinson editors), Pergamon Press, Oxford, 1981.
    b) T.Saegusa, S.Kobayashi, Y.Ito and N.Yasuda, J.Amer.Chem.Soc. 90, 4182 (1968); T.Saegusa, S.Kobayashi and Y.Ito, J.Org.Chem. 35, 211 (1970).
    c) P.M.Blum and B.P.Roberts, J.C.S.Perkin II, 1978, 1313;
    d) D.S.Matteson and R.A.Bailey, Chem.Ind.(London), 1967, 191; R.W.Stackman, J.Macromol.Sci.Chem. 2, 225 (1968).
11. for an early dispute concerning free radical catalysis see D.H.Shaw and H.O.Pritchard, Can.J.Chem. 45, 2749 (1967); T.Fujimoto, F.M.Wang and B.S. Rabinovitch, ibid. 50, 3251 (1972) and ref. 4b).
12. L.A.Singer and S.S.Kim, Tetrahedron Lett. 1974, 1881; S.S.Kim, ibid. 1977, 1274.
13. H.Langhals and C.Rüchardt, Chem.Ber. 114, 3831 (1981); E.Wistuba and C. Rüchardt, Tetrahedron Lett. 1981, 3389, 4069.
14. For the procedure see W.Bernlöhr, H.-D.Beckhaus, K.Peters, H.-G.v.Schnering and C.Rüchardt, Chem.Ber. in print; E.Koch, Angew.Chem. 95, 185 (1983); Angew.Chem.,Int.Ed.Engl. 22, 225 (1983).

(Received in Germany 25 July 1983)