

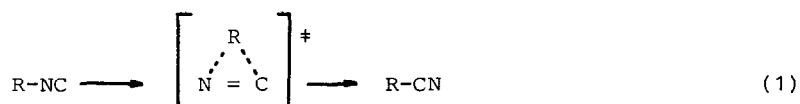
FLASH PYROLYSIS OF ISONITRILES, A STEREOSPECIFIC HIGH YIELD
REACTION

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Summary: Nitriles are obtained from isonitriles in almost quantitative yields and with almost complete retention of the stereochemistry by a convenient flash pyrolytic procedure.

The isonitrile-nitrile rearrangement (1) has been investigated so far mainly for its theoretical background as prototype of an uncatalysed thermal reaction¹⁻³).

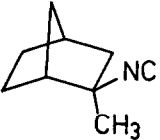
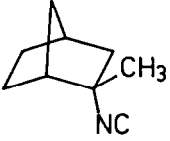


Application of this reaction in synthesis has been scarce due to difficulties which are encountered when this high temperature process is performed in solution. Hydrocarbon side products RH, R_{-H} or even R-R are obtained in appreciable yields^{2,4}) (see table 1), and the stereochemical integrity of the migrating groups is only partly retained. Both of these disturbing results are not explained by the generally accepted concerted mechanism of this rearrangement (1). They are, however, a logic consequence of the free radical chain mechanism (2) proposed recently in the course of a kinetic study of this reaction in solution⁵).



It was possible to suppress this chain for the kinetic study of process (1) by certain inhibitors⁵), by particularly careful degassing^{4,6}) or by conducting the reaction in the gas phase in the sealed sample pan of a differential-scanning-calorimeter without solvent^{4,5}). It was to be expected therefore, that under these conditions the yields and the stereochemical results of the isonitrile-nitrile rearrangements are also improved.

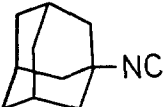
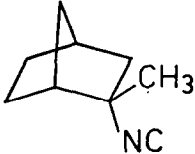
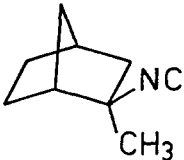
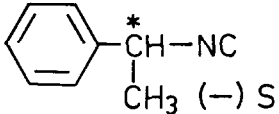
Table 1: Preparative Isonitrile-Nitrile Rearrangements in Solution

R-NC	Lit.	Solvent T°C	% RCN % RH, R _H	retention of stereochemistry
$\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_6\text{H}_5\text{CH}_2-\overset{*}{\text{C}}-\text{NC} \\ \\ \text{C}_2\text{H}_5 \end{array}$	2	a) 280	86 ^{b)} -	90% ^{c)}
$\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_6\text{H}_5\text{CH}_2-\overset{*}{\text{C}}-\text{NC} \\ \\ \text{COOC}_2\text{H}_5 \end{array}$	2	a) 280	92 ^{b)} -	9% ^{c)}
$\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_6\text{H}_5-\overset{*}{\text{C}}-\text{NC} \\ \\ \text{C}_2\text{H}_5 \end{array}$	2	a) 280	21 67	19% ^{c)}
$\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_6\text{H}_5-\overset{*}{\text{C}}\text{H}-\text{NC} \end{array}$	4	d) 230	83 6	41% ^{c)}
 exo	4	d) 250	68 ^{e)} 25	88%-exo ^{e)} 12%-endo
 endo	4	d) 250	76 ^{e)} 16	64%-endo ^{e)} 36%-exo

a) in diphenyl ether; b) crude yield; c) optical yield; d) in hexadecane; e) exo- and endo- refers to the orientation of the CN-group, gc-yield.

Conducting the reaction by flash-pyrolysis⁷⁾ proved to be the most convenient alternative (table 2). Almost quantitative yields and complete retention of the stereochemistry make this procedure now an easy way of transferring (optically active) primary amines into carboxylic acids with retained stereochemistry. This is the reverse of the classic degradation reactions of acids⁸⁾. The saponification of the nitriles in acid solution required for this transformation is a well developed reaction. Even optically active 1-phenylpropionitrile, which is sensitive to racemisation was successfully saponified to optical active hydratropic acid without racemisation⁹⁾. Because the opti-

Table 2: Isonitrile-Nitrile Rearrangement by Flash-Pyrolysis at 10^{-2} Torr ⁷⁾

R-NC	g	T°C	time min. a)	% RCN b)	remarks
$\text{H}_3\text{C}-(\text{CH}_2)_4-\overset{\text{CH}_3}{\underset{\text{CH}_3}{\text{C}}}-\text{NC}$	1.0	540	25	90	8% RH and R _H
	0.10	540	2	92	side products
	0.20	540	30	98	-
	0.10	540	5	80	<1% of isomeric
	0.60	540	25	97	exo-nitrile
	0.50	540	20	95	<1% of isomeric endo-nitrile, 1% RH, R _H
	1.0	500	-	98	o.y.=97.4% c,d)
	1.2	500	30	98	
	1.3	500	35	99	
	3.9	500	120	97	

a) time required for sample evaporation at 25°C; b) isolated yields. Products were identified by comparison with authentic samples; c) yields determined by g.c.; optical yields o.y. based on optical rotation; d) o.p. of starting material was ≥ 0.95 ; optical yields are corrected values.

cal resolution of chiral primary amines is usually a comparably easy process, this sequence of reactions may prove valuable for the synthesis of optical active pyrethroid acids ¹⁰⁾ or non steroidal antiinflammatory agents ¹¹⁾.

We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for support of this work and Miss M. Lutterbeck for technical assistance.

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6. Oxygen apparently is responsible for chain initiation.
7. An apparatus like that shown on p. 28 of ref. 3 was used with a 50 x 2.4 cm quartz tube.
8. cf. Organic Reactions Vol. 3, 267, 307, 337 (1964).
9. 3.3g S(-)-1-phenyl-propionitrile was heated in a mixture of 3.8 ml conc. H₂SO₄, 3.8 ml acetic acid and 1.2 ml water for 1.5h under reflux. S(+)-2-phenyl-propanoic acid was isolated in the usual way in 85% yield and 100% optical yield. In addition 5% S(+)-2-phenyl-propanoic acid amide with ≥ 99% optical yields was obtained.
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(Received in Germany 18 April 1984)