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Nitroimidazoles: Part XX—Reactions of 2,4-Dinitroimidazole with 2-Haloethanols, 3-Chloropropionitrile & Propylene Oxide†‡

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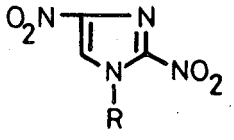
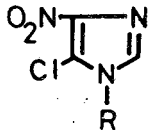
The reaction of 2,4-dinitroimidazole (**1**) with 2-chloroethanol, 3-chloropropanol or 3-chloropropionitrile gives 2-chloro-4-nitroimidazole (**7**) and not 4-chloro-5-nitroimidazole (**3**) as claimed in earlier literature. **1** and 2-bromoethanol likewise yield 2-bromo-4-nitroimidazole (**11**). **7** is methylated to isomeric methyl derivatives **8** and **13** and **11** to **12** and **14**. In the reaction of **1** with 3-chloropropionitrile, other products **9**, **10** and **16** have been isolated. **1** is unaffected by 2-chloropentane. 2-Chloroethanol and 1-methyl-2,4-dinitroimidazole (**2**) afford **8**. HCl formed from hot 2-chloroethanol in the presence of nitroimidazoles seems to be responsible for the displacement of NO_2 group at position-2 with chlorine. **1** and propylene oxide yield imidazooxazoline (**18**) and the dinitro alcohol (**19**) along with a small amount of the isomer **20**. **19** is transformed to imidazooxazoline (**21**) by excess propylene oxide or piperidine. **7** and propylene oxide afford isomeric alcohols **26** and **27**, the latter being readily transformed to **18**. Piperidine opens the oxazoline ring in **18** to yield **25**. ^1H and ^{13}C NMR data are used to derive new structures.

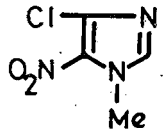
In an earlier publication[1] of this series, we had commented on literature reports[2-4] that the reaction of 2,4-dinitroimidazole (**1**) with hot 2-chloroethanol led to the formation of 4-chloro-5-nitroimidazole (**3**). While we offered a tentative rationalisation of this interesting phenomenon, we had suggested the possibility of the product being in fact 2-chloro-4-nitroimidazole (**7**). We have now repeated the reaction and identified the product as **7** by comparison with an authentic sample[1] as well as by conversion into two N-methyl derivatives which were identical with known 1-methyl-2-chloro-4-nitro-(**8**)- and 5-nitro(**13**)-imidazoles[1] and different from **4** and **6** which would be the expected methylation products of **3**. **7** is formed



1 R = H
2 R = Me



3 R = H
4 R = Me
5 R = CH_2CH_2CN



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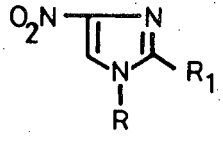
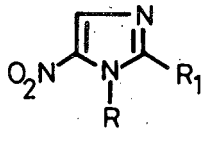
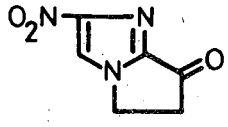


7 R = H; R_1 = Cl
8 R = Me; R_1 = Cl
9 R = CH_2CH_2CN; R_1 = Cl
10 R = $CH_2CH_2CONH_2$; R_1 = Cl
11 R = H; R_1 = Br
12 R = Me; R_1 = Br



13 R = Me; R_1 = Cl
14 R = Me; R_1 = Br
15 R = Me; R_1 = NO_2



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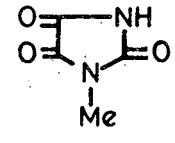

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†Contribution No. 710.
‡Part XIX: *Indian J Chem*, **22B** (1983) 342.

from **1** also by the action of hot phosphorus oxychloride or hydrochloric acid although the latter reagent left **1** unaffected in the cold. We have also shown that the reaction occurs as well with commercial 2-chloroethanol which is acidic as it does with the reagent neutralized over sodium bicarbonate. The same transformation occurs with 3-chloropropanol, but **1** is practically unaffected by excess boiling 1-chloropentane for 20 hr.

The action of hot 2-bromoethanol (commercial or distilled as such or neutralized over sodium bicarbonate) on **1** gave 2-bromo-4-nitroimidazole (**11**) in good yield. The chemical shift of the imidazole C–H in DMSO-d_6 suggests that **11** is a 1*H*-4-nitroimidazole[5]. Methylation of **11** with diazomethane afforded a mixture of known 2-bromo-1-methyl-4-nitro-(**12**)- and 5-nitro-(**14**)-imidazoles which were separated and identified using PMR and ^{13}C NMR spectral data (Tables 1 and 2). Thus **12** showed a pronounced shift for the imidazole proton going from $CDCl_3$ to DMSO-d_6 which **14** did not. In the ^{13}C NMR spectra, C-5 of **12** was seen at 123.3 ppm as a large doublet (J = 206 Hz) the two limbs of which were further split into a quartet (J = 2.7 Hz). The C-4 of **14** was seen only as a doublet at 132.5 ppm (J = 204 Hz). These were in conformity with our earlier observations[5]. Methylated products of **3** (Br instead of Cl) would have given a signal for C-2 as a doublet (J = ~210-230 Hz) with further fine structure[5].

The reaction of **1** with 3-chloropropionitrile has been reported[6] to give **3** as the major and **5** as the minor products. We have identified the major product again to be **7**. Likewise the structure of **5** may have to be revised to **9**. Additionally we obtained the corresponding amide **10**. The structure of **9** and **10** were supported by PMR data. A very small amount of a byproduct was also isolated by us, slightly contaminated with **7**. We have assigned tentatively structure (**16**) to it on the basis of PMR ($CDCl_3$, DMSO-d_6) (Table 1) and mass spectral data. **16** arises presumably from **9**, but the mechanism is not clear.

Boiling 2-chloroethanol as well as phosphorus oxychloride converted **2** into **8**. A similar reaction of the first reagent with **15** afforded a mixture of products in which **13** could be detected (TLC, mass M^+ at m/z 161, 163), while the reaction of **15** with phosphorus oxychloride was complex and gave a small amount of the imidazolidinetrione (**17**)[7]. The latter was presumably formed by nuclear chlorination and hydrolytic loss of NO_2 and Cl groups. From all these

Table 1—PMR Data of Various Nitroimidazoles and Nitroimidazo-oxazolines

Compd No.	δ(ppm) in $CDCl_3$ for protons at			δ (ppm) in DMSO-d_6 for protons at		
	C-4	C-5	Others	C-4	C-5	Others
9	—	7.91	4.38 (*t*, NCH_2), 2.93 (*t*, CH_2CN)	—	8.61	4.38 (*t*, NCH_2), 3.15 (*t*, CH_2CN)
10	—	7.92	4.39 (*t*, NCH_2), 5.44 (*bh*, $CONH_2$); 2.73 (*t*, $COCH_2$)	—	8.45	7.43, 6.97 (2*t*, $CONH_2$), 4.28 (*t*, NCH_2), 2.65 (*t*, $COCH_2$)
11				—	8.40	
12	—	7.80	3.75 (N–CH_3)	—	8.54	3.69 (N–CH_3
14	7.95	—	4.01 (N–CH_3)	8.11	—	3.89 (N–CH_3)
16	—	7.88	4.35 (*t*, NCH_2), 2.92 (*t*, CH_2CO)		8.55	4.25 (*t*, NCH_2), 2.88 (*t*, CH_2CO)
18	7.67	—	5.57 (*m*, CH–O), 4.66, 4.09 (2*dd*, CH_2), 1.71 (*d*, CH_3)	7.84	—	5.64 (*m*, CH–O), 4.63, 4.06 (2*dd*, CH_2), 1.57 (*d*, CH_3)
19	—	8.00	4.75 (*m*), 4.28 (*m*) (together CH_2–CH–), 1.98 (*bm*, OH), 1.37 (*d*, CH_3)	—	8.68	5.11 (*h*, OH), 4.44, 4.24 (2*dd*, CH_2), 4.00 (*m*, CH–O), 1.13 (*d*, CH_3)
20	—	8.13	5.22 (*m*, CH), 3.89 (*m*, CH_2), 1.67 (*d*, CH_3)	—	8.87	5.20 (*m*, OH, CH), 3.64 (*m*, CH_2), 1.52 (*d*, CH_3)
21	—	7.54	5.43 (*m*, CH–O), 4.43, 3.89 (2*dd*, CH_2), 1.67 (*d*, CH_3)	—	8.11	5.47 (*m*, CH–O), 4.44, 3.92 (2*dd*, CH_2), 1.54 (CH_3)
22	—	7.54	5.09 (*m*, CH–Me), 4.70 (*m*, CH_2), 1.61 (*d*, CH_3)	—	8.25	5.08 (*m*, CH–Me), 4.72 (*m*, CH_2), 1.48 (*d*, CH_3)
25	7.88	—	3.83-4.36 (*m*, N–CH_2CH–O), 3.09-3.38 (*m*, CH_2–N–CH_2), 2.13 (*d*, OH), 1.56-2.00 [*m*, C–$(CH_2)_3$–C] 1.17 (*d*, CH_3)	7.96	—	4.94 (*d*, OH), 3.52-4.12 (*m*, N–CH_2–CH–O), 3.16-3.38 (*m*, CH_2–N–CH_2), 1.49-1.77 [*m*, C–$(CH_2)_3$–C], 0.95 (*d*, CH_3)
26	—	7.91	3.67-4.40 (*m*, CH_2–CH), 2.55 (*d*, OH), 1.32 (*d*, CH_3)		8.45	5.11 (*bs*, OH), 3.78-4.16 (*m*, CH_2CH), 1.12[b] (*d*, CH_3)
27	7.90	—	4.46 (*m*, CH_2), 4.17 (*m*, CH), 2.16 (*bs*, OH), 1.34 (*d*, CH_3)	8.13	—	5.08 (*d*, OH), 4.30 (*m*, CH_2), 3.89 (*m*, CH), 1.12 (*d*, CH_3)

[a] Numbering arbitrary for bicyclic nitroimidazoles in Tables 1 and 2.
[b] Actually seen as a triplet with the central limb shorter than the other two; virtual coupling?

Table 2—Carbon-13 NMR Data of Some Nitroimidazoles and Nitroimidazo-oxazolines

Compd No.	C-4		C-5		C-2	Other C-δ [multiplicity[a]; $J_{(Hz)}$]
	δ ppm (multiplicity)	$J_{(Hz)}$	δ ppm (multiplicity)	$J_{(Hz)}$	δ ppm (multiplicity)	
10	144.5(?)(*d*)		123.1($d \times t$)	C(5)H(5) 208 C(5)H(CH_2) 4	131.4(?)(*m*)	170.4 (*t*, C=O, 4.5), 43.6 (*t*, N$-CH_2$, 144); 34.2 (*t*, CH_2CO, 130)
12			123.3($d \times q$)	C(5)H(5) 206 C(5)H(CH_3) 2.7	120.8(*m*)	35.6 (q^b, N$-CH_3$, 143)
14	132.5(*d*)	C(4)H(4) 204			127.8(*m*)	35.6 (q^c, N$-CH_3$, 145)
18	134.5(*d*)	C(4)H(4) 201			160.4(?)	86.0 (*d*, CH$-$O, 158), 51.9 (*t*, N$-CH_2$, 155), 20.4 (*q*, CH_3, 126)
19	142.0(?)(*m*)		126.3($d \times t$)	C(5)H(5) 208 C(5)H(CH_2) 4.4	142.0(?)(*m*)	64.6 (*d*, C$-$OH, 145), 56.8 (*t*, N$-CH_2$, 143), 20.2 (*q*, CH_3, 126)
21	146.9(?)(*d*)	C(4)H(5) 4	114.2	C(5)H(5) 205	156.4(*d*) (J=10 Hz)	84.4 (*d*, C$-$O, 150), 50.2 (*t*, N$-CH_2$, 150); 20.0 (*q*, CH_3, 126)
26	144.5(?)(*d*)	C(4)H(5) 4.9	123.9($d \times t$)	C(5)H(5) 206 C(5)H(CH_2) 4	131.9(?)(*m*)	64.6 (*d*, C$-$OH, 145), 54.2 (*t*, N$-CH_2$, 144), 20.3 (*q*, CH_3,126)
27	131.9(*d*)	C(4)H(4) 203	138.9(?)(*m*)		138.9(?)(*m*)	66.5 (*d*, C$-$OH, 146) 53.2 (*t*, N$-CH_2$, 145), 20.9 (*q*, CH_3, 127)

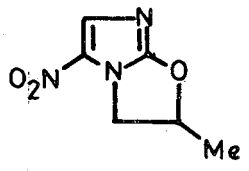
[a] Only primary splitting by one bond C$-$H coupling noted; all signals unless otherwise stated showed further small coupling.
[b] Further splitting due to coupling with C$-$5H, J=2 Hz.
[c] No further splitting.

observations, it appears that the transformation of **1** to **7** with hot 2-chloroethanol, 3-chloropropanol or 3-chloropropionitrile is simply mediated by hydrogen chloride generated readily from the reagents in the presence of **1**. This does not obviously occur with 2-chloropentane.

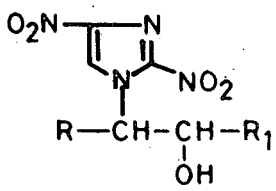
It is reported[4] in one of the publications on the reaction of **1** with 2-chloroethanol that **1** and ethylene oxides, e.g. propylene oxide led to the formation of the imidazooxazoline (**18**) and the 2,4-dinitroimidazolyl-1-isopropanol (**19**), the latter being further transformed into an isomeric imidazooxazoline (**21**). The structure of **18** was substantiated by X-ray crystallographic studies. Since the formation of **23** cannot be ruled out in the cyclisation of **19**, we considered it desirable to repeat the reaction and verify structures of products using NMR techniques[5]. In our hands, the reaction afforded **18** and **19** and, in very low yield, **20**, arising by the attack of 2,4-dinitroimidazole on the more substituted carbon atom of propylene oxide. **18** was formed obviously by the spontaneous cyclisation of the 5-nitroisomer of **19**. Treatment of **19** with hot ethanolic propylene oxide or piperidine gave **21** in low yield. Structure (**23**) for this product was easily ruled out, since in the ^{13}C NMR spectrum, the proton-bearing imidazole carbon atom seen at 114.2 ppm was a doublet with J=205 Hz, less than the expected $^1J_{C,H}$ for C-2 in **23** (210-233 Hz)[5]. Other PMR data, especially solvent-induced shifts (Table 1) and ^{13}C NMR data (Table 2) were consistent with our postulates for these classes of compounds[5]. It was again noted that unlike in the open chain series, e.g. **19**, in the bicyclic series, e.g. **21**, there was no detectable coupling of C-5 with N$-CH_2$ protons in the ring. In the treatment of **19** with piperidine a small amount of an impure product **22** was obtained, contaminated with **21**, which we believe, was formed from **20** accompanying **19**. The UV absorption spectra of **18** (λ_{max} 334 nm; log ε 3.97) and **21** (λ_{max} 324 nm; logε 3.87) matched those of 2-methoxy-1-methyl-5-nitro- (λ_{max} 331 nm; logε 4.01) and 4-nitro- (λ_{max} 324 nm; logε 3.82)-imidazoles[5] respectively and differed from that of 5-methoxy-1-methyl-4-nitroimidazole (λ_{max} 307 nm; logε 3.88).

18 underwent facile ring-opening with piperidine to yield **25** with appropriate NMR and UV data. The reaction of **21** with piperidine was sluggish and complex; but there was mass spectral evidence for the formation of **24** in the reaction of **19** with piperidine.

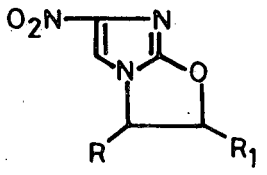
Lastly we studied the reaction of **7** with propylene oxide and found it to give a mixture of **26**, **27** and **18**,**27** was found to go over to **18** spontaneously on keeping and thus the structure of **18** became secure. Attempts to cyclise **26** to **21** under several conditions failed,



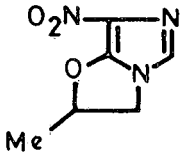
18



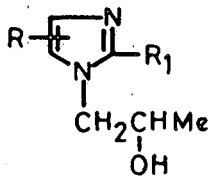
19 R = H; R_1 = Me
20 R = Me R_1 = H



21 R = H; R_1 = Me
22 R = Me; R_1 = H



23



24 R = 4-NO_2; R_1 = piperidino
25 R = 5-NO_2; R_1 = piperidino
26 R = 4-NO_2; R_1 = Cl
27 R = 5-NO_2; R_1 = Cl

highlighting the low reactivity of Cl in the 2-chloro-4-nitro derivative (**26**). Structures **26** and **27** were again supported by NMR data (Tables 1 and 2).

Experimental Procedure

Action of 2-*chloroethanol on* 2,4-*dinitroimidazole* (**1**): *Formation of* 2-*chloro*-4-*nitroimidazole* (**7**)

A mixture containing **1** (3 g) and 2-chloroethanol (commercial; 30 ml) was heated under reflux for 16 hr and the resultant solution set aside overnight. The solvent was evaporated off *in vacuo* and the crystalline residue filtered with ether to give **7** (2.3 g), m.p. and mixed m.p. with authentic sample[1], 204-8°.

Methylation of **7** *with diazomethane*

A suspension of **7** (1.5 g) in methanol (30 ml) was treated with diazomethane (from 6 g nitrosomethyl urea and 100 ml ether) overnight. A small amount of unidentified insoluble solid, m.p. > 290° was filtered off. The filtrate was concentrated to a small volume and treated with ether to give crude **8**, (200 mg), m.p. 136-44°. The mother liquor was evaporated and the residue (0.8 g) chromatographed over silica gel, elution being done with chloroform-2% methanol. Fractions of 25 ml were collected. The first fraction gave **13** (0.1 g), m.p. 78-80°; M^+ at *m/z* 161, 163, identical with an authentic sample. Mixed m.p. with 4-chloro-1-methyl-5-nitroimidazole (**6**)[5] was depressed. Fractions 2 and 3 gave mixtures of **8** and **13**. Fractions 4-6 gave **8** (0.3 g) which was mixed with the earlier product and crystallised from methylene chloride-ether to afford pure **8** (0.25 g), m.p. 146-50°; M^+ at *m/z* 161, 163 identical with an authentic sample; mixed m.p. with 5-chloro-1-methyl-4-nitroimidazole (**4**) was depressed[5].

Action of 2-*chloroethanol on* **2**

A mixture containing **2** (0.5 g) and 2-chloroethanol (10 ml) was heated under reflux for 22 hr. The solution was concentrated *in vacuo* and the residue filtered with ether to give crude **8** (0.3 g). Crystallization from methylene chloride–ether gave pure **8**, m.p. and mixed m.p. 150-52°.

Action of 2-*chloroethanol on* **15**

Treatment of **15** (1 g) with 2-chloroethanol (10 ml) for 22 hr and evaporation of the solution gave a gum which showed 3 spots on TLC (silica; Chloroform-3% methanol); the fastest one had M^+ at *m/z* 161, 163 and had the same R_f as **13**.

Action of $POCl_3$ *on* **15**: *Formation of trione* (**17**)

A solution of **15** (0.5 g) in pyridine (3 ml) was treated with phosphorus oxychloride (0.8 ml) and heated at 80° for 1 hr. After evaporation of solvent, the residue was treated with ice-cold water and extracted with methylene chloride. Evaporation of the methylene chloride extract gave a gum (0.15 g) which was chromatographed on a column of silica gel. Elution with chloroform – 2% methanol gave the trione **17** (10 mg), m.p. 145-8°; M^+ at *m/z* 128, identical with an authentic sample prepared by the action of oxalyl chloride on N-methylurea[7].

Table 3—Analytical Data for Nitroimidazoles and Nitroimidazo-oxazolines

Compd No.	Mol. formula	Calc (%)			Found (%)		
		C	H	N	C	H	N
11	$C_3H_2BrN_3O_2$	18.77	1.05	21.89	18.90	1.27	22.04
12	$C_4H_4BrN_3O_2$	23.32	1.96	20.40	23.97	2.28	20.04
14	$C_4H_4BrN_3O_2$	23.32	1.96	20.40	23.83	2.19	19.88
17	$C_4H_4N_2O_3$	37.51	3.15	21.87	37.65	3.42	22.55
18	$C_6H_7N_3O_3$	42.60	4.17	24.85	43.09	4.53	24.88
19	$C_6H_8N_4O_5$	33.34	3.73	25.92	33.35	4.03	25.97
21	$C_6H_7N_3O_3$	42.60	4.17	24.85	42.82	4.41	25.19
25	$C_{11}H_{18}N_4O_3$	51.95	7.14	22.03	51.83	7.38	22.11
26	$C_6H_8ClN_3O_3$	35.05	3.92	20.44	35.36	4.11	20.46
27	$C_6H_8ClN_3O_3$	35.05	3.92	20.44	35.03	4.69	19.60

Action of 2-*bromoethanol on* **1**

A suspension of **1** (8 g) in 2-bromoethanol (commercial; 40 ml) was heated under reflux and with stirring for 18 hr at 120-25°. The solvent was evaporated off *in vacuo* and the residue triturated with ether. The resultant solid was filtered off and crystallized from chloroform-ether to afford **11** (4.2 g), m.p. 202-6°; M^+ at *m/z* 191, 193. Essentially the same results were obtained when distilled reagent was used as such or after neutralization over solid sodium bicarbonate.

Methylation of **11** *with diazomethane*

11 (5.5 g) in tetrahydrofuran (10 ml) and methanol (70 ml) was treated with diazomethane (from 20 g nitrosomethyl urea in 500 ml ether). After being left overnight, the solution was evaporated to give a mixture of **12** and **14** (TLC), which were separated by chromatography over silica gel. Elution with chloroform gave **14** (2.5 g), m.p. 109-12° (from methylene chloride-ether-hexane) (lit.[8], m.p. 117°); M^+ at *m/z* 205, 207. Further elution gave a mixture of **14** and **12**. Chloroform – 3% methanol eluted **12**, which was recrystallised similarly: 0.5 g, m.p. 143-45° (lit.[8], m.p. 155°); M^+ at *m/z* 205, 207.

Action of 3-*chloropropionitrile on* **1**

A mixture containing **1** (4 g) and 3-chloropropionitrile (purum, Fluka; 50 g) was heated at 100° for 20 hr. The solvent was evaporated *in vacuo*, the residue taken in water (10 ml), neutralised (*p*H 8) with saturated aq sodium carbonate and extracted with ethyl acetate. The ethyl acetate extract on evaporation *in vacuo* gave a gum (3 g) which was subjected to chromatography over silica gel (75 g). Elution with chloroform gave an oil (0.3 g) which showed no imidazole proton in PMR ($CDCl_3$).

Elution with chloroform – 2% methanol gave a gummy solid (1.6 g) which was triturated with methylene chloride and filtered off to give **7** (0.8 g), m.p. and mixed m.p. with an authentic sample 204-8°. The mother liquor on keeping deposited crystals in succession of **16**, **9**, and 3-chloropropionamide (100 mg), m.p. 98-100°.

9: ~10 mg, m.p. 102-5° (methylene chloride-hexane); M^+ at *m/z* 200, 202, IR (KBr) 2250 cm^{-1} ($\nu C{\equiv}N$).
16: ~10 mg, m.p. 96-100° (methylene chloride-hexane); M^+ at *m/z* 167; IR (KBr) 1710 cm^{-1} ($\nu C{=}O$).

Elution with chloroform-5% methanol gave **10** (0.3 g), m.p. 150-54° (methanol-ether); M^+ at *m/z* 218, 220; IR (nujol) 1670, 1690 cm^{-1} (νCO). Further elution with chloroform-10% methanol gave **1** (0.2 g), m.p. and mixed m.p. with an authentic sample, 258-60°.

The aqueous solution after the extraction of ethyl acetate was acidified to *p*H 2 with conc. hydrochloric acid and extracted with chloroform. On evaporating the solvent, a gum (0.3 g) was obtained which was found to be a mixture of **1** and **7** (by TLC).

Action of propylene oxide on **1**

A mixture containing **1** (4.8 g), propylene oxide (30 ml) and ethanol (200 ml) was warmed with stirring at 40-50° till dissolution occurred. The solution was set aside at room temperature for 2 days and evaporated *in vacuo*. The residual gum (8 g) was chromatographed over silica gel.

Elution with chloroform gave a gum (1.2 g) which became crystalline on trituration with hexane. Recrystallisation from methylene chloride-ether-hexane gave **18** (0.6 g), m.p. 70-2°; M^+ at *m/z* 169. Elution with chloroform – 4% methanol gave a gummy material (5.6 g) which upon trituration with ether and a few drops of methylene chloride gave **19** (2.7 g), m.p. 92-94° (lit.[4] m.p. 72-3°); M^+ at *m/z* 216.

The mother liquor from the above crystallisation was concentrated to give a second crop (0.5 g), m.p. 95-110°, which was warmed with ethanol and filtered. The insoluble part was recrystallised from methanol to give **20** (10 mg), m.p. 140°; $M^+ - HNO_2$ at *m/z* 169.

Cyclisation of **19**: (*a*) *Using propylene oxide*

19 (0.2 g), ethanol (10 ml) and propylene oxide (10 ml) were heated under reflux for 4 days, with addition of three 5 ml portions of propylene oxide every 24 hr. The solvents were evaporated off to give a gum which became crystalline with ethanol. Two crystallisations from the same solvent gave **21** (10 mg), m.p. 152-54°; M^+ at *m/z* 169.

The mother liquor gave starting material.

(*b*) *Using piperidine*

19 (0.4 g) and piperidine (0.2 ml) were mixed together in benzene (4 ml) and set aside for 30 min. The solution was evaporated and the residue chromatographed on silica gel, the column being eluted with chloroform-2% methanol. The first 5 fractions of 5 ml each were combined and evaporated to give a gum (0.15 g), which became crystalline with ether. Two crystallisations from methylene chloride–ether gave **21** (50 mg), m.p. 145-47°, identical with the earlier product.

The mother liquor gave a solid (50 mg), m.p. 70-75°, considered to be a mixture of **22** and **21**; M^+ at *m/z* 169; λ_{max} 324 nm (log ε 3.81).

Later fractions gave starting material (100 mg).

When the reaction was conducted in methanol-methylene chloride under reflux, an additional product **24** was formed as a gum; M^+ at *m/z* 254.

Action of piperidine on **18**

A solution of **18** (0.1 g) in benzene (1 ml) containing piperidine (0.12 ml) was set aside at room temperature for 3-4 hr and evaporated. The residual gum was dissolved in chloroform and the solution filtered through silica gel to give **25** (0.1 g), m.p. 150-52°; M^+ at *m/z* 254; λ_{max} 370 nm (log ε 3.92).

Action of propylene oxide on **7**

A suspension of **7** (22.8 g) in ethanol (300 ml) containing propylene oxide (150 ml) and powdered potassium hydroxide (100 mg) was stirred at room temperature for 6 days. The resultant solution was evaporated, the gummy residue dissolved in ethyl acetate–hexane (1:1) and chromatographed over silica gel, elution being carried out with the same solvent mixture. Fractions of 50 ml were collected. The earlier fractions gave mixtures of **18**, **26** and **27**. The later fractions consisted of **26** and were combined and evaporated. Trituration of the resultant gum with hexane gave **26** (10.5 g), m.p. 100-101° (from methylene chloride–methanol–ether); M^+ at *m/z* 205, 207.

Rechromatography of the earlier fractions as before gave first a mixture of **18** and **27** (7.5 g) and later **26** (5.5 g), m.p. 100-101°. The former mixture was again chromatographed over silica gel in methylene chloride to give **18** (1 g) in the earlier fractions, m.p. 70-72° identical with an authentic sample, and **27** in the later fractions as a gum (0.5 g); M^+ at *m/z* 205, 207.

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