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REACTION OF N-ALKOXYCARBONYLAZIRIDINES WITH NITRILES

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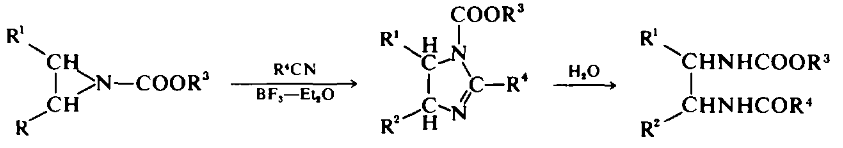
Abstract—The acid catalysed reaction of acetonitrile or benzonitrile with N-alkoxycarbonylaziridines, **1a** and **1b** yields the corresponding 1-alkoxycarbonyl-2-imidazolines, **2ax**, **2ay**, and **2bx**. The imidazolines obtained by the reaction of N-ethoxycarbonyl-2,3-tetramethyleneaziridine (**1c**) with acetonitrile or benzonitrile are labile and are readily hydrolysed to *trans*-cyclohexane-1,2-diamine derivatives (**3cx** or **3cy**). The nitrile-addition supposedly proceeds S_N2 type C—N bond cleavage and C—N bond formation.

N-Alkoxycarbonylaziridines are readily accessible by the addition of alkoxycarbonylnitrenes to olefins[1] or by the addition of iodine isocyanate to olefins and the subsequent alcoholysis and base-treatment.[2] They react with nucleophiles in the presence of an acid catalyst.[3,4] This article describes an acid catalysed reaction of N-alkoxycarbonylaziridines with nitriles, thus providing a new route to 2-imidazolines.

The reaction of 1-methoxycarbonyl-2-phenylaziridine (**1a**)[2] with acetonitrile and a catalytic amount of boron trifluoride etherate gave 1-methoxycarbonyl-2-methyl-4-phenyl-2-imidazoline (**2ax**) in 82% yield. The structure was elucidated as follows. IR absorptions of **2ax** at 1740 cm^{-1} and 1630 cm^{-1} are due to an N-methoxycarbonyl and an imino group respectively. The NMR signal (Table 2) at δ 2·30 is due to the Me proton on C-2. The aziridine **1a** also reacted with benzonitrile at 100°, affording **2ay** as a sole product.

The aziridine **2b** having an attached 8-membered ring reacted with acetonitrile to give **2bx** and no accompanying transannular products were detected. The purification of the product **2by** resulting from the reaction of **2b** and benzonitrile was unsuccessful. The imidazolines, **2cx** and **2cy**, which were obtained by the reactions of **2c** with acetonitrile and with benzonitrile, were unstable to moisture and the isolation could not be accomplished. However the spectral data (Table 2) suggested the formation of **2cx** and **2cy**. Distillation or chromatographic purification of **2cx** resulted



1 **2** **3**

a: $R^1 = H, R^2 = Ph, R^3 = Me$.
b: $R^1, R^2 = —(CH_2CH_2CH{=}CHCH_2CH_2)—, R^3 = Et$.
c: $R^1, R^2 = —(CH_2)_4—, R^3 = Et$.
x: $R^4 = Me$.
y: $R^4 = Ph$.

Table 1. Reaction of 1 with nitriles

Aziridine	Nitrile	Product	Reaction Time (hr)	Reaction Temp (°)	Yield (%)
1a	MeCN	**2ax**	4	81	82
1a	PhCN	**2ay**	4	100	56
1b	MeCN	**2bx**	8	81	67
1c	MeCN	**3cx**	6	81	45
1c	PhCN	**3cy**	6	100	50

Table 2. Physical properties of the new compounds

Compound	b.p. (°/mmHg) |m.p. (°)|	IR (cm^{-1})[a]	NMR (δ)[b]
2ax[c]	140/0·08	1740, 1630, 760 700	2·30 (s, 3H, CH_3), 3·35 (d, J = 9·6 Hz, 1H, CH), 3·58 (s, 3H, CH_3), 3·90 (d, J = 9·3 Hz, 1H, CH), 4·84 (dd, J = 9·6, 0·3 Hz, 1H, CH), 7·07 (s, 5H, Ph),
2ay[d]	170/0·08 (bath temp)	1720, 1630	3·65 (s, 3H, CH_3), 3·95 (d, J = 8·0 Hz, 1H, CH), 4·35 (d, J = 9·6 Hz, 1H, CH), 5·25 (dd, J = 8·0, 9·6 Hz, 1H, CH), 7·30 (s, 10H, Ph)
2bx[e]	160/0·09	1725, 1660, 1650	0·8–2·5 (m, 8H, methylenes), 1·30 (t, 3H, CH_3), 2·30 (s, 3H, CH_3), 3·7–4·2 (m, 2H, methines), 4·26 (q, 2H, CH_2), 5·5–5·8 (m, 2H, CH=CH)
2cx[f]		1720, 1620	1·0–2·2 (m, 8H, methylenes), 1·35 (t, 3H, CH_3), 2·33 (s, 3H, CH_3), 2·5–3·3 (m, 2H, methines), 4·25 (q, 2H, CH_2)
2cy[f]		1715, 1615	1·0–2·2 (m, 8H, methylenes), 0·95 (t, 3H, CH_3), 2·60 (m, 1H, CH), 3·29 (m, 1H, CH), 3·87 (q, 2H, CH_2), 7·30 (m, 5H, Ph)
3cx[g]	|134–135|[j]	3300, 3250, 1690 1640, 1540[h]	1·20 (t, 3H, CH_3), 1·1–2·7 (m, 8H, methylenes), 1·80 (s, 3H, CH_3), 3·2–3·8 (m, 2H, methines), 4·08 (q, 2H, CH_2), 5·1 (br s, 1H, NH), 6·3 (br s, 1H, NH)
3cy[i]	|175–176|[j]	3350, 3300, 1690 1640, 1550[h]	1·20 (t, 3H, CH_3), 0·7–3·0 (m, 8H, methylenes), 3·2–4·5 (m, 2H, methines), 4·10 (q, 2H, CH_2), 5·2 (br s, 1H, NH), 7·2 (br s, 1H, NH), 7·7 (s, 5H, Ph)

[a] Neat liq film unless otherwise stated.

[b] Recorded in deuteriochloroform soln.

[c] MS: *m/e* (relative abundance) 218 (M^+, 42), 141 (100), 140 (58), 90 (51). Found: C; 66·1, H; 6·6, N; 12·3%. $C_{12}H_{14}N_2O_2$ requires: C; 66·0, H; 6·5, N; 12·8%.

[d] MS: *m/e* (relative abundance) 280 (M^+, 17), 193 (100), 90 (21), 77 (12). Found: C; 72·5, H; 5·8, N; 10·0%. $C_{17}H_{16}N_2O_2$ requires: C; 72·8, H; 5·8, N; 10·0%.

[e] MS: *m/e* (relative abundance) 236 (M^+, 43), 198 (77), 197 (78), 95 (77), 42 (100). Found: C; 66·1, H; 8·6, N; 11·9%. $C_{13}H_{20}N_2O_2$ requires: C; 66·1, H; 8·5, N; 11·9%.

[f] Not isolated in a pure form.

[g] MS: *m/e* (relative abundance) 228 (M^+, 2), 169 (36), 140 (40), 112 (42), 111 (40), 97 (50), 57 (50), 44 (100). Found: C; 57·9, H; 8·9, N; 12·2%. $C_{11}H_{20}N_2O_3$ requires: C; 57·9, H; 8·8, N; 12·3%.

[h] KBr.

[i] MS: *m/e* (relative abundance) 290 (M^+, 8), 169 (34), 105 (100), 77 (48). Found: C; 66·5, H; 7·9, N; 9·7%. $C_{16}H_{22}N_2O_3$ requires: C; 66·2, H; 7·6, N; 9·7%.

[j] Recrystallized from n-hexane-ethyl acetate (1 : 1).

in hydrolysis to give N-acetyl-N′-ethoxycarbonylcyclohexane-1,2-diamine (**3cx**). Similarly column chromatography of **2cy** afforded bisamide **3cy**. The configuration of the two amino groups was proved to be trans by the following sequence. Hydrolysis of the crude **2cx** with conc hydrochloric acid, followed by sulfonylation with benzenesulfonyl chloride, yielded *trans*-N,N′-bisbenzenesulfonylcyclohexane-1,2-diamine.* Thus the attack of the nitrile to the aziridine ring occurred in a trans fashion.** The mechanism of the reaction can be interpreted as shown in the scheme. Since the presence of a Lewis acid is necessary, direct nucleophilic attack by nitriles is excluded. Boron trifluoride coordinates to the O atom of **1c**, whereas acetonitrile attacks the aziridine ring to afford a zwitter ion **4**, which subsequently cyclizes to **2cx**. The stereochemistry clearly indicates an S_N2 type reaction path.[3,4] Formation of bisamide **3cx** can be understood in terms of the intermediacy of 2-hydroxyimidazolidine **5** which isomerizes to **3cx** *via* a 6-membered cyclic array.

Since aziridines react with nitriles only in the form of the unstable aziridinium salts,[6] the present reaction† constitutes one of useful tools in organic

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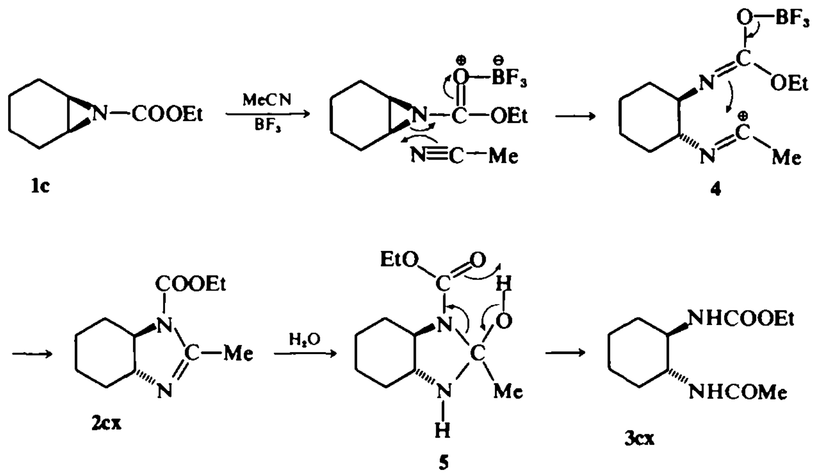
*The *trans* isomer is recorded to melt at 154–155°, while the *cis* isomer melts at 165–166°. See Ref 5.

**Acid catalysed hydration of aziridine is reported to yield *trans*-2-amino alcohols exclusively. As to the stereochemistry of the ring opening of the aziridines, see Ref 2.

†Acid catalysed reactions of epoxides with nitriles have been recorded to afford 2-oxazolidinium salts or 2-amino alcohols. See Ref 7. Episulphides also react with nitriles to provide 2-thiazolines. See Ref 8.



SCHEME

syntheses to prepare 2-imidazolines and 1,2-diamines.*

EXPERIMENTAL

IR spectra were recorded on a Shimadzu spectrophotometer IR-27 G, NMR spectra on a JEOL C-60-H spectrometer and mass spectra on a Hitachi RMU-6L spectrometer. All temps are uncorrected.

Reaction of aziridines with acetonitrile

A typical procedure. To a mixture of boiling acetonitrile (15 ml) and BF_3-etherate (0·02 ml) aziridine **1a** (0·40 g, 2·3 mmol) was added drop by drop under N_2 and refluxing was continued for 4 hr. After cooling, the acid was neutralized with anhyd Na_2CO_3 and the soln was concentrated *in vacuo*. The product was purified by preparative layer chromatography on alumina (elution with dichloromethane). Table 2 lists the physical properties of the products.

Hydrolysis of **2cx**. A mixture of **2cx** (200 mg) and conc HCl (2 ml) was heated at 120° in a sealed tube for 12 hr. After cooling HCl was removed *in vacuo*, and the residue was treated with 10% NaOH aq soln (5 ml) and benzenesulfonyl chloride (0·5 ml). After stirring at room temperature overnight, work-up gave colorless needles, mp 151–152° (benzene). An authentic sample prepared according to the reported procedure[5] melted at 150–152°. NMR and IR spectra of both were completely identical.

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*An alternative route to 1,2-diamines involves the reaction of sodium azide with aziridines followed by hydrogenolysis. See Ref 5.