Nitroacetamidation of Styrenes

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Reaction of styrenes with nitronium tetrafluoroborate in acetonitrile affords good yields of products of nitroacetamidation. In all cases addition is highly regioselective to give Markownikoff products. With *trans*-β-methylstyrene, conversion of the initial product of nitroacetamidation into epimeric imidazolines proves a *cis*-nitroacetamidation. In contrast the *trans*-addition to 1-phenylcyclohexene is proved by n.m.r. analysis of the epimeric nitroamides. *trans*-Stilbene gives only the *threo*-nitroamide by *cis*-addition but *cis*-stilbene gives a little of the *erythro*-nitroamide in addition to the *threo*-nitroamide. Products from the stilbenes are related to the known *threo*-1-acetamido-2-benzamido-1,2-diphenylethane. The course of these nitroacetamidations is compared with those of related additions. The nitroacetamidation of the less nucleophilic alkenes hex-1-ene, oct-1-ene, cyclohexene, and cyclopentene gives poor yields of nitroamides.

The diversity of electrophilic additions to alkenes affording vicinally substituted products of synthetic importance has recently increased. In particular, methods of addition of a nitrogen and of a second heteroatom substituent have been developed. By use of dimethyl(methylthio)sulphonium tetrafluoroborate,[1] azasulphenylation procedures, by appropriate choice of the nitrogen nucleophile, can lead to vicinal additions with the introduction of nitrogen at different oxidation levels. Thus, access is possible to vicinally substituted aminosulphides, azidosulphides, or nitrosulphides. We and others have shown that by use of alternative sulphur electrophiles such as diphenyl disulphide[2] or arylsulphenyl compounds[3] addition in acetonitrile affords products of acetamidosulphenylation. Similarly, acetamidoseleniation[4] is possible. Although products of nitroacetamidation would be of considerable synthetic interest, no efficient method to such products has been described. In this paper we describe such a procedure based on use of nitronium tetrafluoroborate in acetonitrile.

Nitroacetamidation represents the addition of two nitrogen substituents to an alkene and is the subject of few reports in the literature: the addition of nitronium tetrafluoroborate to propene, isobutene, and but-2-ene in acetonitrile gives[5] nitroamides in poor yield, and addition to 2-methylbut-2-ene has been reported.[6] By contrast many examples of addition of nitronium salts to alkenes in diverse solvents have been described. Thus, nitrofluorination is possible using nitronium tetrafluoroborate in hydrogen fluoride–pyridine[7] or in lower yields in acetonitrile–sulphur dioxide[8] or by using nitric acid–hydrogen fluoride.[9] Nitroacetoxylation is achieved[10] by use of nitronium tetrafluoroborate in acetic anhydride or by the (more investigated) use of acetyl nitrate.[11–16] Less importantly, additions of nitric acid, nitryl chloride, and nitryl iodide gave, respectively, products of nitrohydroxylation,[17] nitrochlorination,[18] and nitroiodination.[19] As part of the complex chemistry of reaction of alkenes with the oxides of nitrogen, formation of nitronitrates[20] by reaction of dinitrogen pentaoxide (nitronium nitrate) has been noted. However, none of these additions permit a generally applicable direct or indirect route to vicinal nitroamides. The report[5] of use of nitronium tetrafluoroborate in acetonitrile describes addition to propene in 50% yield and to isobutene in 23% yield with formation in both cases of a Markownikoff product. Addition to *cis*- or *trans*-but-2-ene gives a nitroamide (13% yield) of undefined stereochemistry.

Following preliminary investigations with a number of alkenes we have developed an efficient procedure for nitroacetamidation typified by addition to styrene. At −70 °C (bath temperature) nitronium tetrafluoroborate adds rapidly to styrene in acetonitrile–dichloromethane. After a brief reaction time and aqueous work-up the crude nitroamides were purified by crystallisation or by chromatography. With styrenes satisfactory yields (see Table) were obtained by reaction at −70 °C but with less reactive alkenes (*e.g.* cyclohexene or hex-1-ene) even at −40 °C only poor yields of nitroamides were obtained. At higher reaction temperatures extensive polymer formation was observed. In order to minimise the formation of side-products it is important that reactions are conducted in the rigorous absence of water.

Table. Nitroacetamidation of alkenes

Alkene	Reaction temperature (°C)	Product	Yield (%)[a]
Styrene	−70	(**2**)	63
4-Bromostyrene	−70	(**3**)	84
3-Nitrostyrene	−70	(**4**)	40
4-Methylstyrene	−70	(**5**)	51
α-Methylstyrene	−70	(**6**)	28
1-Phenylcyclohexene	−70	(**7**)	59
trans-β-Methylstyrene	−70	(**11**)	61
cis-β-Methylstyrene	−70	(**11**) and (**16**)	38 and 5
trans-Stilbene	−70	(**13**)	72
cis-Stilbene		(**13**) and (**18**)	39 and 6
Hex-1-ene	−10	(**21**)	16
Oct-1-ene	−10	(**22**)	28
Cyclopentene	−10	(**23**)	13[b]
Cyclohexene	−10	(**24**) and (**25**)	20[c]

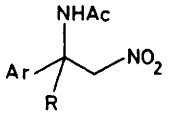
[a] Yields are based on pure isolated products after recrystallisation. [b] Impure product. [c] Mixture of isomers not separable by chromatography.

For styrene the assignment of structure to the adduct follows from both analysis of the ^{1}H n.m.r. spectrum and from previous studies. Reaction of nitromethane with the amide (**1**) has been reported[21] to give (**2**), the expected product of Markownikoff addition to styrene. We have confirmed that the product obtained by reaction of nitromethane with (**1**) is identical with that obtained by nitroacetamidation of styrene. Further

$$PhCH(NHAc)_2$$
(**1**)

support for this assignment comes from observation of a coupling between the methine proton at δ 5.75 in (**2**) and the amide proton at δ 6.80. In a similar manner structures are assigned to the adducts (**3**) and (**4**) of 4-bromostyrene and 3-nitrostyrene, respectively, which are again the products of

Markownikoff addition. In the case of the more reactive 4-methylstyrene the product of double nitration (**5**) is isolated in 51% yield. In each of the additions to these styrenes only a single regioisomer, the Markownikoff product, is observed. The Markownikoff addition to α-methylstyrene to give (**6**) is recognised from the relative chemical shifts in the ^{13}C n.m.r. spectrum of CH_2NO_2 and Ph*C*(CH_3)NHAc at δ_C 80.65 and 58.40 p.p.m. respectively, and is confirmed by other spectral data (^1H n.m.r. and mass).



(**2**) Ar = Ph, R = H

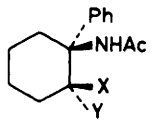
(**3**) Ar = 4-BrC_6H_4, R = H

(**4**) Ar = 3-$NO_2C_6H_4$, R = H

(**5**) Ar = 2-NO_2-4-$CH_3C_6H_3$, R = H

(**6**) Ar = Ph, R = CH_3

Addition to 1-phenylcyclohexene gives a single product. Epimerisation of this product under mildly basic conditions to give mainly a different product clearly establishes an initial Markownikoff addition. Discrimination between the epimers (**7**) and (**8**) is easily made from their ^1H n.m.r. spectra. In the initially formed nitroamide (**7**) the methine proton ($CHNO_2$) at δ 5.92 is observed as a triplet (*J* 4 Hz). Following equilibration the methine proton ($CHNO_2$) in the more stable nitroamide (**8**) is observed at δ 4.98 as a quartet (*J* 12 and 4 Hz). These results indicate equilibration of an axial nitro group to a more favoured equatorial position. In view of the much greater preference for a phenyl group to occupy an equatorial site relative to a nitrogen substituent[22] an initial *trans* addition to 1-phenylcyclohexene to give (**7**) is suggested. This view is confirmed by comparison of the ^1H n.m.r. spectra of (**7**) and (**8**) with those of the related fluoroamides (**9**) and (**10**). The proof[23] of the structure of the *cis*-fluoroamide (**10**) by *X*-ray crystallographic analysis and the relative chemical shift data for the methine protons in the amides (**7**)—(**10**) [δ 5.92 for (**7**), 4.98 for (**8**), 5.53 for (**9**), and 4.63 for (**10**)] permits the unequivocal assignments to (**7**) and (**8**) and hence the conclusion that 1-phenylcyclohexene undergoes *trans*-nitroacetamidation.



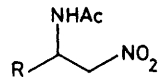
(**7**) X = H, Y = NO_2

(**8**) X = NO_2, Y = H

(**9**) X = H, Y = F

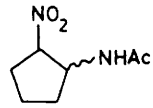
(**10**) X = F, Y = H

Addition to *trans*-β-methylstyrene gives predominantly a single product with a trace of a minor product. The two products are readily equilibrated under basic conditions and can be separated by chromatography. Structures were proved by separate reduction with aluminium amalgam and subsequent cyclisation to give imidazolines which were spectroscopically characterised. Thus the initially formed major product (**11**) on reduction gave the amine (**12**) which was cyclised to give the imidazoline (**19**). Similarly, the epimer (**16**) on reducion gave the amine (**17**) which was cyclised to give a second imidazoline (**20**). The structures of the imidazolines (**19**) and (**20**) are unambiguously assigned on the basis of the relative chemical shifts of the methyl protons at δ 1.28 in the imidazoline (**19**) obtained from the initial product of nitroacetamidation of *trans*-β-methylstyrene, and at δ 0.70 in the imidazoline (**20**) obtained from (**16**), the product of epimerisation of (**11**). This assignment is supported by chemical shift data concerning related examples[24] in the literature. Hence the nitroamide (**11**) is formed by *cis*-addition in a Markownikoff manner to *trans*-β-methylstyrene.

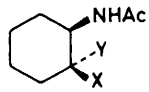


(**21**) R = n-C_4H_9

(**22**) R = n-C_6H_{13}



(**23**)

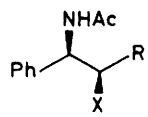


(**24**) X = H, Y = NO_2

(**25**) X = NO_2, Y = H

Addition to *trans*-stilbene gives a single nitroamide (**13**) in good yield but *cis*-stilbene gives a mixture of the two nitroamides (**13**) and (**18**). Discrimination between these nitroamides was made by conversion of the product (**13**) from *trans*-stilbene *via* the acetamidoamine (**14**) into the known[25] *threo*-1-acetamido-2-benzamido-1,2-diphenylethane (**15**). The observation of the single product, the *threo*-nitroamide (**13**), from *trans*-stilbene indicates reaction by *cis*-addition. Observation of two products from *cis*-stilbene suggests that under the reaction conditions *cis*-stilbene undergoes partial equilibration to the more stable *trans*-stilbene. Similarly, *cis*-β-methylstyrene gives a mixture of the *threo*- and *erythro*-nitroamide (**11**) and (**16**).

Additions to aliphatic alkenes, *e.g.* hex-1-ene and oct-1-ene, and to cyclohexene and cyclopentene are less satisfactory. Although products of nitroacetamidation can be isolated, extensive formation of polymers leads to lower yields of nitroamides.



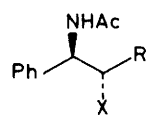
(**11**) R = CH_3, X = NO_2

(**12**) R = CH_3, X = NH_2

(**13**) R = Ph, X = NO_2

(**14**) R = Ph, X = NH_2

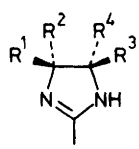
(**15**) R = Ph, X = NHBz



(**16**) R = CH_3, X = NO_2

(**17**) R = CH_3, X = NH_2

(**18**) R = Ph, X = NO_2



(**19**) R^1 = CH_3, R^2 = R^3 = H, R^4 = Ph

(**20**) R^1 = CH_3, R^2 = R^4 = H, R^3 = Ph

In the case of terminal alkenes reaction is regiospecific. Hex-1-ene and oct-1-ene give the nitroamides (**21**) and (**22**), respectively, in poor yield. Cyclopentene gives a single isomer (**23**) and cyclohexene gives a mixture of stereoisomers (**24**) and (**25**) which are difficult to separate.

These results establish the potential synthetic utility of nitroacetamidation of styrenes and other electron-rich alkenes. Introduction of two different nitrogen substituents offers the possibility of subsequent elaboration by a variety of procedures. The observations of consistent Markownikoff addition but with variable *cis*- or *trans*-addition has parallels in the addition of other electrophilic nitronium salts.

Acetyl nitrate adds to *trans*-β-methylstyrene[12,15] and to *trans*-stilbene[12,15] with *cis*-addition but to 1-phenylcyclopentene[14] and to 1-phenylcyclohexene[14] with mainly *trans*-addition. Hence these major addition pathways are the same as those observed in our study in acetonitrile. However, in additions of acetyl nitrate substantial elimination to give nitroalkenes[14] is observed in contrast to our results in acetonitrile. With less nucleophilic alkenes such as *trans*-but-2-ene and cyclohexene, addition of acetyl nitrate occurs[11] to give (typically) low yields of mixtures of the possible nitroacetates. Addition of dinitrogen pentaoxide (nitronium nitrate) to cyclohexene in chloroform gives[20] a complex product mixture in which only the *cis*-nitronitrate *trans*-nitronitrate could be characterised. *cis*-Addition of dinitrogen pentaoxide to *trans*-stilbene occurs[20] but in higher yield.

Earlier results and our present study indicate that the observed stereochemistry of addition of nitronium salts to alkenes is variable. We observe near exclusive *trans*-addition to 1-phenylcyclohexene and near exclusive *cis*-addition to *trans*-stilbene and *trans*-β-methylstyrene. Yet in our addition to cyclohexene and in the above examples of additions of acetyl nitrate and dinitrogen pentaoxide little stereoselectivity is observed.

These results establish the utility of nitronium tetrafluoroborate as a reagent for efficient nitroacetamidation of styrenes and confirm the dual stereochemical pathways previously observed in addition of nitronium salts and alkenes.

Experimental

Acetonitrile (Fisons HPLC Grade) was distilled from phosphorus pentaoxide or calcium hydride. Dichloromethane was distilled from phosphorus pentaoxide. Nitronium tetrafluoroborate (Aldrich) was washed successively with dry nitromethane and dichloromethane and then dried *in vacuo* at 50 °C for 3 h. Alkenes were purified by percolation through active basic alumina. N.m.r. spectra (^1H and ^{13}C) were measured for deuteriochloroform solutions with a Varian XL 100 instrument with tetramethylsilane as internal standard. I.r. spectra were measured with a Perkin-Elmer 157 spectrophotometer. Mass spectra were measured with a Kratos MS 30 spectrometer at 70 eV. Flash chromatography was performed on Macherey Nagel silica gel 60. All m.p.s were taken in open ended capillary tubes and are uncorrected. Elemental analyses were made at University College, London. All products were shown to be homogeneous by t.l.c.

Nitroacetamidation: Typical Procedure.—A solution of an alkene (*ca.* 10 mmol) in dichloromethane was added rapidly to a solution of nitronium tetrafluoroborate (*ca.* 10 mmol) in a mixture of acetonitrile (20 ml) and dichloromethane (20 ml) at −70 °C (bath temperature). After 5 min aqueous sodium hydrogen carbonate (10 ml) was added and the mixture was allowed to warm to room temperature. The organic solvents were then evaporated off and the residue was extracted with dichloromethane (3 × 20 ml). Evaporation of the dried ($MgSO_4$) and combined extracts gave a crude product which was purified by crystallisation and/or flash chromatography on silica gel (ethyl acetate eluant). The following compounds were prepared.

N-(2-*Nitro*-1-*phenylethyl*)*acetamide* (**2**) (84%) from styrene, m.p. 135—138 °C (from dichloromethane) (lit.,[21] 138—139 °C); $\nu_{max.}$($CHCl_3$) 3 440m, 3 320w, 1 675s, 1 550s, 1 495s, and 1 370s cm^{-1}; δ_H (100 MHz; $CDCl_3$) 2.02 (3 H, s, CH_3CO), 4.84 (2 H, m, CH_2NO_2), 5.75 (1 H, m, C*H*NH), 6.80 (1 H, br, NH), and 7.40 (5 H, s, Ph); δ_C($CDCl_3$) 170.05 (CO), 138.95 (quaternary, aromatic), 129.57 (aromatic), 128.52 (aromatic), 127.83 (aromatic), 79.13 (CH_2NO_2), 52.18 (*C*HNH), and 22.81 p.p.m. (*C*H_3CO); *m/z* 162 (12.9%), 148 (1.7), 120 (100), and 106 (28.3).

N-[1-(4-*Bromophenyl*)-2-*nitroethyl*]*acetamide* (**3**) (84%) from 4-bromostyrene, m.p. 135—138 °C (from dichloromethane) (Found: C, 41.6; H, 3.8; Br, 27.4; N, 9.7. $C_{10}H_{11}BrN_2O_3$ requires C, 41.8; H, 3.8; Br, 27.9; N, 9.7%); $\nu_{max.}$($CHCl_3$) 3 430m, 3 310w, 1 685s, 1 560s, 1 495s, and 1 370s cm^{-1}; δ_H (100 MHz; [$^2H_6$]acetone) 2.00 (3 H, s, CH_3CO), 4.80 (2 H, m, CH_2NO_2), 5.75 (1 H, m, C*H*NH), 7.28 (2 H, d, *J* 9 Hz, ArH), 7.51 (2 H, d, *J* 9 Hz, ArH), and 7.7 (1 H, br d, *J* 8 Hz, NH); δ_C([$^2H_6$]acetone) 170.29 (CO), 136.50 (quaternary, aromatic), 132.22 (aromatic) 128.74 (aromatic), 122.48 (quaternary, aromatic), 78.05 (CH_2NO_2), 51.06 (*C*HNH), and 22.88 p.p.m. (*C*H_3CO); *m/z* 242 (2.8%), 240 (4.7), 200 (35.1), 198 (37.0), 186 (9.6), 184 (13.1), and 43 (100).

N-[2-*Nitro*-1-(3-*nitrophenyl*)*ethyl*]*acetamide* (**4**) (40%) from 3-nitrosytrene, m.p. 122—123 °C (from dichloromethane–methanol) (Found: C, 51.0; H, 8.5; N, 14.9. $C_{10}H_{11}N_3O_5$ requires C, 51.1; H, 8.5; N, 14.9%); $\nu_{max.}$($CHCl_3$) 3 420w, 3 300w, 1 680s, 1 560s, 1 530m, 1 510m, 1 370m, and 1 350s cm^{-1}; δ_H (100 MHz; [$^2H_6$]acetone) 2.00 (3 H, s, CH_3CO), 5.06 (2 H, d, *J* 8 Hz, CH_2NO_2), 5.95 (1 H, *J* 8 Hz, CHN), and 7.6—8.4 (5 H, complex, N*H* and ArH); δ_C([$^2H_6$]acetone) 170.55 (CO), 141.43 (quaternary, aromatic), 134.66 (aromatic), 134.51 (aromatic), 130.98 (aromatic), 123.81 (aromatic), 122.73 (aromatic), 78.59 (CH_2NO_2), 51.60 (*C*NH), and 22.85 p.p.m. (*C*H_3CO); *m/z* 207 (3.7%), 165 (80.2), and 43 (100).

N-[1-(4-*Methyl*-2-*nitrophenyl*)-2-*nitroethyl*]*acetamide* (**5**) (51%) from 4-methylstyrene, m.p. 192—193 °C (from dichloromethane–methanol) (Found: C, 49.0; H, 5.0; N, 15.6. $C_{11}H_{13}N_3O_5$ requires C, 49.4; H, 4.8; N, 15.7%); $\nu_{max.}$(Nujol) 3 270m, 1 665s, 1 545s, 1 525s, 1 510m, 1 370s, and 1 325s cm^{-1}; δ_H (100 MHz; [$^2H_6$]acetone) 1.90 (3 H, s, CH_3CO), 2.46 (3 H, s, CH_3), 4.98 (2 H, m, CH_2NO_2), 6.22 (1 H, m, C*H*NH), 7.66 (2 H, m), 7.84 (1 H, d, *J* 2 Hz) (both aromatic), and 8.1 (1 H, br, NH); δ_C([$^2H_6$]acetone) 140.01 (quaternary, aromatic), 135.39 (aromatic), 131.36 (aromatic), 121.87 (aromatic), 125.75 (aromatic), 78.08 (CH_3NO_2), 48.01 (CHNH), 22.61 (*C*H_3CO), and 20.63 p.p.m. (CH_3); *m/z* 221 (100%), 208 (9.1), 179 (66.3), and 165 (57.4).

N-(1-*Methyl*-2-*nitro*-1-*phenylethyl*)*acetamide* (**6**) (28%) from α-methylstyrene, m.p. 147—148 °C (from dichloromethane) (Found: C, 59.2; H, 6.3; N, 12.5. $C_{11}H_{14}N_2O_3$ requires C, 59.5; H, 6.3; N, 12.6%); $\nu_{max.}$($CHCl_3$) 3 440m, 3 340w, 1 680s, 1 550s, 1 500s, and 1 370m cm^{-1}; δ_H (100 MHz; [$^2H_6$]acetone) 1.65 (3 H, s, CH_3), 1.96 (3 H, s, CH_3CO), 5.17 (1 H, d, *J* 12 Hz) and 5.64 (1 H, d, *J* 12 Hz), 7.2—7.6 (5 H, m, ArH), and 7.62 (1 H, br s, NH); δ_C([$^2H_6$]acetone) 170.50 (CO), 143.82 (quaternary aromatic), 129.27 (aromatic), 126.93 (aromatic), 126.03 (aromatic), 125.74 (aromatic), 80.65 (CH_2NO_2), 58.40 (quaternary), 126.03 (aromatic), 125.74 (aromatic), 80.65 (CH_2NO_2), 58.40 (quaternary), 27.58 (CH_3), and 23.55 p.p.m. (*C*H_3CO); *m/z* 176 (100%), 134 (44.6), and 120 (95.1).

trans-N-(2-*Nitro*-1-*phenylcyclohexyl*)*acetamide* (**7**) (59%) from 1-phenylcyclohexene, m.p. 182—185 °C (from dichloromethane) (Found: C, 63.7; H, 6.9; N, 10.5. $C_{14}H_{18}N_2O_3$ requires C, 64.1; H, 6.9; N, 10.7%); $\nu_{max.}$($CHCl_3$) 3 430m,

3 320w, 1 675s, 1 545s, 1 495s, and 1 355m cm $^{-1}$; δ_H (100 MHz; [$^2H_6$]acetone) 1.40 1.90 (6 H, complex), 1.86 (s, CH_3CO) 2.70 (2 H, br, CH_2CPh), 5.92 (1 H, t, *J* 4.0 Hz, $CHNO_2$), and 7.2—7.6 (6 H, complex, Ph and NH); δ_C(CD_3CN–CD_3OH) 171.10 (CO), 143.66 (quaternary, aromatic), 129.20 (aromatic), 128.50 (aromatic), 127.15 (aromatic), 88.69 ($CHNO_2$), 60.08 (quaternary), 28.26 (cycloalkyl), 26.59 (cycloalkyl), 23.97 (CH_3CO), 21.24 (cycloalkyl), and 20.44 p.p.m. (cycloalkyl); *m*/*z* 216 (27%), 174 (15.7), and 157 (40.6).

threo-N-(2-*Nitro*-1-*phenylpropyl*)*acetamide* (**11**) (61%) from *trans*-β-methylstyrene, m.p. 150—152 °C (from dichloromethane) (Found: C, 59.3; H, 6.3; N, 12.8. $C_{11}H_{14}N_2O_3$ requires C, 59.5; H, 6.3; N, 12.6%); $\nu_{max.}$ 3 430m, 3 310w, 1 680s, 1 550s, 1 495s, and 1 365m cm^{-1}; δ_H (100 MHz; [$^2H_6$]acetone) 1.36 (3 H, d, *J* 7 Hz, CH_3), 1.92 (3 H, s, CH_3CO), 5.12 (1 H, m, $CHNO_2$), 5.56 (1 H, dd, *J* 10 and 7 Hz, C*H*NH), 7.3—7.6 (5 H, complex, Ph), and 8.1 (1 H, br d, NH); δ_C([$^2H_6$]acetone) 169.95 (CO), 139.04 (quaternary, aromatic), 129.60 (aromatic), 128.95 (aromatic), 128.46 (aromatic), 87.10 ($CHNO_2$), 56.93 (CHNH), 22.84 (CH_3CO), and 17.37 p.p.m. (CH_3); *m*/*z* 176 (25.6%), 148 (7.0), and 134 (100).

erythro- *and* threo-N-(2-*Nitro*-1-*phenylpropyl*)*acetamide* (**16**) *and* (**11**) *from* cis-β-*Methylstyrene*. The crude product mixture was separated by flash chromatography [eluant ethyl acetate–dichloromethane (2:3)] to give *threo-N*-(2-nitro-1-phenylpropyl)acetamide (**11**) (38%) and then *erythro-N*-(2-nitro-1-phenylpropyl)acetamide (**16**) (5%).

threo-N-(2-*Nitro*-1,2-*diphenylethyl*)*acetamide* (**13**) (72%) from *trans*-stilbene, m.p. 176—179 °C (from dichloromethane) (Found: 67.4; H, 5.7; N, 9.8. $C_{16}H_{16}N_2O_3$ requires C, 67.6; H, 5.7; N, 9.9%); $\nu_{max.}$($CHCl_3$) 3 440m, 3 300w, 1 670s, 1 550s, 1 495s, and 1 360m cm^{-1}; δ_H (100 MHz; $CDCl_3$) 1.98 (3 H, s, CH_3CO), 6.00 (2 H, m, 2 CH), 6.98 (1 H, br d, *J* 10 Hz, NH), and 7.24—7.32 (10 H, complex, 2 Ph); δ_C($CDCl_3$) 169.82 (CO), 136.82 (quaternary, aromatic), 131.46 (quaternary, aromatic), 130.07 (aromatic), 129.89 (aromatic), 127.33 (aromatic), 94.23 ($CHNO_2$), 55.78 (CHNH), and 23.25 p.p.m. (CH_3CO); *m*/*z* 238 (0.2%), 196 (4.4), 148 (11.3) and 106 (100).

erytho- *and* threo-N-(2-*Nitro*-1,2-*diphenylethyl*)*acetamide* (**18**) *and* (**13**) *from* cis-*Stilbene*. The product mixture was separated by column chromatography [eluant benzene–ethyl acetate (1:1)] to give *threo-N*-(2-nitro-1,2-diphenylethyl)-acetamide (**13**) (39%) and *erythro-N*-(2-nitro-1,2-diphenylethyl)acetamide (**18**) (6%), m.p. 176—177 °C (ethyl acetate); $\nu_{max.}$($CHCl_3$) 3 440w, 3 310w, 1 680s, 1 550s, and 1 500s cm^{-1}; δ_H [100 MHz; $CDCl_3$–$(CD_3)_2SO$] 1.66 (3 H, s, CH_3CO), 5.98 (1 H, d, *J* 12 Hz, $CHNO_2$), 6.06 (1 H, m, C*H*NH), 7.22 (1 H, br, NH), and 7.2—7.7 (10 H, complex, 2 Ph); *m*/*z* (chemical ionisation, NH_3) 285.0655 (46%). $C_{16}H_{17}N_2O_3$ requires (*M* + 1), 285.1233.

General Procedure for Aliphatic Alkenes.—A solution of an alkene (*ca.* 10 mmol) in acetonitrile (10 ml) was added to a stirred solution of nitronium tetrafluoroborate in acetonitrile (40 ml) at −40 °C. The mixture was then allowed to warm up to −10 °C, whereupon aqueous sodium hydrogen carbonate (10 ml) was quickly added. After evaporation the residue was extracted with dichloromethane (3 × 25 ml). The combined extracts were dried (magnesium sulphate) and evaporated to give an oil from which the desired nitroacetamide was isolated by flash chromatography (20:1 ethyl acetate–methanol). The following compounds were thus prepared.

N-(1-*Nitromethylpentyl*)*acetamide* (**21**) (16%) from hex-1-ene, m.p. 113—115 °C (from dichloromethane) (Found: C, 50.9; H, 8.5; N, 14.9. $C_8H_{16}N_2O_3$ C, 51.0; H, 8.5; N, 14.9%); $\nu_{max.}$($CHCl_3$) 3 440m, 3 320w, 1 680s, 1 550s, 1 510s, and 1 380m cm^{-1}; δ_H($CDCl_3$) 0.89 (3 H, m, CH_3), 1.2—1.8 (6 H, complex, $[CH_2]_3$), 2.01 (3 H, s, CH_3CO), 4.45 (1 H, br, C*H*NH), 4.56 (2 H, d, CH_2NO_2), and 6.22 (1 H, br, NH); δ_C($CDCl_3$) 170.32 (CO), 78.07 (CH_2NO_2), 47.81 (CHNH), 31.15 (alkyl), 28.07 (alkyl), 23.16 ($COCH_3$), 22.88 (alkyl), and 13.85 p.p.m. (CH_3); *m*/*z* 142 (0.4%), 128 (1.7), and 43 (100).

N-(1-*Nitromethylheptyl*)*acetamide* (**22**) (28%) from oct-1-ene, m.p. 119.5 °C (from dichloromethane) (Found: C, 55.3; H, 9.1; N, 12.9. $C_{10}H_{20}N_2O_3$ requires C, 55.6; H, 9.3; N, 13.0%); $\nu_{max.}$($CHCl_3$) 3 440m, 3 325m, 1 675s, 1 550s, 1 500s, and 1 375s cm^{-1}; δ_H($CDCl_3$) 0.9 (3 H, br, CH_3), 1.2—1.4 (8 H, br, $CH_3[CH_2]_4$), 1.4—1.6 (2 H, br, CH_2CHNH), 1.98 (3 H, s, CH_3CO), 4.4 (1 H, br, C*H*NH), 4.45 (2 H, m, CH_2NO_2), and 6.0 (1 H, br, NH); δ_C($CDCl_3$) 170.19 (CO), 78.05 (CH_2NO_2), 47.80 (CHNH), 31.56, 31.43, 28.84, 25.96, and 23.22 (all CH_2), 22.53 (CH_3CO), and 14.01 p.p.m. (CH_3); *m*/*z* 217 (0.2%), 170 (4.0), 156 (5.7), 128 (34.9), 114 (25.6), and 43 (100).

N-(2-*Nitrocyclopentyl*)*acetamide* (**23**) (13%) from cyclopentene as a low melting solid (lit.,[26] 113—115 °C); $\nu_{max.}$($CHCl_3$) 3 440w, 3 340w, 1 670s, 1 550s, 1 510m, and 1 370m cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.5—3.5 (6 H, br, $[CH_2]_3$), 1.9 (3 H, s, CH_3CO), 4.5 (1 H, m, C*H*NH), 5.0 (1 H, m, $CHNO_2$), and 6.7 (1 H, br, NH); *m*/*z* 172 (1.25%), 126 (12.9), and 84 (100). Although attempted chromatographic purification or recrystallisation failed to afford a pure sample of compound (**23**) the above spectra data are in excellent agreement with the literature.

cis- *and* trans-N-(2-*Nitrocyclohexyl*)*acetamide* (**25**) *and* (**24**) (20%) from cyclohexene, $\nu_{max.}$ 3 440m, 3 320w, 1 665s, 1 550s, 1 510s, and 1 365m cm^{-1}; δ_H($CDCl_3$) 1.2—2.6 (br, $[CH_2]_4$), 1.97 and 1.99 (both s, CH_3CO), 4.85 (br, C*H*NH), 5.20 (br, $CHNO_2$), and 6.3 and 6.6 (both br, NH); δ_C($CDCl_3$) 170.09 and 169.89 (both CO), 83.63 and 81.85 (both $CHNO_2$), 46.97 and 45.47 (both CHNH), 30.31, 30.01, 29.66, 27.86, and 26.86 (all CH_2), and 23.24 p.p.m. (CH_3CO); *m*/*z* 186.1185 (M^+, 0.2%). $C_8H_{14}N_2O_3$ requires *M*, 186.1004. The two isomers could not be separated by chromatography.

Epimerisation. General Procedure.—The nitroacetamide (*ca.* 1 mmol) was dissolved in saturated ethanolic sodium hydrogen carbonate and the solution was refluxed for 12 h. When the solution had cooled, one drop of conc. hydrochloric acid was added and the ethanol was evaporated off. The residue was dissolved in dichloromethane and the extract was washed with saturated aqueous sodium chloride, dried (magnesium sulphate), and evaporated to give an oil. Flash chromatography [eluant dichloromethane–ethyl acetate (60:40)] gave a clean separation of both isomers. Thus prepared were the following compounds.

erythro-N-(2-*Nitro*-1-*phenylpropyl*)*acetamide* (**16**). *threo-N*-(2-Nitro-1-phenylpropyl)acetamide (**11**) gave starting material (45%) and erythro-N-(2-*nitro*-1-*phenylpropyl*)*acetamide* (**16**) (24%), m.p. 104.106 °C (from diethyl ether) (Found: C, 59.2; H, 6.3; N, 12.7. $C_{11}H_{14}N_2O_3$ requires C, 59.5; H, 6.3; N, 12.6%); $\nu_{max.}$($CHCl_3$) 3 440m, 3 320w, 1 675s, 1 550s, 1 495s, and 1 380s cm^{-1}; δ_H([$^2H_6$]acetone) 1.58 (3 H, d, *J* 7 Hz, CH_3), 1.98 (3 H, s, CH_3CO), 5.14 (1 H, m, $CHNO_2$), 5.72 (1 H, dd, *J* 10 Hz, CHNH), 7.3—7.6 (5 H, complex, Ph), and 8.0 (1 H, br, d, NH); δ_C([$^2H_6$]acetone) 170.43 (CO), 138.78 (quaternary, aromatic), 129.42 (aromatic), 128.88 (aromatic), 128.02 (aromatic), 86.72 ($CHNO_2$), 56.41 (CHNH), 22.83 (CH_3CO), and 15.55 p.p.m. (CH_3); *m*/*z* 176 (21.9%), 148 (16.6), 134 (96.5), and 106 (100).

cis-N-(2-*Nitro*-1-*phenylcyclohexyl*)*acetamide* (**8**). *trans-N*-(2-Nitro-1-phenylcyclohexyl)acetamide (**7**) gave starting material (9.5%) and cis-N-(2-*nitro*-1-*phenylcyclohexyl*)*acetamide* (**8**) (81%), m.p. 141—142 °C (from dichloromethane) (Found: C, 63.6; H, 6.8; N, 10.6. $C_{14}H_{18}N_2O_3$ requires C, 64.1; H, 6.9; N, 10.7%); $\nu_{max.}$($CHCl_3$) 3 410m, 1 685s, 1 555m, 1 495s, and 1 370m cm^{-1}; δ_H([$^2H_6$]acetone) 1.4—2.9 (6 H, br, $[CH_2]_3$), 2.14 (3 H, s, CH_3CO), 2.48 (2 H, br, CH_2CHNO_2), 4.98 (1 H, dd, *J* 12 Hz, C*H*NO_2), 7.2—7.5 (5 H, complex, Ph), and 8.00 (1 H, s, N*H*);

$\delta_C(CD_3CN)$ 170.41 (CO), 141.95 (quaternary, aromatic), 129.37 (aromatic), 128.47 (aromatic), 126.47 (aromatic), 94.45 ($CHNO_2$), 62.20 (quaternary), 32.85 (cycloalkyl), 28.13 (cycloalkyl), 23.34 (cycloalkyl), 23.15 (CH_3CO), and 21.11 p.p.m. (cycloalkyl; *m/z* 262.1477 (M^+, 0.15%). $C_{14}H_{18}N_2O_3$ requires *M*, 262.1317.

threo-N-(2-*Amino*-1-*phenylpropyl*)*acetamide* (**12**).—Strips of aluminium amalgam (1.0 g) were added to a solution of *threo*-N-(2-nitro-1-phenylpropyl)acetamide (**11**) (0.22 g, 1 mmol) in wet ethyl acetate (100 ml) and the mixture was stirred until all evolution of hydrogen had ceased. The inorganic salts formed were then filtered off and thoroughly washed with ethyl acetate (3 × 25 ml). Evaporation of the combined filtrate and washings, followed by azeotropic removal of the last traces of ethyl acetate with tetrachloromethane, gave an oil. Trituration with diethyl ether gave threo-N-(2-*amino*-1-*phenylpropyl*)*acetamide* (**12**) (0.19 g, 100%) as a low melting, unstable, white solid, $\nu_{max.}(CHCl_3)$ 3 400m, 3 320s, 1 660s, and 1 500s cm^{-1}; $\delta_H(CDCl_3)$ 1.08 (3 H, d, *J* 7 Hz, CH_3), 2.04 (3 H, s, CH_3CO), 2.35 (2 H, br s, NH_2), 3.29 (1 H, m, C*H*NH_2), 4.82 (1 H, dd, *J* 8 and 4 Hz, C*H*NHCO), and 7.1—7.5 (6 H, complex, Ph and NHCO); $\delta_C(CDCl_3)$ 170.57 (CO), 141.40 (quaternary, aromatic), 128.52 (aromatic), 127.13 (aromatic), 126.59 (aromatic), 58.99 (*C*NHCO), 50.89 (CNH_2), 23.05 (CH_3CO), and 20.62 p.p.m. (CH_3); *m/z* 174 (0.29%), 148 (5.2), 106 (42.1), and 44 (100).

erythro-N-(2-*Amino*-1-*phenylpropyl*)*acetamide* (**17**). Similarly *erythro-N*-(2-nitro-1-phenylpropyl)acetamide (**16**) gave *erythro-N*-(2-amino-1-phenylpropyl)acetamide (**17**) (100%) an unstable, low melting solid, $\nu_{max.}(CHCl_3)$ 3 400m, 3 320m, 1 660s, and 1 505s cm^{-1}; $\delta_H(CDCl_3)$ 1.02 (3 H, d, *J* 7 Hz, CH_3), 1.98 (3 H, s, CH_3CO), 2.2 (2 H, br, NH_2), 3.15 (1 H, m, C*H*NH_2), 4.84 (1 H, dd, *J* 8 and 6 Hz, C*H*NH), 6.9 (1 H, br, NH), and 7.30 (5 H, s, Ph); $\delta_C(CDCl_3)$ 170.23 (CO), 139.51 (quaternary, aromatic), 128.34 (aromatic), 127.74 (aromatic), 127.35 (aromatic), 59.34 (CHNH), 50.56 ($CHNH_2$), 22.97 (CH_3CO), and 20.54 p.p.m. (CH_3); *m/z* 174 (0.12%), 149 (7.8), 106 (18.9), and 44 (100).

threo-N-(2-*Amino*-1,2-*diphenylethyl*)*acetamide* (**14**). Similarly threo-N-(2-*amino*-1,2-*diphenylethyl*)*acetamide* (**14**) was obtained from *threo-N*-(2-nitro-1,2-diphenylethyl)-acetamide (**13**) (100%), m.p. 120—121 °C (from dichloromethane–diethyl ether) (Found: C, 75.3; H, 7.1; N, 10.8. $C_{16}H_{18}N_2O$ requires C, 75.6; H, 7.1; N, 11.0%); $\nu_{max.}(CHCl_3)$ 3 410m, 1 665s, and 1 500s cm^{-1}; $\delta_H(CDCl_3)$ 1.56 (2 H, br, NH_2), 1.87 (3 H, s, CH_3CO), 4.28 (1 H, d, *J* 6 Hz, C*H*NH_2), 5.12 (1 H, m, C*H*NHCO), and 7.1—7.5 (13 H, complex, NH and 2 Ph); $\delta_C(CDCl_3)$ 170.30 (CO), 142.11 (quaternary, aromatic), 140.57 (quaternary, aromatic), 128.79 (aromatic), 128.26 (aromatic), 128.14 (aromatic), 127.20 (aromatic), 127.04 (aromatic), 126.76 (aromatic), 126.26 (aromatic), 59.84 (methine), 59.39 (methine), and 22.77 p.p.m. (CH_3CO); *m/z* 254 (0.1%) and 106 (100).

threo-1-*Acetamido*-2-*benzamido*-1,2-*diphenylethane* (**15**).—Benzoyl chloride (1 ml) was added slowly to a suspension of the amine (**14**) (0.45 g) in aqueous sodium hydroxide (10 ml; 5% solution) and the reaction mixture was shaken for 30 min. The solid product was isolated by filtration, washed [ether (3 × 20 ml)] and recrystallised from ethyl alcohol–water to give *threo*-1-acetamido-2-benzamido-1,2-diphenylethane (**15**) (0.5 g, 79%), m.p. 246—248 °C (lit.,[25] 251 °C); $\nu_{max.}(CHCl_3)$ 3 440, 3 350, and 1 660 cm^{-1}; $\delta_H(CHCl_3)$ 1.90 (3 H, s), 5.42 (2 H, m), 7.0—7.8 (17 H, complex).

trans-4,5-*Dihydro*-2,4-*dimethyl*-5-*phenyl*-1H-*imidazole* (**19**).—*threo-N*-(2-amino-1-phenylpropyl)acetamide (0.50 g, 2.6 mmol) (**12**) was heated under reflux in xylene (50 ml) for 72 h. After having cooled, the xylene solution was extracted with dil. hydrochloric acid (3 × 20 ml) and the combined extracts were washed with diethyl ether. The aqueous phase was neutralised (potassium hydroxide) and re-extracted with dichloromethane (3 × 20 ml). Evaporation of the combined dichloromethane extracts and then Kugelrohr distillation (oven temperature 84 °C; 0.5 Torr) gave *trans*-4,5-dihydro-2,4-dimethyl-5-phenyl-1*H*-imidazole (**19**) (0.45 g, 99%) a pale yellow oil, $\nu_{max.}(CHCl_3)$ 3 410m, 3 150m, and 1 630s cm^{-1}; $\delta_H(CDCl_3)$ 1.28 (3 H, d, *J* 6 Hz, CH_3), 1.98 (3 H, s, CH_3C=N), 3.74 (1 H, m, C*H*CH_3), 4.36 (1 H, d, *J* 8 Hz, CHC_6H_5), 5.62 (1 H, br, NH), and 7.30 (5 H, s, Ph); $\delta_C(CDCl_3)$ 162.83 (C=N), 143.99 (quaternary, aromatic), 128.43 (aromatic), 127.10 (aromatic), 126.30 (aromatic), 72.65 (C-5), 67.30 (C-4), 21.48 (CH_3), and 14.87 p.p.m. (CH_3C=N); *m/z* 174.1097 (M^+, 29.5%). $C_{11}H_{14}N_2$ requires *M*, 174.1157.

cis-4,5-*Dihydro*-2,4-*dimethyl*-5-*phenyl*-1H-*imidazole* (**20**).—Similarly, *erythro-N*-(2-amino-1-phenylpropyl)acetamide (**17**) gave *cis*-4,5-dihydro-2,4-dimethyl-5-phenyl-1*H*-imidazole (**20**) (80%) (distilled at oven temperature 100 °C; 0.1 Torr), $\nu_{max.}(CHCl_3)$ 3 410m, 3 160s, and 1 630s cm^{-1}; $\delta_H(CDCl_3)$ 0.70 (3 H, d, *J* 7 Hz, C*H*$_3$), 2.06 (3 H, s, CH_3C=N), 4.26 (1 H, m, C*H*CH_3), 4.96 (1 H, d, *J* 10 Hz, CHC_6H_5), 6.20 (1 H, br s, NH), and 7.1—7.4 (5 H, complex, Ph); $\delta_C(CDCl_3)$ 164.98 (C=N), 138.21 (quaternary, aromatic), 128.84 (aromatic), 128.46 (aromatic), 127.76 (aromatic), 127.45 (aromatic), 126.59 (aromatic), 67.11 (CHC_6H_5), 60.03 ($CHCH_3$), 17.33 (CH_3), and 14.30 p.p.m. (CH_3C=N); *m/z* 172.1242 (M^+, 33.0%).

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