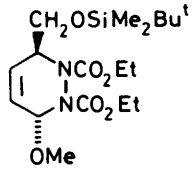
Reductive Cleavage of the Nitrogen–Nitrogen Bond in Hydrazine Derivatives

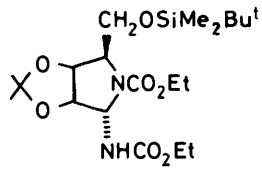
John M. Mellor* and Neil M. Smith
Department of Chemistry, The University, Southampton SO9 5NH

The reductions of the 1,2-disubstituted hydrazines (**4**)—(**7**) having the activating groups toluene-*p*-sulphonyl, acetyl, ethoxycarbonyl, and trifluoroacetyl respectively have been studied with zinc in acetic acid, aluminium amalgam, sodium in liquid ammonia, sodium in ethanol, and Raney nickel. Satisfactory conditions have been defined for the reductive cleavage of each of these substituted hydrazines (**4**)—(**7**). The Diels–Alder adduct (**12**) of cyclopentadiene and diethyl azodicarboxylate has been oxidised, by *m*-chloroperoxybenzoic acid to give the epoxide (**20**), by osmium tetraoxide to give the diol (**21**), and *via* hydroboration to give the alcohol (**22**). Using sodium in liquid ammonia these hydrazine derivatives (**20**)—(**22**) and others have been reduced by cleavage of the nitrogen–nitrogen bond to give derivatives of oxygenated cyclic diamines.

Although the reaction of the esters of azodicarboxylic acid with many different dienes to give Diels–Alder adducts is well established,[1] with the exception of a single recent example these adducts have not been used in the synthesis of diamine derivatives *via* a reductive cleavage of the nitrogen–nitrogen bond. Recently Forrest and Schmidt[2] reported the transformation of the Diels–Alder adduct (**1**) *via* several steps to the amide (**2**). A key step was the reductive cleavage of the hydrazine derivative (**3**) carried out in unstated yield by sodium in liquid ammonia. In this paper we report our studies of the reductive cleavage of hydrazine derivatives. Following preliminary studies which establish the optimum conditions for cleavage of different hydrazine derivatives, we show that products readily obtained from Diels–Alder adducts of cyclic dienes are efficiently reduced to give derivatives of cyclic diamines. Such diamines are the present focus of much synthetic interest.[3,4] This route based on elaboration of Diels–Alder adducts of cyclic dienes with azo-dienophiles complements similar routes[5] which stereospecifically afford sugar derivatives by the elaboration of Diels–Alder adducts of furans or cyclic dienes with substituted ethylenes.



(**1**)



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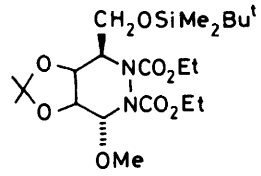
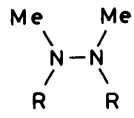


(**3**)



(**4**) R = $SO_2C_6H_4Me$
(**5**) R = COMe

Previous studies of the reductive cleavage of the nitrogen–nitrogen bond in hydrazine derivatives have established that cleavage to give amine derivatives may be achieved by hydrogenation,[6] by reduction with aluminium[7] or boron hydrides,[8] or by successive single electron and proton transfers.[9] In general, non-aromatic hydrazines are much more difficult to reduce than aromatic hydrazines, and partially substituted hydrazines are more resistent to reduction than fully substituted hydrazines.

Simple alkylhydrazines are readily cleaved to give amines by hydrogenation[6] under acidic conditions. However their amide derivatives[9] are resistant to hydrogenolytic cleavage. Thus reductive cleavage of some cyclic hydrazines in the synthesis of amino sugars[10] can require hydrogenation under elevated pressure conditions.

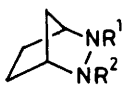
Reductive cleavage of the nitrogen–nitrogen bond in aliphatic hydrazines[7,8] by aluminium hydride or boron hydride is very sluggish. These reagents can be efficiently used to reduce the carbonyl functionality in hydrazide derivatives, but forcing conditions are required to give amine products.

Our attention focussed on the methods of possible nitrogen–nitrogen cleavage by successive electron and proton transfers. The constraints imposed by the choice of a good dienophile for the Diels–Alder reaction establish that the most efficient route involving a reductive cleavage would be by cleavage of a diacyl hydrazide or related compound. Variation of the acyl moiety controls the relative electron affinity of the hydrazine derivative to be cleaved. Hence the choice of acyl moiety could dictate the appropriate dissolving metal conditions necessary to effect cleavage of the nitrogen–nitrogen bond. The control by acyl substitution of the ease of reduction of hydrazine derivatives has been demonstrated in an electrochemical study[11] by Horner and Jordan. The importance of adequate activation of the hydrazine derivative is shown[2] by the successful reduction using sodium in liquid ammonia of the diacylhydrazine derivative (**3**) which contrast with the failure to reduce the nitrogen–nitrogen bond in an unactivated hydrazine[12] using sodium in liquid ammonia. Zinc has been used as an alternative reducing agent,[13] but examples indicate the resistance to cleavage of the nitrogen–nitrogen bond with this metal as an electron source. The lack of comparative data relating the degree of activation of hydrazine derivatives with the possible metal reducing agents prompted us to examine briefly the behaviour of some metals with some simple hydrazine derivatives. The hydrazine derivatives (**4**)—(**7**) were chosen to illustrate different degrees of activation with respect to dissolving metal reductants.

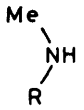
In the Table the results of the attempted reduction of the hydrazine derivatives (**4**)—(**7**) are described. The ditosylhydrazine (**4**) can be reductively cleaved to give the toluene-*p*-sulphonyl derivative (**9**) of methylamine by zinc in acetic acid or by aluminium amalgam. Under similar conditions the less

Table. Results of the attempted reduction of hydrazine derivatives (4)—(7)

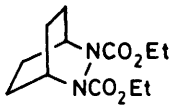
Compound reduced	Reagent used and product (yield %)				
	Zinc–$MeCO_2H$	Aluminium amalgam	Sodium–NH_3	Sodium–ethanol	Raney nickel
(4)	(9) (62)	(9) (87)	Complex	Complex	(9) (35)
(5)	No reaction	No reaction	(10) (75)	No reaction	No reaction
(6)	No reaction	No reaction	(13) (100)	Complex	No reaction
(7)	(8) (28)	(14) (100)	Complex	Complex	Complex



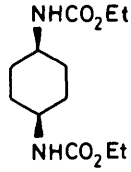
(6) $R^1 = R^2 = CO_2Et$
(7) $R^1 = R^2 = COCF_3$
(8) $R^1 = COCF_3$; $R^2 = H$



(9) $R = SO_2C_6H_4Me$
(10) R = COMe



(18)



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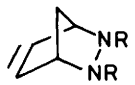
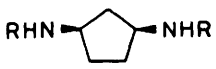
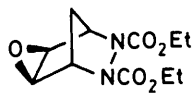


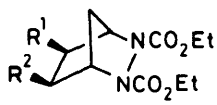
(11) $R = CO_2Bu^t$
(12) $R = CO_2Et$



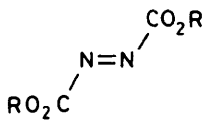
(13) $R = CO_2Et$
(14) $R = COCF_3$



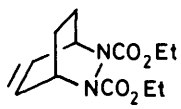
(20)



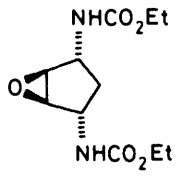
(21) $R^1 = R^2 = OH$
(22) $R^1 = OH$, $R^2 = H$



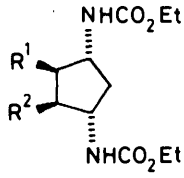
(15) R = Bu^t
(16) R = Et



(17)



(23)



(24) $R^1 = R^2 = OH$
(25) $R^1 = R^2 = OCOMe$
(26) $R^1 = OH$, $R^2 = H$
(27) $R^1 = OCOC_6H_4NO_2$, $R^2 = H$

activated hydrazine derivatives (5) and (6) are inert. However, both are efficiently cleaved by sodium in liquid ammonia: *N*-methylacetamide (10) is obtained from compound (5) and the carbamate (13) is obtained from (6).

The hydrazine derivative (7) is available by Diels–Alder reaction[14] of cyclopentadiene with di-t-butyl azodicarboxylate (15) which affords the adduct (11). Subsequent hydrogenation, hydrolysis in acid, and trifluoroacetylation gives the hydrazine derivative (7). The reaction of compound (7) with zinc and acetic acid affords only the amide (8) in addition to unchanged starting material. Although only a complex mixture is obtained by the attempted reaction of compound (7) with sodium in liquid ammonia, the reduction with aluminium amalgam affords the amide (14) quantitatively. Neither sodium in ethanol nor Raney nickel proved to be satisfactory reagents for effecting the cleavage of the hydrazine derivatives (4)—(7). However, the results in the Table clearly establish the optimum reaction conditions. For the less activated compounds (5) and (6), sodium in liquid ammonia is required to effect nitrogen–nitrogen bond cleavage. For the more activated compound (4), zinc in acetic acid or aluminium amalgam are adequate reducing agents and the more activated (7) is only efficiently reduced by aluminium amalgam.

The ready availability of Diels–Alder adducts of the esters of azodicarboxylic acid [for example (16)] prompted us to examine the sodium–liquid ammonia cleavage of further compounds prepared from such adducts in order to establish the general applicability of this reaction using vigorous conditions. Hydrogenation of the Diels–Alder adduct (17) from cyclohexa-1,3-diene[15] gave the hydrazine derivative (18), which was reductively cleaved by sodium in liquid ammonia to give the known[16] amide (19) in 81% yield. The successful reduction of compound (18) shows that the strain in the bicyclo[2.2.1] framework of compound (6) is not a major factor facilitating cleavage.

Three more functionalised hydrazine derivatives (20)—(22) were prepared for study. Epoxidation of the Diels–Alder adduct (12)[17] afforded the *exo*-epoxide (20) as the sole product. Oxidation of the adduct (12) with osmium tetraoxide, and *via* hydroboration, afforded the diol (21) and the known[18] alcohol (22) respectively. In both cases only *exo*-products were obtained.

Each of the three hydrazine derivatives (20)—(22) was reduced to give cleaved products in good yield. From the epoxide (20) the cleaved product (23) was identified by spectroscopic features which established that the epoxide function was retained and that the stereochemistry was preserved. Similarly, in the reductive cleavage of compound (21) the diol product (24) showed spectroscopic features that indicated the symmetry of the product, and hence the preservation of the relative stereochemistry through the conditions of reductive cleavage. Characterisation of the diol (24) as the diacetate (25) confirmed this analysis. Reduction of the alcohol (22) afforded compound (26) as the only product. The structure of the alcohol (26), which was further characterised as a *p*-nitrobenzoate (27), is assigned with the

assumption that in common with all the other examples of cleavage of a bicyclic skeleton reported in this paper, the relative stereochemistry is preserved. These successful reductions contrast with the failure of attempted hydrogenations. For example the epoxide (**20**) is stable to hydrogenation.

The successful reduction of the hydrazine derivatives (**20**)—(**22**) shows that the procedure using sodium in liquid ammonia is not affected by the presence of the epoxide or hydroxyl functionality. The utility of the method is increased by the absence of any epimerisation *via* possible anionic intermediates in the course of reaction. Hence, by the reductive cleavage of products easily obtained by elaboration of Diels–Alder adducts, derivatives of cyclic diamines are available stereospecifically. Such diamines[3,4,19] constitute the aglycone components of new aminoglycoside antibiotics. Thus *cis*-1,3- and *cis*-1,4-deoxyinosadiamines are important constituents of fortimicins, istamycins, and sannamycins.

Experimental

M.p.s. were determined in a capillary tube and are uncorrected. I.r. spectra were obtained using a Perkin-Elmer 157G grating spectrometer. ^1H and ^{13}C N.m.r. spectra were obtained using a Varian Associates XL-100 spectrometer and a Bruker spectrometer. Tetramethylsilane was used as internal standard and deuteriochloroform was used as the solvent unless otherwise stated. Mass spectra were obtained at 70 eV unless otherwise stated, using a Kratos MS-30 spectrometer equipped with a DS 505 Data System. Flash chromatography was carried out on Macherey Nagel silica gel 60. All reactions were carried out under nitrogen. Organic solutions were dried over anhydrous magnesium sulphate and solvent evaporation was carried out at reduced pressure using a rotatory evaporator. Elemental analyses were performed at University College, London. Ether refers to diethyl ether.

2,3-*Bis*(*trifluoroacetyl*)-2,3-*diazabicyclo*[2.2.1]*heptane* (**7**).—Di-t-butyl azodicarboxylate[14] (**15**) (5 g) and cyclopentadiene (1.8 ml) in ether were stirred at room temperature for 24 h. Further cyclopentadiene (1.8 ml) was added and the solution was stirred for a further 24 h. Removal of the solvent afforded as a crystalline solid di-t-butyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**11**) (6.08 g, 94%), m.p. 102–105 °C (lit.,[14] 99—100 °C); $\nu_{max.}$ ($CHCl_3$) 1 740 and 1 695 cm^{-1}; δ (60 MHz) 1.5—1.75 (20 H, complex, 7-H and CMe_3), 5.1 (2 H, br, 1-H and 4-H), and 6.5 (2 H, m, 5-H and 6-H).

Di-t-butyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**11**) (2 g, 0.0067 mol) in methanol (50 ml) was stirred under hydrogen (1 atm) at room temperature in the presence of platinum dioxide (40 mg) until no further hydrogen was absorbed (2 h). Catalyst residues were filtered off and the solvent removed under reduced pressure. The residue (1.96 g) was taken up into trifluoroacetic acid (10 ml) and the resulting yellow solution was stirred at room temperature for 30 min. Trifluoroacetic anhydride (2.5 ml) was added and the mixture was stirred at room temperature for 18 h. The solvent was removed under reduced pressure to give a gummy solid. Recrystallisation (ether) gave as white crystals 2,3-*bis*(*trifluoroacetyl*)-2,3-*diazabicyclo*[2.2.1]*heptane* (**7**) (1.08 g, 55%), m.p. 138—139 °C (Found: C, 37.2; H, 2.8; N, 9.6. $C_9H_8F_6N_2O_2$ requires C, 37.0; H, 2.7; N, 9.6%); $\nu_{max.}$ ($CHCl_3$) 1 755 and 1 715 cm^{-1}; δ (100 MHz) 2.0 (6 H, complex, 5-H, 6-H, and 7-H) and 4.95 (2 H, br, 1-H and 4-H); δ_C (p.p.m.) 29.58, 38.88, 62.32, 115.81, and 153.75; *m/z* 290 (M^+, 13%).

Diethyl 2,3-*Diazabicyclo*[2.2.2]*oct-5-ene*-2,3-*dicarboxylate* (**17**).—Cyclohexa-1,3-diene (3 g) and diethyl azodicarboxylate (6 g) in cyclohexane (200 ml) were irradiated (Pyrex; 400-W medium-pressure mercury lamp) for 12 h according to the procedure of Askani.[15] Work-up afforded diethyl 2,3-diazabicyclo[2.2.2]oct-5-ene-2,3-dicarboxylate (**17**)[15] (7.4 g, 82%); δ (60 MHz) 1.25 (6 H, t, *J* 7 Hz, Me), 1.3—2.4 (4 H, complex, 7-H and 8-H), 4.2 (4 H, q, *J* 7 Hz, CO_2CH_2), 4.9 (2 H, br s, 1-H and 4-H), and 6.6 (2 H, m, 5-H and 6-H).

Diethyl 2,3-*Diazabicyclo*[2.2.2]*octane*-2,3-*dicarboxylate* (**18**).—Diethyl 2,3-diazabicyclo[2.2.2]oct-5-ene-2,3-dicarboxylate (**17**) (1 g) in methanol (50 ml) was hydrogenated (1 atm) over platinum dioxide (40 mg) at room temperature to afford on work-up, as an oil, diethyl 2,3-diazabicyclo[2.2.2]octane-2,3-dicarboxylate (**18**)[15] (0.99 g, 98%); δ (60 MHz) 1.25 (6 H, t, *J* 7 Hz, Me), 1.3—2.4 (8 H, complex, 5-H, 6-H, 7-H, and 8-H), and 4.0—4.4 (6 H, complex, 1-H, 4-H, and CO_2CH_2).

Diethyl 5,6-*Epoxy*-2,3-*diazabicyclo*[2.2.1]*heptane*-2,3-*dicarboxylate* (**20**).—Diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**12**)[17] (2.1 g, 8.7 mmol) and *m*-chloroperoxybenzoic acid (5.5 g, 0.032 mol) in chloroform (150 ml) were heated under reflux for 23 h. The cold reaction mixture was washed with aqueous sodium hydrogen carbonate (2 × 100 ml) and then with aqueous sodium carbonate (100 ml). The organic phase was dried, filtered, and concentrated to afford a brown oil (2.3 g). Column chromatography (eluant ethyl acetate) of a portion (0.70 g) of this oil afforded a colourless but rather unstable oil (0.69 g, 94%) which was further purified by bulb-to-bulb distillation (oven temperature 85—90 °C; 1 mmHg) to give as an oil, *diethyl* 5,6-*epoxy*-2,3-*diazabicyclo*[2.2.1]*heptane*-2,3-*dicarboxylate* (**20**) [Found: M^+, 256.1352, $C_{11}H_{16}N_2O_5$ requires M^+, 256.1055 (C.I.; NH_3)]; *m/z* 257 (100%), and 256 (49%); $\nu_{max.}$ ($CHCl_3$) 1 750—1 700 cm^{-1}; δ (360 MHz) 1.3 (7 H, complex, 7-H and Me), 1.82 (1 H, d, *J* 11 Hz, 7-H), 3.55 (2 H, s, 5-H and 6-H), 4.25 (4 H, q, *J* 7 Hz, CO_2CH_2), and 4.80 (2 H,br s, 1-H and 4-H); δ_C (p.p.m.) 14.45, 26.25, 47.42, 61.45, 62.76, and 158.01.

Diethyl 5,6-*Dihydroxy*-2,3-*diazabicyclo*[2.2.1]*heptane*-2,3-*dicarboxylate* (**21**).—To diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**12**)[17] (1 g, 4.2 mmol) in t-butyl alcohol (10 ml), water (2.5 ml), and pyridine (0.35 ml) was added trimethylamine *N*-oxide dihydrate (0.65 g) and then osmium tetraoxide [0.5% solution in t-butyl alcohol (0.4 ml)]. The mixture was heated under reflux for 4 h and then cooled to room temperature. Aqueous sodium metabisulphite (10 ml; 20% solution) was added and the solvent removed under reduced pressure. To the residue, water (20 ml) and then dilute hydrochloric acid were added to afford an acidic solution. This solution was extracted with ethyl acetate (3 × 200 ml), and the organic extract was dried, filtered, and concentrated to afford a crude product as an oil (0.82 g). Column chromatography (eluant ethyl acetate) afforded a colourless oil, which was further purified by bulb-to-bulb distillation (oven temperature 135—140 °C; 1 mmHg) to give an oil (0.76 g, 67%) which slowly crystallised on standing affording *diethyl* 5,6-*dihydroxy*-2,3-*diazabicyclo*[2.2.1]*heptane*-2,3-*dicarboxylate* (**21**), m.p. 104.5—106 °C (Found: C, 48.3; H, 6.7; N, 10.2. $C_{11}H_{18}N_2O_6$ requires C, 48.2; H, 6.6; N, 10.2%); $\nu_{max.}$ ($CHCl_3$) 3 400, 1 740, 1 720, and 1 690 cm^{-1}; δ (360 MHz) 1.29 (6 H, t, *J* 7 Hz, Me), 1.65 and 2.08 (2 H, ABq, *J* 11 Hz, 7-H), and 3.9—4.4 (10 H, complex, 1-H, 4-H, 5-H, 6-H, OH and CO_2CH_2); δ_C (p.p.m.) 14.42, 27.5, 31.17, 62.94, 70.39, and 157.56; *m/z* (C.I; NH_3) 274 (14%) and 275 (15%) (M^+ and $M^+ + 1$).

Diethyl 5-*Hydroxy*-2,3-*diazabicyclo*[2.2.1]*heptane*-2,3-*dicarboxylate* (**22**).—To a solution of diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**12**)[17] (0.98 g, 4.1

mmol) in dry tetrahydrofuran (10 ml), a solution of borane–tetrahydrofuran complex (4.2 ml of 1M-solution; 4.2 mmol) in tetrahydrofuran (40 ml) was added during 15 min at 0—5 °C. The clear solution was stirred for 3 h and a solution (24.8 ml) 30% hydrogen peroxide in 3M-aqueous sodium hydroxide (1:1) was added at 0—5 °C. The mixture was allowed to slowly warm to room temperature and then left for 12 h. After removal of the solvents under reduced pressure, the aqueous residue was partitioned with ethyl acetate (2 × 200 ml). The combined organic layers were dried, filtered, and concentrated under reduced pressure to afford an oily residue (1.1 g). Column chromatography (eluant, ethyl acetate) gave as a colourless oil the known[18] diethyl 5-hydroxy-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (**22**) (0.9 g, 86%); $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 740 cm^{-1}; δ (60 MHz) 1.29 (6 H, t, *J* 7 Hz, Me), 1.3—2.7 (4 H, complex, 6-H and 7-H), and 3.6—4.7 (8 H, complex, 1-H, 4-H, 5-H, OH, and CO_2CH_2); *m/z* 258 (M^+, 6.7%).

Reduction by Sodium in Ammonia: Typical Procedure.—The hydrazine (*ca.* 1—3 mmol) was stirred in dry liquid ammonia (100 ml) under reflux. Small lumps of sodium metal were added until a permanent blue colour persisted. During a further 1.5 h the blue colour was maintained by the addition of further sodium. An excess of solid ammonium chloride was then added in portions and the solvent was allowed to evaporate. Typically the residue was taken up in methylene dichloride (100 ml), but less soluble residues were taken up in ethyl acetate (100 ml). Following filtration, the solvent was removed from the filtrate to afford a crude reaction product, which was purified either by crystallisation or by flash column chromatography (eluant ethyl acetate or ether). The following products were then obtained.

cis-1,3-*Bis*(*ethoxycarbonylamino*)*cyclopentane* (**13**) (100%) from diethyl 2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (**6**), m.p. 111—112 °C (from ether) (Found: C, 54.1; H, 8.2; N, 11.55. $C_{11}H_{20}N_2O_4$ requires C, 54.1; H, 8.25; N, 11.5%); $\nu_{max.}$ ($CHCl_3$) 3 450, 3 360, and 1 710 cm^{-1}; δ (100 MHz) 1.27 (6 H, t, *J* 7 Hz, Me), 1.3—2.1 (5 H, complex, 2-H, 4-H, and 5-H), 2.25—2.55 (1 H, m, 2-H), 3.75—4.25 (6 H, complex, 1-H, 3-H, and CO_2CH_2), and 5.66 (2 H, br, NH); δ_C (p.p.m.) 14.71, 31.71, 39.81, 51.14, 60.79, and 156.65; *m/z* 244 (M^+, 0.1%).

N-*Methylacetamide* (**10**) (75%) from *N,N'*-diacetyl *N,N'*-dimethylhydrazine (**5**)[19] as a low melting solid (lit., m.p. 26—28 °C[20]) with spectral features identical with literature data[21] (^{1}H n.m.r.).

cis-1,3-*Bis*(*ethoxycarbonylamino*)-4,5-*expoxycyclopentane* (**23**) (48%) from diethyl-5,6-epoxy-2,3-diazabicyclo-[2.2.1]heptane-2,3-dicarboxylate (**20**), m.p. 119—119.5 °C [from ether–light petroleum (b.p. 60—80 °C)] (Found: C, 51.1; H, 7.1; N, 10.8. $C_{11}H_{18}N_2O_5$ requires C, 51.2; H, 7.0; N, 10.8%); $\nu_{max.}$ ($CHCl_3$) 3 420, 3 360, 3 280, and 1 710 cm^{-1}; δ (100 MHz) 1.29 (6 H, m, Me), 1.5 (1 H, d, *J* 16 Hz, 2-H), 2.30 (1 H, m, 2-H), 3.55 (2 H, s, 4-H and 5-H), 4.0—4.2 (6 H, complex, 1-H, 3-H, and CO_2CH_2), and 6.35 (2 H, br, NH); δ_C (p.p.m.) 14.43, 38.1, 50.54, 58.62, 62.23, and 156.61; *m/z* 240 (*M* − 18, 4%).

cis-1,3-*Bis*(*ethoxycarbonylamino*)*cyclopentane*-4,5-*diol* (**24**) (59%) from diethyl 5,6-dihydroxy-2,3-diazabicyclo-[2.2.1]heptane-2,3-dicarboxylate (**21**), m.p. 108—110 °C (from ether); $\nu_{max.}$ ($CHCl_3$) 3 440 and 1 705 cm^{-1}; δ (360 MHz) 1.25 (6 H, t, *J* 7 Hz, Me), 1.4—2.1 (2 H, complex, 2-H), 3.7—4.2 (10 H, complex, 1-H, 3-H, 4-H, 5-H, CO_2CH_2, and OH), and 5.37 (2 H, m, NH). The diol was further characterised by reaction with acetic anhydride in pyridine as the *diacetate* (**25**), m.p. 146—147 °C (from ether) (Found: C, 50.1; H, 6.5; N, 7.7. $C_{15}H_{22}N_2O_8$ requires C, 50.3; H, 6.2; N, 7.8%); $\nu_{max.}$ ($CHCl_3$) 3 440, 3 360, 1 745sh and 1 715 cm^{-1}; δ (100 MHz) 1.26 (6 H, t, *J* 7 Hz, Me), 2.09 (6 H, s, COMe), 1.3—2.9 (2 H, complex, 2-H), 3.9—4.3 (6 H, complex, 1-H, 3-H, and CO_2CH_2), 5.26 (2 H, complex, 4-H and 5-H), and 5.90 (2 H, br, NH); δ_C (p.p.m.) 14.57, 20.69, 33.9, 53.17, 61.11, 75.50, 156.26, and 170.31.

cis-1,3-*Bis*(*ethoxycarbonylamino*)*cyclopentan*-4-*ol* (**26**) (65%) as an oil from diethyl 5-hydroxy-2,3-diazabicyclo-[2.2.1]heptane-2,3-dicarboxylate (**22**); $\nu_{max.}$ ($CHCl_3$) 3 680, 3 550, 3 440, 1 750sh, and 1 710 cm^{-1}; δ (100 MHz) 1.26 (6 H, t, *J* 7 Hz, Me), 1.3—2.7 (4 H, complex, 2-H and 5-H), 3.6—4.3 (8 H, complex, 1-H, 3-H, 4-H, OH, and CO_2CH_2), and 4.9—5.7 (2 H, br, NH); *m/z* 153 (100%). This alcohol was further characterised as the p-*nitrobenzoate ester* (**27**), m.p. 168—169 °C [from ethyl acetate–light petroleum (b.p. 40—60 °C)] (Found: C, 52.9; H, 5.6; N, 10.3. $C_{18}H_{23}N_3O_8$ requires C, 52.8; H, 5.7; N, 10.3%); $\nu_{max.}$ ($CHCl_3$) 3 440, 1 720, 1 530, and 1 510 cm^{-1}; δ (100 MHz) 1.25 (6 H, t, *J* 7 Hz, Me), 1.8—2.3 (4 H, complex, 2-H and 5-H), 4.0—4.4 (6 H, complex, 1-H, 3-H, and CO_2CH_2), 4.8—5.6 (3 H, complex, 4-H and NH), and 8.1—8.3 (4 H, aromatic).

cis-1,4-*Bis*(*ethoxycarbonylamino*)*cyclohexane* (**19**) (81%) from diethyl 2,3-diazabicyclo[2.2.2]octane-2,3-dicarboxylate (**18**), m.p. 121—123 °C (lit.,[16] 123—124.5 °C) (from ether); $\nu_{max.}$ ($CHCl_3$) 3 440 and 1 730 cm^{-1}; δ (100 MHz) 1.25 (6 H, t, *J* 7 Hz, Me), 1.66 (8 H, complex, 2-H, 3-H, 5-H, and 6-H), 3.65 (2 H, br, 1-H and 4-H), 4.10 (4 H, q, *J* 7 Hz, CO_2CH_2), and 4.82 (2 H, br, NH); *m/z* 258 (M^+, 0.3%).

Reduction by Zinc in Acetic Acid: N-*Methyltoluene*-p-*sulphonamide* (**9**).—*N,N'*-Dimethyl-*N,N'*-ditosylhydrazine (**4**) (190 mg, 0.5 mmol) and zinc dust (500 mg, 8 mmol) were stirred in glacial acetic acid (15 ml) at 80 °C for 2 h. The cold reaction mixture was poured into aqueous sodium carbonate (10% solution; 50 ml) and the suspension extracted with methylene dichloride (3 × 50 ml). The combined organic layers were washed with water (50 ml), dried, and filtered. Evaporation of methylene dichloride afforded as white crystals *N*-methyltoluene-p-sulphonamide (**9**) (119 mg, 61%), m.p. 75—76 °C (lit.,[22] 76.5—78.5 °C); δ (60 MHz) 2.4 (3 H, s), 2.6 (3 H, d, *J* 5 Hz), 5.0 (1 H, br), and 7.25—7.85 (4 H, complex).

2-*Trifluoroacetyl*-2,3-*diazabicyclo*[2.2.1]*heptane* (**8**).—The reduction of 2,3-ditrifluoroacetyl-2,3-diazabicyclo-[2.2.1]heptane (**7**) by the above procedure using zinc in acetic acid and subsequent column chromatography (eluant ethyl acetate) afforded as an unstable oil 2-*trifluoroacetyl*-2,3-*diazabicyclo*[2.2.1]*heptane* (**8**) (28%) (Found: M^+ 194.0576. $C_7H_9F_3N_2O$ requires M^+, 194.0655); *m/z* 194 (M^+, 38%); $\nu_{max.}$ ($CHCl_3$) 3 250, 3 160, 1 750, and 1 680 cm^{-1}; δ (60 MHz) 1.5—2.2 (6 H, complex, 5-H, 6-H, and 7-H), 3.8—4.1 (2 H, complex, NH and 4-H), and 4.72 (1 H, br, 1-H). The starting material (**7**) was also recovered (42%).

Reduction by Aluminium Amalgam: Typical Procedure.—The hydrazine (*ca.* 0.5—1 mmol) was dissolved in ethyl acetate–water (9:1; 45 ml). Strips of aluminium amalgam (2 g) were added and the reaction mixture was stirred for 15 min at room temperature and then heated under reflux for a further 1 h. From the cold suspension the solids were removed by filtration and washed with ethyl acetate (50 ml) and then methylene dichloride (50 ml). The combined filtrate and washings were concentrated under reduced pressure and the residue taken up in methylene dichloride (100 ml). The resulting solution was dried, filtered, and concentrated to afford a crude reaction product which was purified by recrystallisation where necessary.

N-*Methyltoluene*-p-*sulphonamide*[21] (**9**) (87%) from *N,N'*-dimethyl-*N,N'*-ditosylhydrazine (**4**), as white crystals, m.p. 75—76 °C, identical with a sample prepared by zinc reduction (m.p., t.l.c., ^{1}H n.m.r.).

cis-1,3-*Bis*(*trifluoroacetamido*)*cyclopentane* (**14**) (99%) from

2,3-bis(trifluoroacetyl)-2,3-diazabicyclo[2.2.1]heptane (**7**), m.p. 121—122.5 °C (from ether) (Found: C, 37.1; H, 3.4; N, 9.6. $C_9H_{10}F_6N_2O_2$ requires C, 37.0; H, 3.4; N, 9.6%); $\nu_{max.}$(Nujol) 3 300, 3 100, and 1 695 cm^{-1}; δ (100 MHz) 1.6—2.1 (5 H, complex, 2-H, 4-H, and 5-H), 2.52 (1 H, m, 2-H), 4.25 (2 H, m, 1-H and 3-H), and 7.4 (2 H, br, NH); *m/z* 292 (M^+, 2%).

Reduction by Raney Nickel: N-*Methyltoluene*-p-*sulphonamide* (**9**).—*N,N'*-Dimethyl-*N,N'*-ditosylhydrazine (**4**) (240 mg, 0.6 mmol) and Raney nickel (2 g; W2) were stirred in ethanol (50 ml) under reflux for 30 min. After being cooled, the nickel was removed by filtration and washed with ethanol (2 × 50 ml) and methylene dichloride (50 ml). The combined filtrate and washings were concentrated under reduced pressure to give as white crystals *N*-methyltoluene-*p*-sulphonamide[21] (**9**) 85 mg, 35%), identical with a sample prepared by zinc reduction (m.p., t.l.c., ^1H n.m.r.).

Attempted Hydrogenation of Diethyl 5,6-*Epoxy*-2,3-*diazabicyclo*[2.2.1]*heptane*-2,3-*dicarboxylate* (**20**).—Diethyl 5,6-epoxy-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (**20**) (150 mg) in glacial acetic acid (50 ml) was stirred under hydrogen (1 atm) at room temperature for 9 h in the presence of platinum oxide (30 mg). After work-up the starting material (**20**) was recovered quantitatively.

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