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STUDIES IN THE 3-AZABICYCLO[3.3.1]NONANE SYSTEM

A NOVEL ROUTE TO DERIVATIVES OF 3-AZABICYCLO[3.3.1]NONAN-7-ONE

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Abstract—A two step synthesis of several 3-substituted 1,5-dinitro-3-azabicyclo[3.3.1]nonan-7-ones from 3,5-dinitroanisole is described. These aminoketones show no spectral evidence of transannular interaction, but a derived 7α(*endo*) alcohol was found to exhibit such an interaction, indicating a preferred chair-chair conformation. A novel rearrangement involving ring contraction to form a 3-azabicyclo[3.2.1] octane derivative is reported.

ALTHOUGH 3-azabicyclo[3.3.1]nonane (**1**) constitutes part of the ring skeleton of the diterpene alkaloids,[1] many simpler derivatives[2] are also known. In particular, the 9- and 6-ketones isopseudopelletierine[3] (**2**), and 3-benzyl-3-azabicyclo[3.3.1]nonan-6-one[4] (**3**), have been synthesized, but neither 3-azabicyclo[3.3.1]nonan-7-one (**4**) nor any of its derivatives has been reported.

In view of several reports[5] that derivatives of **1** prefer to be in a chair-chair conformation, it was of interest to examine the possibility of transannular interaction[6] between the amine and carbonyl functions in a compound of type **4**. The aminoketones **2**[3c] and **3**[4] have been found to exhibit no such interaction.

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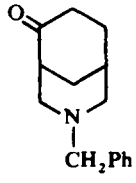

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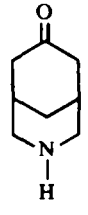

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Entry into the 3-azabicyclo[3.3.1]nonane system is often achieved [1b, 2e, 2f, 3, 7] by means of the Mannich reaction. The particular route selected involves the use of metadinitrobenzenes partially reduced by sodium borohydride.[7] Examples of 3-azabicyclo[3.3.1]nonane derivatives that have been prepared in this way are the compounds **6**–**9**.[7d] In the present study, 3,5-dinitrobenzamide, on $NaBH_4$ reduction, followed immediately by Mannich condensation with methylamine and formaldehyde, afforded in good yield the amide **5**. When a methanol—THF solution of **5** was treated

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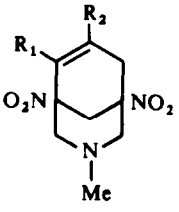
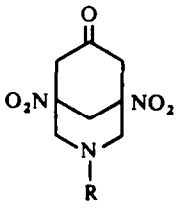
successively with aqueous sodium hypochlorite and dilute HCl, a 12% yield of aminoketone **11** was obtained after chromatographic separation.

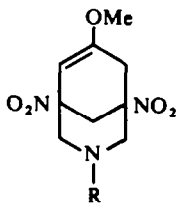
This method however proved unsuitable for the syntheses of aminoketones **10**, **12**, and **13**, and a superior route was developed. Reduction–Mannich condensation treatment of 3,5-dinitroanisole led to the vinyl ether **15**, which on dilute acid



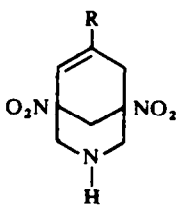
5: $R_1 = H, R_2 = CONH_2$
6: $R_1 = R_2 = H$
7: $R_1 = CH_3, R_2 = H$
8: $R_1 = Cl, R_2 = H$
9: $R_1 = CH{=}CHPh, R_2 = H$
23: $R_1 = H, R_2 = CH_3$
24: $R_1 = H, R_2 = CO_2Et$



10: R = H
11: R = Me
12: R = Et
13: R = CH_2Ph



14
15
16
17



18: R = $CONH_2$
19: R = CO_2Me

hydrolysis was converted quantitatively to the aminoketone **11**. Extension of this sequence to include the use of ethylamine and benzylamine led to the oily vinyl ethers **16** and **17** respectively, from which the aminoketones **12** and **13** were formed in good yield. Although ammonia could be employed smoothly in the Mannich condensation step to form the amide **18** or the ester **19**, 3,5-dinitroanisole under these conditions furnished the vinyl ether **14** in only 7% yield after separation (preparative TLC) from the 3-methyl analogue **15**, presumably formed by methylation of **14** by formaldehyde. Hydrolysis of **14** gave the partially crystalline aminoketone **10**, which could not be further purified.

The $\nu_{C=O}$ values of **11**, **12** and **13** are identical in $CHCl_3$, and exhibit a negligible variation in CCl_4 (Table). This strongly suggests that the amine and carbonyl functions in these compounds exert no interaction on each other. The values are higher than those of some other bicyclic ketones (Table), although the values reported for the diketone and aminoketone **2** are of the same order.

A change in the electronic structure of the amine nitrogen as a result of amine-carbonyl interaction would be expected to induce a shift in the NMR signal of the N-substituent. The aminoketones **11**, **12** and **13** give signals at τ 7·59s; 7·36q and 8·97t (J = 7 c/s); and 2·70 m (aromatic H) and 6·32s (benzylic H) respectively. The fact that these values are very similar to those exhibited by the corresponding vinyl ethers (Experimental) and by olefin **6** and its N-ethyl* and N-benzyl* analogues, is interpreted as additional evidence for the absence of interaction.

Evidence of transannular interaction was however obtained by comparison of the IR and NMR spectra of the aminoalcohols **20** and **21**. The former was prepared by

* R. T. Wall, unpublished observations.

TABLE. COMPARISON OF $\nu_{C=O}$ VALUES OF AMINOKETONES 11, 12 AND 13 WITH SEVERAL BICYCLIC KETONES

Ketone	$\nu_{C=O}(CCl_4)$	$\nu_{C=O}(CHCl_3)$
11	1734	1727
12	1732	1727
13	1731	1727
2	1733[3b]	
	1730, 1710[3c]	1710[3c]
3	1700[4]	
bicyclo[3.3.1]nonan-3-one	1717, 1706[15]	
1,5-dimethylbicyclo[3.3.1]nonane-3,7-dione	1729[16]	

hydroboration of 7.[7d] Its IR spectrum contains a band at 3623 cm^{-1} (Nujol) due to the free, i.e. *exo*, 7-OH group. This stereochemical assignment was confirmed by the NMR spectrum, in which the broad multiplet at 5·45 τ due to the carbinol proton has a half-band width[8] of 20 c/s, indicating diaxial coupling of this proton with the C_6 proton and the C_8 proton. Sodium borohydride reduction of aminoketone **11** gave the alcohol **21**, in which strong intramolecular H-bonding[9] was apparent from broad IR absorption ($CHCl_3$) at 3450–3100 cm^{-1}, unaffected by dilution. In addition, the half-band width[8] (in $CDCl_3$–D_2O) of the NMR multiplet at 5·80 τ due to the C_7 proton is 11 c/s, and the doublet at 7·63 τ (4H, C_6 and C_8H) has J = 3 c/s, indicating that the OH group is axial (*endo*). In $CDCl_3$, the multiplet is much broader (J_{base} = 30 c/s) due to additional coupling with the OH proton. Indeed, the OH proton gives rise to a doublet at 2·90 τ, indicating that this proton is not undergoing rapid exchange, but is constrained by the N atom. The value of J_{HCOH} is 12 c/s.

There is considerable evidence[10] that J_{HCOH} exhibits a dependence on the dihedral angle Φ analogous to the Karplus relation,[11] i.e. $J_{HCOH} = A\cos^2\Phi$. Unusually large values of J^{trans}_{HCOH} (ca. 12 c/s) have been reported[10f, 10g] for compounds in which the OH hydrogen is constrained by H-bonding to be *anti* to the carbinol hydrogen. A similar value of J_{HCOH} for aminoalcohol **21** indicates a transoid arrangement (Φ = 180°) of the H—C—O—H bonds in accord with the chair–chair structure **22**. The altered environment of the N-Me group in **21** gives rise to significant variations in the IR C—H stretching frequency (2822 cm^{-1}) and the NMR singlet (7·49 τ) compared with many similar compounds, for which values in the ranges 2790–2813 cm^{-1} and 7·57–7·66 τ respectively are observed.

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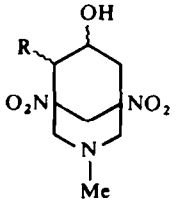
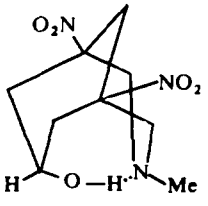


20: R = α-CH_3; β-OH
21: R = H; α-OH



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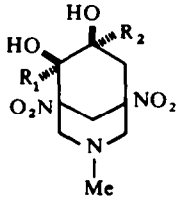
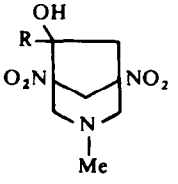


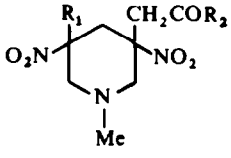
25: $R_1 = R_2$ = H
26: R_1 = CH_3, R_2H
27: R_1 = H, R_2 = Me



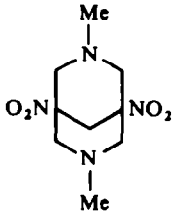
28: R = H
29: R = Me

Until very recently,[12] no nitropiperidine derivatives were known. While attempting to prepare derivatives of 3,5-dinitropiperidine by oxidative cleavage of the cyclohexene ring in compounds of type **6**, a novel rearrangement involving loss of one ring C atom was discovered.

Treatment of **6**[7d] with osmium tetroxide by the method of Baran[13] yielded the 6,7-*cis*-diol **25**, which on exposure to sodium metaperiodate in methanol for 18 hr under nitrogen was converted into a brown partially solid oil. This material exhibited OH, N-Me, NO_2 and CO absorption in the IR. Careful recrystallization gave a pale brown crystalline solid, too unstable to be prepared analytically pure. Spectral data however conclusively showed the product to be 1,5-dinitro-3-methyl-3-azabicyclo-[3.2.1]octan-6-ol **28**. The mass spectrum showed the correct molecular weight of 231, with additional peaks confirming the presence of two NO_2 groups and a OH group. Absorption in the IR ($CHCl_3$) occurred at 3595 (sharp band due to a free OH group), 2805 (N Me), 1549 (asym NO_2 str) and 1371 (sym NO_2 str) cm^{-1}. The CO region was transparent. The NMR spectrum contained a multiplet at 5·50 τ (1H, carbinol proton), an apparent triplet at 6·73 τ (2H, J = 10 c/s, bridge protons), and a singlet at 7·59 τ (3H, NMe).



30: R_1 = CHO, R_2 = H
31: R_1 = R_2 = H
32: R_1 = Ac, R_2 = H
33: R_1 = H, R_2 = Me



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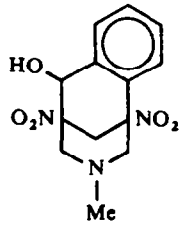


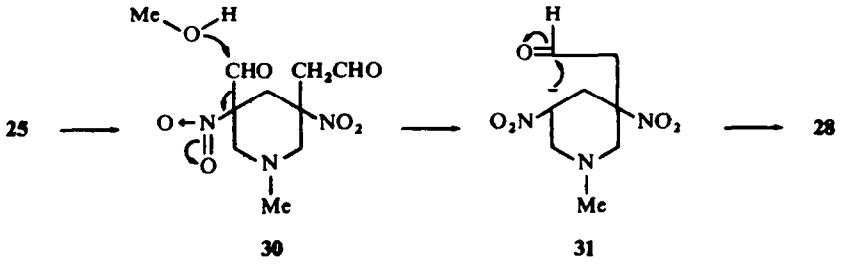
35

The alcohol **28** must be formed by loss of formic acid from the intermediate dialdehyde **30**, followed by intramolecular cyclization of **31** (Scheme 1). Indeed, TLC analysis of the crude product revealed the presence of a small amount of a compound less polar than **28**, probably **31**. The IR CO absorption (1720 cm^{-1}) which disappeared on purification was also assigned to **31**. When a longer reaction time (60 hr) was used, only the alcohol **28** was present. On standing, **28** was decomposed to amorphous material insoluble in chloroform, with evolution of nitrous acid (odour detectable).

Hydroxylation of **7**[7d] afforded the diol **26**, which on sodium metaperiodate treatment (15 hr) exhibited similar behaviour by yielding a mixture of unchanged **26**, alcohol **28**, and a less polar compound, probably aldehyde **31**. In this case also, the product showed IR carbonyl absorption, due to the formation of aldehyde **31** from ketoaldehyde **32** by loss of acetic acid.

Under the same conditions used in the preparation of **6**, 4-chloro-3,5-dinitrotoluene afforded **23**. Conclusive evidence for the absence of a Cl atom in **23** was provided by a quartet in the NMR spectrum at 6·80 τ (2H, J = 10·5 c/s) due to the bridge protons. Similar signals were observed for the analogous ester **24**, and vinyl ether **15** at 6·77 τ (J = 11 c/s) and 6·85 τ (J = 12 c/s) respectively. Reaction between **23** and osmium tetroxide produced much tar and only a low yield of diol **27**, which was completely

SCHEME 1



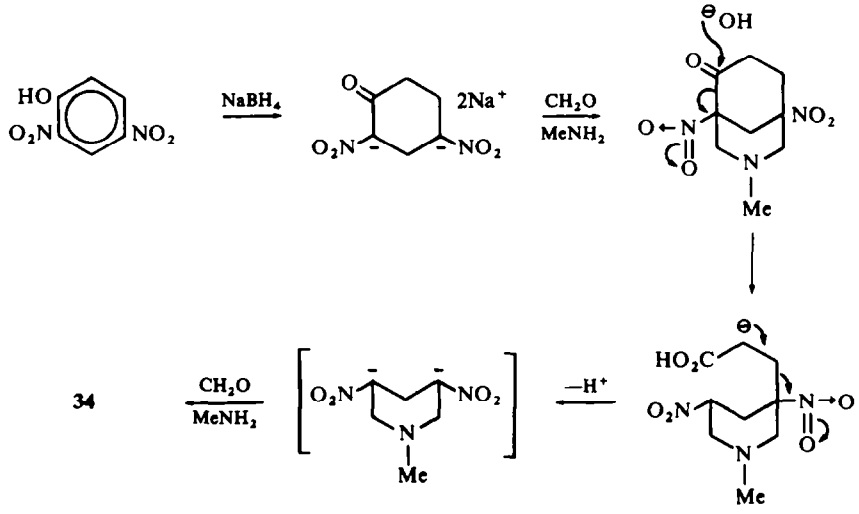
converted with sodium metaperiodate (52 hr) to a brown oil. This material had IR OH (3450 cm^{-1}) N-Me, CO (sharp band at 1725 cm^{-1}) and NO_2 absorption, consistent with a mixture of alcohol **29** and ketone **33**. In addition, TLC analysis revealed the presence of two components and NMR singlets at 7·57, 7·83, and 8·60 τ were assigned to NMe, MeCO and CH_3COH groups respectively. The continued presence of ketone **33** after reaction times long enough to cause complete cyclization of aldehyde **31** may be due to the lower reactivity of the ketonic carbonyl.

The more vigorous cleavage procedure of ozonolysis produced no useful result. Olefin **23** formed in very low yield material which lacked IR N-Me absorption.

Of all the metadinitroaromatics subjected to reduction and Mannich condensation, the only one to yield an anomalous product was 2,4-dinitrophenol. Under the conditions used to prepare **6**, 2,4-dinitrophenol afforded in very low yield a crystalline compound analysing for $C_9H_{16}N_4O_4$ and having a mass spectral molecular weight of 244. This product was not a 3-azabicyclo[3.3.1]nonane, but had the novel bispidine[14] structure **34**. Peaks corresponding to losses of 46 (NO_2) and 92 ($2NO_2$) m/e were observed in the mass spectrum. IR bands (CCl_4) at 2812 and 2798 cm^{-1} were attributed to two N-Me groups, and those at 1551 and 1353 cm^{-1} to nitro groups. The NMR spectrum ($CDCl_3$) contained a singlet at 7·64 τ (6H, 2NMe), and an AB quartet at 7·13 τ (J = 11 c/s, bridge protons) with an overlapping signal at 7·34 τ (10H in all, $4NCH_2$). The formation of **34** may be rationalized as in Scheme 2. The existence of the suggested intermediate (essentially 1,3-dinitropropane) finds parallels in the formation of 1,3,5-trinitropentane by sodium borohydride reduction of the sodium salt of picric acid,[7b] and of 1,5-dinitropentane by acid treatment of the monopotassium salt of 2,5-dinitrocyclohexanone.[17]

In contrast, the product from 2,4-dinitronaphthol was obviously the alcohol **35**, having ν_{OH}^{Nujol} 3500 cm^{-1} in addition to aromatic, N-Me and NO_2 bands. This was confirmed by an NMR (CF_3CO_2H) hydroxyl proton signal at 4·28 τ, shifted by D_2O exchange. The aromatic protons gave rise to multiplets at 2·27 τ (3H) and 2·70 τ (1H). Two quartets at 5·45 τ (J = 10 c/s) and 6·18 τ (J = 14 c/s) were assigned to the bridge and NCH_2 protons respectively, and a singlet at 6·80 τ to the N-Me group. In this case, therefore, the ring containing the NO_2 groups has remained intact. Because the aromatic ring in **35** prevents the OH group becoming ketonic, this compound is not prone to the type of breakdown that results in the formation of the bispidine **34**.

SCHEME 2



EXPERIMENTAL

NMR spectra were recorded on a Perkin Elmer R.S.10 60 Mc/S spectrometer (solvent was $CDCl_3$ with TMS as internal standard), IR spectra on a Unicam S.P.100 spectrophotometer, and mass spectra on an A.E.I. M.S.9. Chromatoplates employed Kieselgel G (Merck) Silica, with 20% EtOAc in light petroleum as the solvent system, and were developed in I_2 vapour. M.ps were determined on a Kofler hot-stage microscope and are uncorrected. Unless otherwise stated, organic extracts were washed with brine and dried over $MgSO_4$ prior to evaporation. The formaldehyde and methylamine used were respectively 40% and 25% aqueous solns.

Amide **5**

Following the procedure used in the preparation of **6**,[7d] the reaction mixture from reduction and Mannich condensation of 3,5-dinitrobenzamide (2 g) was acidified (HOAc), stirred for 2 hr, and suction-filtered. Filtered solid was washed (H_2O), dried, and combined with solid obtained by extracting the filtrate with $CHCl_3$, yield 1·70 g (67%), m.p. 201–203° (colourless plates from EtOH). (Found: C, 44·53; H, 4·98, N, 20·62. $C_{10}H_{14}N_4O_5$ requires: C, 44·45; H, 5·22; N, 20·73%); ν^{Nujol} 3460, 3170, 2808, 1696 (amide I CO), 1659 (C=C), 1618 (amide II CO), 1551 and 1352 cm^{-1}; NMR (CF_3CO_2H) τ 2·4 (broad m, NH), 2·84 (m, olefinic H), 6·46 and 6·78 (s, NCH_2), 6·65 (s, NCH_3). M = 270 *m/e*.

Aminoketone **11** *from amide* **5**

NaOCl soln[18] (0·798 N; 18 ml) was added over 15 min to a stirred soln of **5** (3·24 g; 12 mM) in THF (35 ml) and MeOH (25 ml) at $< -5°$ (ice–salt bath). The mixture was allowed to warm to room temp, stirred for 30 min, heated at 55–65° for 10 min, and 6N HCl (2 ml) was carefully added. The clear red soln was refluxed on the steam bath for 30 min, cooled, basified with solid K_2CO_3, filtered, and extracted thoroughly with $CHCl_3$. The extract was evaporated, leaving a semi-solid red oil containing **5** and five other compounds, two of which predominated (TLC). Thorough extraction with hot CCl_4 separated most of the amide from a red oil (2·7 g). Preparative TLC (thickness 1 mm, using light petroleum: EtOAc 1:1) afforded from the least polar band crude **11** (336 mg; 12% based on consumed amide) m.p. 120–121° as colourless needles from CCl_4. (Found: C, 44·23; H, 5·45; N, 17·22. $C_{19}H_{13}N_3O_5$ requires: C, 44·45; H, 5·39; N, 17·28%); ν^{CHCl_3} 2808, 1727, 1551, 1369 cm^{-1}.

Vinyl ether **15**

A soln of 3,5-dinitroanisole (2 g; prepared from sym trinitrobenzene[19]) in THF (30 ml), formamide (20 ml) and MeOH (10 ml) was reduced by $NaBH_4$ (1·5 g), treated with formaldehyde and methylamine, and acidified carefully with HOAc (violent effervescence). Extraction gave a red oil (1·7 g; 66%) which solidified on standing, and was recrystallized with difficulty from EtOH, m.p. 110–111° as colourless crystals which yellowed on exposure to light. (Found: C, 46·81; H, 5·79; N, 16·39. $C_{10}H_{15}N_3O_5$ requires: C, 46·69; H, 5·88; N, 16·33%); ν^{CCl_4} 2800, 1669, 1552, 1369, 1342 and 1235 cm^{-1}; NMR τ 5·00 (m, olefinic H), 6·43 (s, OCH_3), 6·85 (apparent t, J = 12 c/s, bridge H), 7·24 (broad s, allylic H), 7·4–7·7 (complex, NCH_2), and 7·62 (s, NCH_3).

Vinyl ether **16**

Using ethylamine (35% aqueous soln) in the Mannich step, a red oil (1·79 g) was formed, consisting of one major component and several more polar ones. Pure **16** was obtained by preparative TLC (thickness 1 mm, plates run twice in light petroleum: EtOAc 4:1) as a pale yellow oil (283 mg; 10%); ν^{CCl_4} 3097, 1553, 1370, 1340 and 1233 cm^{-1}; NMR τ 4·98 (m, olefinic H), 6·40 (s, OMe), 6·77 (apparent t, J = 11 c/s, bridge H), 7·25 (broad s, allylic H), 7·37 (q, J = 7 c/s, $C\underline{H}_2CH_3$), 7·4–7·7 (complex, NCH_2), and 8·94 (t, J = 7 c/s, $CH_2C\underline{H}_3$).

Vinyl ether **17**

When benzylamine (35% aqueous soln) was used, the red oily product (2·63 g) comprised two components, the less polar predominating. Preparative TLC afforded **17** as a pale yellow oil (814 mg; 24%); ν^{CCl_4} 3091 (=C—H), 3070 and 3030 (ar =C—H), 1670, 1554, 1497, 1371, 1342 and 1232 cm^{-1}; NMR τ 2·74 (s, ar H), 4·96 (m, olefinic H), 6·31 (s, benzylic H), 6·38 (s, OMe), 6·82 (apparent t, J = 11 c/s, bridge H), 7·25 (broad s, allylic H) and 7·3–7·6 (complex, NCH_2).

Vinyl ether **14**

When concentrated aqueous ammonia was used, the reaction mixture was filtered, and the filtrate extracted with $CHCl_3$. This extract was washed with dilute HCl, affording basic material as an oil which slowly solidified (720 mg). IR showed the presence of NH, C=C, NO_2 and NMe groups, and TLC analysis a two component mixture with the less polar predominant. Preparative TLC (thickness 1 mm, using light petroleum: EtOAc 7:3) furnished from the less polar band crystalline **15** (363 mg), and from the other band the oily vinyl ether **14** (160 mg; 6·5%); ν^{CHCl_3} 1663, 1550, 1366, 1339 and 1236 cm^{-1}; ν^{film} 3400 cm^{-1}; NMR τ 4·93 (m, olefinic H), 6·36 (s, OMe) 6·71 (apparent t, J = 11 c/s, bridge H), 6·87 and 6·95 (s, NCH_2) 7·17 (broad s, allylic H), and 7·93 (s, NH).

Aminoketone **11**

Vinyl ether **15** (182 mg) dissolved in dilute HCl (10 ml) was heated for 2 hr on a steam bath. The cooled soln was basified with dil Na_2CO_3 aq and extracted with $CHCl_3$ to give a crystalline solid (172 mg; 100%) identical with **11** prepared from **5**.

Aminoketone **12**

Similar hydrolysis of **16** (100 mg) afforded **12** as a colourless crystalline solid (71 mg; 75%), m.p. 121–123° as needles from CCl_4. (Found: C, 46·71; H, 5·83; N, 16·31. $C_{10}H_{15}N_3O_5$ requires: C, 46·69; H, 5·88; N, 16·33%); ν^{CHCl_3} 1727, 1553 and 1370 cm^{-1}.

Aminoketone **13**

The solid product from hydrolysis of **17** (100 mg) precipitated from the aqueous acidic soln on cooling, and was totally extractable without basification (67 mg; 70%) m.p. 155–157° as colourless needles from CCl_4. (Found: C, 56·65; H, 4·81; N, 13·26. $C_{15}H_{17}N_3O_5$ requires: C, 56·42; H, 5·37; N, 13·16%); ν^{CHCl_3} 3035, 1727, 1552, 1495 and 1372 cm^{-1}.

Aminoketone **10**

Hydrolysis of **14** (100 mg) gave **10** as a partially crystalline yellow oil. The final m.p. of this material was 170°, but it could not be purified by recrystallization; ν^{CHCl_3} 3400, 1735 (broad band), 1553 and 1361 cm^{-1}.

Amide **18**

Reduction of 3,5-dinitrobenzamide (2 g) by $NaBH_4$ (1·5 g) was followed by addition of a mixture containing concentrated NH_3 (S.G. 0·88; 9 ml), formaldehyde (9 ml) and water (9 ml). The reaction mixture was stirred for 1 hr, with HOAc (9 ml) being added after 15 min. Filtration afforded **18** as a solid which was washed (H_2O) and dried. Extraction of the filtrate ($CHCl_3$, then EtOAc) afforded a semisolid orange oil which was recrystallized (EtOH). The combined solids (710 mg; 29%) were washed thoroughly with hot $CHCl_3$ and hot MeOH to give a colourless powder, m.p. 234–235°. (Found: C, 42·28; H, 4·67; N, 22·02. $C_9H_{12}N_4O_5$ requires: C, 42·19; H, 4·72; N, 21·87%); ν^{Nujol} 3525 (NH), 3458 and 3410 (free amide NH), 3190 broad (bonded amide NH), 1680 (amide I C=O), 1652 (C=C), 1602 (amide II C=O), 1560 sh., 1551 and 1348 cm^{-1}; NMR (CF_3CO_2H) τ 1·60 (d, J = 5·5 c/s, NH), 2·42 (m, amide H), 2·92 (m, olefinic H), 6·50 and 6·78 (both broad s, NCH_2).

Ester **19**

Similar treatment of methyl 3,5-dinitrobenzoate (2 g) gave a clear green solution, which on extraction ($CHCl_3$) furnished a viscous pale yellow oil which slowly solidified (1·85 g; 77%). Washing with hot $CHCl_3$, then hot MeOH gave **19** as a colourless powder, further purified by adding large volumes of CCl_4 and light petroleum to a hot $CHCl_3$ soln, and cooling, m.p. 191–192·5°. (Found: C, 44·40; H, 4·66; N, 15·55. $C_{10}H_{13}N_3O_6$ requires: C, 44·28; H, 4·83; N, 15·49%); ν^{Nujol} 1736, 1664, 1568, 1556, 1346, 1276 and 1250 cm^{-1}; NMR (CF_3CO_2H) τ 1·64 (s, NH), 2·75 (m, olefinic H), 6·02 (s, OCH_3), 6·58 s and 6·7–6·9 (clmplex absorption, NCH_2).

Aminoalcohol **20**

To a suspension of $NaBH_4$ (78 mg) in dry THF (5 ml), and **7** (1·205 g; 5 mM) was added dropwise over 30 min with stirring and under N_2, BF_3 etherate (357 mg; 2·5 mM). The mixture was stirred for 20 hr, and water (2 ml) was carefully added, followed by 3N NaOH (1 ml) and 30% H_2O_2 aq (1 ml). $CHCl_3$ extraction after 40 hr stirring gave a brown crystalline solid (1·21 g) consisting mainly of **7** together with the more polar alcohol **20**. Preparative TLC (thickness 0·6 mm, using light petroleum: EtOAc 7:3; each plate run thrice) afforded from the more polar band crystalline **20**, m.p. 96–97·5° (aq EtOH), in 11% yield; ν^{Nujol} 3623, 2808, 1551 and 1354 cm^{-1}; NMR τ 5·45 (m, carbinol H), 6·65 (q, J = 11 c/s, bridge H), 7·5–7·9 (complex absorption, NCH_2), 7·65 (s, NCH_3) and 8·95 (d, J = 6 c/s. CH_3).

Aminoalcohol **21**

A soln of **11** (73 mg) in EtOH (10 ml) was treated portionwise with $NaBH_4$ (28 mg), and stirred for 8 hr. Brine was added, and $CHCl_3$ extraction yielded crystalline **21** (67 mg; 91%), m.p. 159·5–162·5° as colourless needles from EtOH–CCl_4. (Found: C, 43·91; H, 6·02; N, 17·00. $C_9H_{15}N_3O_5$ requires: C, 44·08; H, 6·17; N, 17·13%); ν^{CHCl_3} 3450–3100, 2820, 1551 and 1342 cm^{-1}.

Iminoolefin **6**[74]

The red oil obtained from *m*-dinitrobenzene (7 g) was recrystallized from light petroleum 60–80° to give 4·34 g (46%) of a colourless solid, m.p. 76° (Lit. 75°); ν^{CCl_4} 3048, 2790, 1547, 1354 and 1338 cm^{-1}; NMR τ 3·89 (s, olefinic H), 6·75 (apparent t, J = 11 c/s, bridge H), 7·20 (broad s, allylic H), and 7·57 (s, NCH_3); M = 227 *m/e*.

Aminoolefin **7**[74]

2,4-dinitrotoluene (4 g) was converted, after recrystallization from EtOH, into a pale yellow solid (2·04 g; 36%), m.p. 97° (Lit. 98°); ν^{CCl_4} 2802, 1553 and 1343 cm^{-1}; NMR τ 4·27 (m, olefinic H), 6·60 and

6·79 (broad s, bridge H), 7·24 (m, allylic H), 7·58 (s, NMe) and 8·36 (d, J = 2 c/s, CH_3). M = 241 *m/e*.

Aminoolefin **23**

From 4-chloro-3,5-dinitrotoluene (5 g) was obtained a yellow crystalline solid (3·0 g; 47%), after one recrystallization from EtOH. Colourless material had m.p. 107–108° (light petroleum 60–90°). (Found: C, 50·13; H, 6·20; N, 17·30. $C_{10}H_{15}N_3O_4$ requires: C, 49·78; H, 6·27; N, 17·42%); ν^{CCl_4} 2800, 1675, 1540, 1370, 1345 cm^{-1}; NMR τ 4·21 (m, olefinic H), 6·80 (q, J = 10·5 c/s, bridge H), 7·35 (broad s, allylic H), 7·60 (s, NCH_3) and 8·17 (s, CH_3).

Ester **24**

This compound was prepared in the usual way in 98% yield from ethyl 3,5-dinitrobenzoate, m.p. 101–102° as colourless feathery crystals from EtOH. (Found: C, 48·15; H, 5·40; N, 13·84. $C_{12}H_{17}N_3O_6$ requires: C, 48·16; H, 5·73; N, 14·04%); IR and NMR in agreement with structure.

Diol **25**

A soln of **6** (885 mg; 3·9 mM) and OsO_4 (1 g; 3·94 mM) in dry pyridine (15 ml) was left for 48 hr at room temp. A soln of $NaHSO_3$ (1·8 g) in water (30 ml) and pyridine (20 ml) was then added. The mixture was stirred for 1 hr and extracted (3 × $CHCl_3$), yielding **25** as a yellow crystalline solid (944 mg; 93%). The analytical sample had m.p. 128–144° (aq. EtOH). Narrowest m.p. range was 150–153° (after 3 × aq. EtOH). (Found: C, 41·40; H, 5·49; N, 15·90. $C_9H_{15}N_3O_6$ requires: C, 41·38; H, 5·79; N, 16·09%); $\nu^{N\ Jol}$ 3487 sharp, 3310 broad, 2808, 1551, 1356 and 1348 cm^{-1}. M = 261 *m/e*.

Diol **26**

Similar hydroxylation of **7** (470 mg) gave **26** (535 mg; 100%), m.p. 128–132° (CCl_4–$CHCl_3$); ν^{Nujol} 3515, 3495, 2813, 1549, 1538 and 1351 cm^{-1}. NMR τ 5·45 (m, carbinol H), 6·60 (apparent t, J = 12 c/s, bridge H), 7·27 and 8·41 (s, OH protons), 7·64 (s, NMe) and 8·58 (s, Me).

Diol **27**

Olefin **23** (1·07 g) on hydroxylation afforded a dark brown oil, which was extracted thoroughly with hot EtOH. The evaporated extract was then extracted with hot light petroleum 60–90°, yielding a small amount of unchanged **23**. Residual material on recrystallization gave diol **27** as a colourless crystalline solid (75 mg), m.p. 138–139° (CCl_4–$CHCl_3$); ν^{Nujol} 3500 sharp, 3330 broad, and 1540 cm^{-1}; NMR ($CDCl_3$–CF_3CO_2H) τ 6·83 (s, NCH_3), 8·15 (s, CH_3) and 8·61 (s, OH H).

Alcohol **28**

(a) *From diol* **25**. To the diol **25** (522 mg) dissolved in MeOH (50 ml) was added sodium metaperiodate (530 mg). The mixture was stirred 18 hr under N_2, brine was added, and the $CHCl_3$ extract was evaporated under reduced press at room temp. The brown oily product slowly solidified, its IR spectrum showed OH, NMe, NO_2 and C=O (1720 cm^{-1}) absorption, and it consisted of one major component and a less polar one. Two recrystallizations performed by dissolving in a little benzene, and, with cooling in an ice–salt bath, adding large volumes of CCl_4 followed by light petroleum 40–60°, gave **28** as a pale brown crystalline solid, m.p. 96–99° (219 mg; 47%). Preparative TLC (thickness 1 mm, using light petroleum: EtOAc 7:3) yielded identical material from the more polar band. Alcohol **28** decomposed on standing by elimination of nitrous acid, and satisfactory analytical figures could not be obtained. M = 231 *m/e*, with peaks corresponding to losses of 1, 17(OH), 46(NO_2), 47 (HONO), 92(NO_2 from M-46) and 93 (HONO from M-46) *m/e*.

(b) *From diol* **26**. Diol **26** (138 mg) after 15 hr afforded a yellow oil (120 mg) containing starting diol (present even after 48 hr) and two less polar compounds. IR carbonyl absorption was again observed. Preparative TLC afforded from the middle band material identical to **28** prepared from **25**.

Treatment of diol **27** *with sodium metaperiodate*

Diol **27** (56 mg) after 52 hr (some diol remained after 24 hr) formed a brown oil (44 mg) consisting of one major component and another less polar; ν^{film} 3450, 2780, 1725, 1550 and 1370 cm^{-1}; NMR: see discussion.

Ozonolysis of olefin **23**

About 10% O_3 in O_2 was passed through a soln of **23** (1 g) in EtOAc (20 ml) at −70° until the colour

had changed from pale yellow to blue-grey (ca. 1 hr). Zn dust (1·2 g) and HOAc (20 ml) were added, and the mixture was stirred for 1 hr at room temp, and filtered. Evaporation of solvents at 5 mm left a red tar, which was dissolved in $CHCl_3$ and chromatographed on neutral Al_2O_3. A small amount (35 mg) of a dark orange oil was recovered, which exhibited IR nitro, but lacked N-Me absorption.

Bispidine **34**

2,4-dinitrophenol (10 g) in THF (25 ml), formamide (50 ml) and EtOH (60 ml) was reduced by $NaBH_4$ (7·5 g). Ice-water (250 ml), followed by a mixture of 37·5 ml each of formaldehyde, methylamine and water, and finally HOAc (37·5 ml) were added. The mixture was stirred for 3 hr and extracted ($CHCl_3$) to give a viscous dark red oil (4·1 g). This was extracted with hot EtOH, and the ethanolic soln was concentrated in stages, each time with cooling and filtering to remove precipitated tar. Finally on cooling was obtained a pale yellow crystalline solid (164 mg), m.p. 117–118° as needles from EtOH. (Found: C, 44·34; H, 6·59. $C_9H_{16}N_4O_4$ requires: C, 44·26; H, 6·60%); Spectra: see discussion.

Alcohol **35**

When treated as above, 2,4-dinitro-1-naphthol (5 g) formed as a basic fraction a viscous brown gum. Recrystallization from EtOH furnished a colourless powder (177 mg), m.p. 190–191° (dec). (Found: C, 53·05; H, 5·13; N, 14·22. $C_{13}H_{15}N_3O_5$ requires: C, 53·24, H, 5·16; N, 14·33%); ν^{Nujol} 3500, 2830, 1530, 800, 770 and 750 cm^{-1}.

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