N-Alkoxy-*N*-acylnitrenium Ions as Possible Intermediates in Intramolecular Aromatic Substitution: Novel Formation of *N*-Acyl-3,4-dihydro-1*H*-2,1-benzoxazines and *N*-Acyl-4,5-dihydro-1*H*,3*H*-2,1-benzoxazepine

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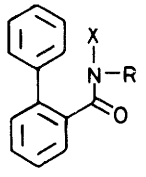
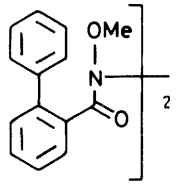
N-Halogeno-*N*-alkoxyamides undergo intramolecular aromatic substitution by thermal- or Lewis acid-catalysed heterolysis of the nitrogen–halogen bond. *N*-Acyl-*N*-alkoxynitrenium ions are likely intermediates. *N*-Chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) yields *N*-methoxyphenanthridone (**11**) quantitatively with $AgBF_4$, while *O*-2-phenylethyl-*N*-chlorobenzohydroxamate (**19**) is converted in good yield into *N*-benzoyl-3,4-dihydro-1*H*-2,1-benzoxazine (**21**) with $AgBF_4$, $AgClO_4$, HgO, and $Hg(OAc)_2$. *N*-Acetyl-3,4-dihydro-1*H*-2,1-benzoxazine (**22**) is formed similarly. *O*-3-Phenylpropyl-*N*-chlorobenzohydroxamate (**23**) cyclises to *N*-benzoyl-4,5-dihydro-1*H*,3*H*-2,1-benzoxazepine (**24**) with $AgBF_4$.

Nitrenium ion intermediates have been postulated in *inter alia* silver-catalysed intramolecular cyclisations of unsaturated *N*-chloroamines, intramolecular rearrangements of saturated *N*-chloroamines,[1,2] and in the cyclisations of *N*-biphenyl)-2-yl-hydroxylamines to form carbazoles with polyphosphoric acid.[3] Aminyl radical reactions are also possible under the conditions of the former cyclisation.[4] MNDO calculations predict that nitrenium ions will be stabilised by adjacent electron-releasing aryl groups in that both singlet and triplet states are lowered in energy.[5] In accordance with this fact, *N*-alkoxy substituents should facilitate the formation of nitrenium ions.

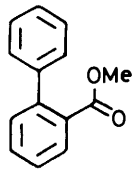
In efforts to form *N*-halogeno-*N*-methoxybiphenyl-2-carboxamides (**2**)—(**4**) from the methoxyamide (**1**) and the corresponding t-butyl hypohalites we have found that only *N*-chloroamide (**4**) can be isolated at room temperature. *N*-Methoxybiphenyl-2-carboxamide (**1**) reacted with t-butyl hypoiodite in t-butyl alcohol or t-butyl hypobromite in benzene[6] in the dark to give *NN'*-bis(biphenyl-2-carbonyl)-*NN'*-dimethoxyhydrazine (**9**), methyl biphenyl-2-carboxylate (**10**), and *N*-methoxyphenanthridone (**11**). *N*-Iodoamines have an N–I dissociation energy of *ca.* 130 kJ mol^{-1}[7] (ref. 7) and if similar *N*-halogen bond strengths pertain, neither (**2**) nor (**3**) would be



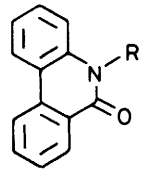
(**1**) R = OMe, X = H
(**2**) R = OMe, X = I
(**3**) R = OMe, X = Br
(**4**) R = OMe, X = Cl
(**5**) R = Ac, X = Cl
(**6**) R = Ac, X = Br
(**7**) R = Me, X = Cl
(**8**) R = Me, X = Br



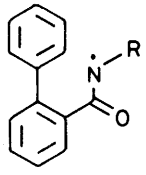
(**9**)



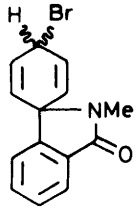
(**10**)



(**11**) R = OMe
(**12**) R = Ac
(**13**) R = Me



(**14**) R = OMe
(**15**) R = Me



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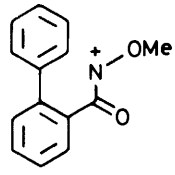
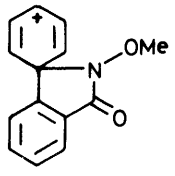
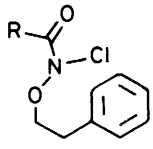


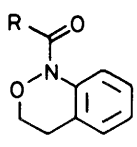
(**17**)



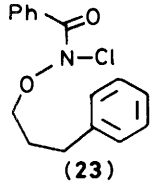
(**18**)



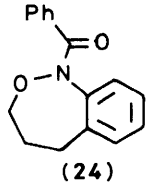
(**19**) R = Ph
(**20**) R = Me



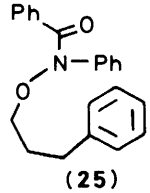
(**21**) R = Ph
(**22**) R = Me



(**23**)

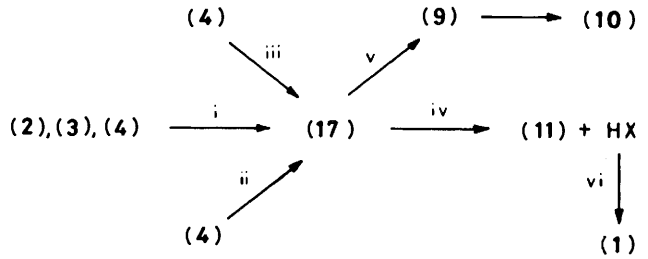


(**24**)



(**25**)

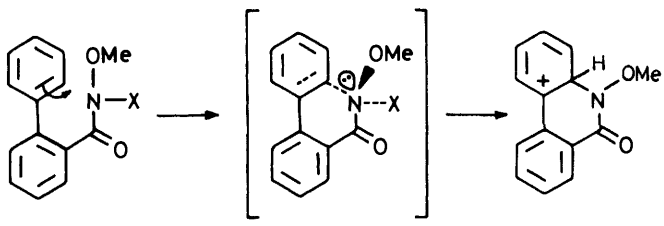
expected to dissociate thermally at room temperature to give the *N*-methoxyamidyl (**14**). Although a radical pathway to (**9**), whilst unlikely, cannot be totally excluded, conclusive evidence that *N*-methoxyphenanthridone (**11**) formation does not involve radicals was derived from the room-temperature photolysis of the *N*-chloroamide (**4**) (> 300 nm, in benzene) which gave only dimer (**9**) (32%) and ester (**10**) (35%). Dimerisation of alkoxyamidyls is known to occur as is the decomposition of (**9**) to (**10**);[8,9] however, we were unable to detect any *N*-methoxyphenanthridone (**11**) even upon photolysis of (**4**) in an adamantane matrix, a medium in which *N*-bromo-*N*-methylbiphenyl-2-carboxamide (**8**) cyclised readily *via* (**15**) to *N*-methylphenanthridone (**13**) and *N*-methyl-3-oxoisoindoline-1-spiro-1′-cyclohexa-2′,5′-dienyl bromides (**16**).[10] Confirmation of the heterolytic pathway for the cyclisation of (**2**) and (**3**) came from refluxing the *N*-chloro-*N*-methoxyamide (**4**) in benzene in the dark for 2 h which gave 50% yields of *N*-methoxyphenanthridone (**11**) and parent amide (**1**) respectively (the *N*-chloroamide was unchanged after the same period in the dark at room temperature). *N*-Methoxyphenanthridone was also formed quantitatively by stirring compound (**4**) for 12 h with an equimolar amount of silver tetrafluoroborate in benzene at room temperature. Stirring with an equivalent of iodine in benzene for 12 h in the dark also gave compounds (**11**) and (**1**) in yields of 58 and 42% respectively. Hydrazine dimers have been formed from the reaction of silver salts of methoxyamides and iodine presumably *via* the *N*-iodoamides.[9] Iodine exchange with the *N*-chloroamide is thus not envisaged since no dimer or ester was produced and iodine most probably behaves as a Lewis acid catalyst. The results, summarised in Scheme 1, could



Scheme 1. *Reagents and conditions:* i, heat, $-X^-$; ii, $AgBF_4$; iii, I_2; iv, $-H^+$; v, (**1**); vi, (**4**)

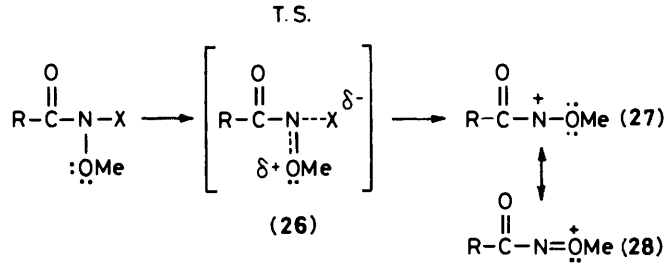
implicate the intermediacy of *N*-biphenyl-2-carbonyl-*N*-methoxynitrenium ion (**17**) formed either by thermal heterolysis (path i) or by silver ion- (path ii) and iodine- (path iii) induced heterolysis of the nitrogen–halogen bond. The nitrenium ion can cyclise to phenanthridone (path iv) or, in the case of (**2**) and (**3**), can react with parent methoxyamide (**1**) to form dimer (**9**) (path v) which decomposes to ester (**10**). In the case of thermal or iodine heterolysis of *N*-chloromethoxyamide (**4**), HCl produced upon cyclisation and re-aromatisation reacts with *N*-chloroamide (**4**) to give amide (**1**) (path vi). No *N*-methylphenanthridone (**13**) or *N*-acetylphenanthridone (**12**) was formed when *N*-bromo-*N*-methyl- (**8**) and *N*-bromo-*N*-acetylbiphenyl-2-carboxamide (**6**) were refluxed in the dark in benzene for 2 h. In addition, treatment of *N*-chloro-*N*-methyl- (**7**) and *N*-acetyl-*N*-chloro-biphenyl-2-carboxamide (**5**) with silver tetrafluoroborate in benzene only afforded unchanged *N*-chloroamides and parent amides.

These results disfavour a concerted process in which the nitrogen-halogen bond cleavage is induced by donation of a pair of electrons from the neighbouring aromatic ring (Scheme 2). Such a process, whilst being slower, might be expected to occur with either or both the *N*-methyl and *N*-acyl substituents



Scheme 2.

present. The methoxy group, as opposed to methyl or acetyl would, however, facilitate N–halogen bond cleavage in (**2**), (**3**), and (**4**) by oxygen stabilisation of the developing positive charge on nitrogen in the transition state [Scheme 3, (**26**)] and the resultant *N*-alkoxynitrenium ion intermediate would be stabilised by resonance [Scheme 3, (**27**) ⟷ (**28**)]. In molecular



Scheme 3.

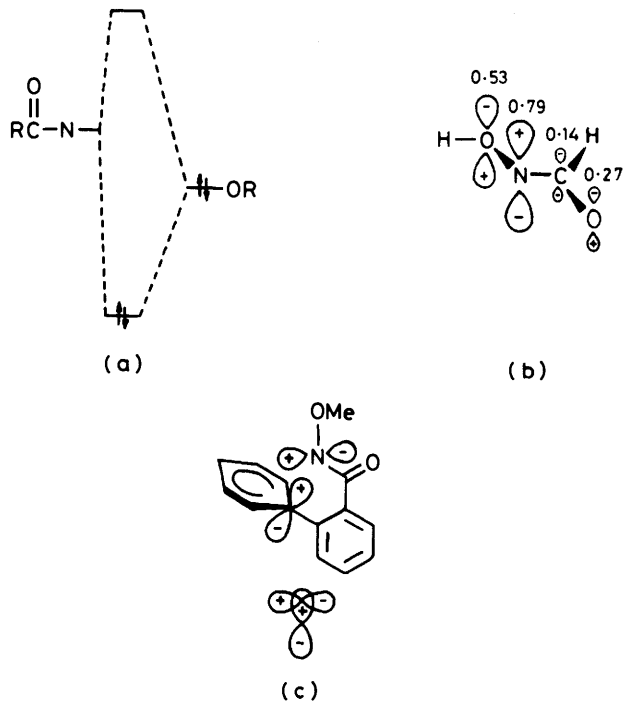


Figure. (a) Electronic stabilisation in alkoxynitrenium ions. (b) LUMO coefficients for *N*-formyl-*N*-hydroxynitrenium ion. (c) Orthogonal orbital overlap in Ar_1–5 cyclisation of nitrenium ion (**17**)

orbital parlance there would be a net electronic stabilisation through overlap between the filled lone pair orbital on oxygen and the vacant orbital on nitrogen [Figure (a)].

These differences in reactivity as well as the similarity in the

Table. Yields of *N*-benzoyl-3,4-1*H*-dihydro-2,1-benzoxazine (**21**)

Reagent[a]	% Yield[b]
$AgBF_4$	67
$AgClO_4$	81
HgO	26
$Hg(OAc)_2$	24

[a] Equimolar quantities. [b] Isolated yield.

ease with which nitrenium ions appear to be formed from *N*-chloroamines[1,2] and *N*-halogeno-*N*-alkoxyamides are also in accord with fully optimised MNDO calculations[11] on the ground states of the model aminyl HNH (**29**), amidyl HNC(O)H (**30**), *N*-acylamidyl HC(O)NC(O)H (**31**), and *N*-hydroxyamidyl HONC(O)H (**32**) radicals. All are predicted to have a π-ground-state at MNDO level of approximation but more significantly the SOMO energies of the aminyl (**29**) and *N*-hydroxyaminyl (**32**) (−5.77 and −5.73 eV respectively) are very similar but much higher than those of the amidyl (**30**) and *N*-acylamidyl (**31**) (−6.92 and −7.51 eV respectively), reflecting their lower oxidation potentials.

MNDO calculations also predict a singlet ground state for the nitrenium ion from *N*-hydroxyformamide with charge deficiency mainly on nitrogen in the LUMO [Figure (b)]. Such π-character would explain the regioselectivity of the nitrenium ion (**17**) for the Ar_2-6 mode of cyclisation. While biphenyl-2-carboxamidyl radicals *e.g.* (**15**), which can react through their Σ-state, afforded mainly Ar_1-5 cyclised products[10,12-14] this mode would be precluded for the nitrenium ion owing to orthogonality between the N $2p_z$ and 1′-C-$2p_z$ orbitals [Figure (c)]. Only *N*-methoxyphenanthridone (**11**) could be detected from the cyclisation of *N*-chloroamide (**4**) with silver tetrafluoroborate in methanol in which the intermediate spirocyclohexadienyl cation (**18**), if formed, would have been solvolysed.[12,14]

We have illustrated the synthetic potential of the reaction by the synthesis of two novel fused heterocyclic systems. *O*-2-Phenylethyl-*N*-chlorobenzohydroxamate (**19**) cyclised in benzene in moderate yields (Table) upon being stirred overnight with an equivalent of silver tetrafluoroborate, silver perchlorate, mercury(II) oxide, or mercury(II) acetate to give the Ar_2-6 product *N*-benzoyl-3,4-dihydro-1*H*-2,1-benzoxazine (**21**). *O*-2-Phenylethyl *N*-chloroacetohydroxamate (**20**) cyclised similarly with silver tetrafluoroborate to give 63% of *N*-acetyl-3,4-dihydro-1*H*-2,1-benzoxazine (**22**). Low yields of polysubstituted 3,4-dihydro-2,1-benzoxazines have only been detected previously from the photolysis of 3,5-dimethyl-2,4-dinitro-t-butylbenzene.[15]

N-Benzoyl-4,5-dihydro-1*H*,3*H*-2,1-benzoxazepine (**24**) has also been synthesized in 35% yield from *O*-3-phenylpropyl-*N*-chlorobenzohydroxamate (**23**) with silver tetrafluoroborate in benzene. To our knowledge no 2,1-benzoxazepines have yet been reported. We have not yet drawn the distinction between direct Ar_2-7 cyclisation or Ar_1-6 spiro cyclisation followed by a 1,2-rearrangement of either the nitrogen or carbon atom.

The *N*-phenyl adduct of the parent hydroxamate, compound (**25**), was also formed in 32% yield presumably by direct electrophilic substitution upon benzene and this interception is additional evidence for the intermediacy of nitrenium ion.

We are continuing to investigate the viability of direct *N*-alkoxyamidation of unsaturated systems using *N*-halogeno-*N*-alkoxyamides as potential nitrenium ion precursors.

Experimental

M.p.s were determined on a Kofler hot stage and are uncorrected. Mass spectra were run on a Varian MAT-212 mass spectrometer equipped with a Varian SS-188 data system as well as on an AEI MS 30 double-beam mass spectrometer. I.r. spectra were run on a Perkin-Elmer Infrared Spectrophotometer, Model 297. 60 MHz N.m.r. spectra were recorded on a Perkin-Elmer R12 A spectrometer with $SiMe_4$ as internal standard. Preparative separations were carried out on a Waters Preparative LC/System 500A (h.p.l.c.) using silica gel. Analytical separations were performed on a Waters Analytical HPLC (μ porasil column) using the model 440 Absorbance Detector linked to a Waters Data Module. Molecular orbital calculations were performed on a Burroughs 6800 computer using the QCPE version of MNDO by W. Thiel.[16] Light petroleum refers to the fraction boiling over the range 40—60 °C.

N-*Bromo*-N-*methylbiphenyl*-2-*carboxamide* (**8**).—Sodium hydride (0.47 g, 19.4 mmol) was added to a solution of t-butyl alcohol (1.60 g, 21.6 mmol) in dry benzene (50 ml) and the reaction mixture was heated gently and stirred for 30 min. The stirred suspension of sodium t-butoxide was diluted with benzene (100 ml) and cooled to room temperature. Bromine (3.11 g, 19.4 mmol) was added dropwise in the dark to the stirred mixture which was maintained (cooling) at room temperature. After 20 min, *N*-methylbiphenyl-2-carboxamide (1.00 g, 4.7 mmol) was added and the mixture was stirred in the dark at room temperature for 1 h. The sodium bromide formed in the reaction was filtered off under suction and the mother liquour concentrated in the dark, under reduced pressure below 40 °C, to give a pale yellow solid (1.5 g). This was recrystallised from benzene–light petroleum as pale yellow prisms of *N*-bromo-*N*-methylbiphenyl-2-carboxamide (**8**) (1.15 g, 85%), m.p. 92—94 °C (decomp.); $\nu_{max.}$ ($CHCl_3$) 1 640 cm^{-1}; δ ($CDCl_3$) 2.97 (3 H, s) and 7.39 (9 H, s) [Found: Br (by iodometry), 27.5%. $C_{14}H_{12}BrNO$ requires Br, 27.54%].

N-*Chloro*-N-*methylbiphenyl*-2-*carboxamide* (**7**).—*N*-methylbiphenyl-2-carboxamide (1.00 g, 4.7 mmol) was stirred for 5 h in the light in a dichloromethane (20 ml) solution of t-butyl hypochlorite (2.55 g, 23.5 mmol) and bromine (2 drops). Removal of the solvent under reduced pressure below 40 °C gave a yellow gum (1.46 g). Analysis by means of the relative n.m.r. *N*-methyl integrals gave a composition of *N*-chloro-*N*-methylbiphenyl-2-carboxamide (**7**) (84.9%) and parent amide (15.1%). Isolation by chromatography yielded pure *N*-chloro-*N*-methylbiphenyl-2-carboxamide (**7**) (0.85 g, 3.5 mmol) [Found: Cl (by iodometry), 14.4%. $C_{14}H_{12}ClNO$ requires Cl, 14.46%].

N-*Acetylbiphenyl*-2-*carboxamide*.—A mixture of biphenyl-2-carboxamide (1.97 g, 10 mmol) and acetic anhydride (2.04 g, 20 mmol) containing a catalytic amount (2 drops) of conc. sulphuric acid was heated at 130 °C for 10 min. After being cooled to 60 °C, the reaction mixture was poured into water (30 ml) and stirred vigorously for 10 min. The pale yellow solid which formed was extracted with chloroform (3 × 20 ml), and the combined extracts were dried (Na_2SO_4) and concentrated to give a yellow oil (2.40 g) which crystallised slowly with time. Recrystallisation from benzene–light petroleum afforded needles of *N*-acetylbiphenyl-2-carboxamide (1.91 g, 80%), m.p. 113—113.5 °C (lit.,[17] 112—113 °C); $\nu_{max.}$ ($CHCl_3$) 1 700, 1 730, and 3 400 cm^{-1}; δ ($CDCl_3$) 2.28 (3 H, s) and 7.2—7.9 (10 H, m).

N-*Acetyl*-N-*bromobiphenyl*-2-*carboxamide* (**6**).—Potassium t-butoxide (1.40 g, 12.5 mmol) and bromine (2.00 g, 12.5 mmol) in dry benzene (40 ml) were stirred together in the dark for 10 min in an ice-bath. After addition of *N*-acetylbiphenyl-2-carboxamide (1.0 g, 4.2 mmol) the reaction mixture was stirred at room temperature in the dark for 1 h. The mixture was filtered under suction and the mother liquour was concentrated

under reduced pressure, below 40 °C in the dark, to give a dark brown gum (1.08 g) of *N*-acetyl-*N*-bromobiphenyl-2-carboxamide (**6**) which could not be crystallised, $\nu_{max.}$ ($CHCl_3$) 1 720 cm^{-1}; δ ($CDCl_3$) 2.15 (3 H, s) and 7.15—7.7 (9 H, m). The presence of positive halogen was indicated by iodometry; percentage composition (by n.m.r.): *N*-acetyl-*N*-bromobiphenyl-2-carboxamide (> 85%) and *N*-acetylbiphenyl-2-carboxamide (< 15%).

N-*Acetyl*-N-*chlorobiphenyl*-2-*carboxamide* (**5**).—*N*-Acetylbiphenyl-2-carboxamide (0.89 g, 3.7 mmol) was stirred with t-butyl hypochlorite (4.56 g, 42 mmol) in benzene (30 ml) containing bromine (2 drops) for 2 h, after which the mixture was stored overnight at 4 °C. Solvent was removed under reduced pressure at 30 °C to yield a pale yellow gum (1.1 g) which could not be crystallised, δ ($CDCl_3$) 2.05 (3 H, s) and 7.15—7.7 (9 H, m) [Found: Cl (by iodometry), 11.7%. $C_{15}H_{12}ClNO_2$ requires Cl, 12.95%].

N-*methoxybiphenyl*-2-*carboxamide* (**1**).—Biphenyl-2-carbonyl chloride (2.73 g, 12.6 mmol), prepared from biphenyl-2-carboxylic acid and thionyl chloride, was added to a vigorously stirred suspension of anhydrous sodium carbonate (5.34 g, 50.4 mmol) and hydroxylamine hydrochloride (3.50 g, 50.4 mmol) in diethyl ether (200 ml).[18] Water (0.5 ml) was added and after being stirred overnight, the solid which formed was separated from the mother liquor by filtration under suction and the insoluble biphenyl-2-carbohydroxamic acid was extracted from the residual sodium carbonate–hydroxylamine hydrochloride with hot chloroform (6 × 100 ml). The extracts were combined with the ether mother liquor, dried (Na_2SO_4), and concentrated to give a white solid (2.5 g). Recrystallisation from chloroform afforded fine needles of biphenyl-2-carbohydroxamic acid (2.50 g, 92.8%), m.p. 132—136 °C; $\nu_{max.}$ ($CHCl_3$) 1 650, 2 900—3 600 br, and 3 425sh cm^{-1}; δ ($CDCl_3$) 3.13 (1 H, s) and 7.2—7.6 (10 H, m); *m/z* 213 (M^+), 181, 167, 153, and 152.

Biphenyl-2-carbohydroxamic acid (1.00 g, 4.7 mmol), anhydrous sodium carbonate (1.49 g, 14.1 mmol), and dimethyl sulphate (0.59 g, 4.7 mmol) were stirred overnight in a mixture of ethanol (20 ml) and water (25 ml). The ethanol was removed under reduced pressure and the aqueous mixture was extracted with chloroform (3 × 20 ml). The combined extracts were dried (Na_2SO_4) and concentrated to give a light brown oil (0.95 g). After purification by preparative h.p.l.c. using chloroform as eluant, the oil product (0.94 g) crystallised slowly with time. Recrystallisation from benzene–light petroleum afforded needles of *N*-methoxybiphenyl-2-carboxamide (**1**) (0.94 g, 87.2%), m.p. 104—105 °C (lit.,[8] 103—105 °C); $\nu_{max.}$ ($CHCl_3$) 1 675 and 3 400 cm^{-1}; δ ($CDCl_3$) 3.3 (3 H, s), 7.2—7.5 (9 H, m), and 9.3 (1 H, br s); *m/z* 228 ($M^+ + 1$) 196, 181, 153, and 152. (Found: C, 73.75; H 5.65; N, 6.05. Calc. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16%).

N-*Chloro*-N-*methoxybiphenyl*-2-*carboxamide* (**4**).—t-Butyl hypochlorite (0.36 g, 3.3 mmol) and *N*-methoxybiphenyl-2-carboxamide (**1**) (0.25 g, 1.1 mmol) were stirred in dry benzene (25 ml) in the dark for 2 h. The mixture was concentrated under reduced pressure, in the dark below 40 °C, to give a light yellow gum of *N*-chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) (0.30 g) which could not be crystallised, $\nu_{max.}$ ($CHCl_3$) 1 720 cm^{-1}; δ ($CDCl_3$) 3.41 (3 H, s) and 7.2—7.6 (9 H, m) [Found: Cl (by iodometry), 13.1%. $C_{14}H_{12}ClNO_2$ requires Cl, 13.55%].

O-2-*Phenylethyl Benzohydroxamate*.—Potassium benzohydroxamate[19] (1.89 g, 10.8 mmol) and 2-phenylethyl bromide (1.99 g, 10.8 mmol) were stirred overnight with sodium carbonate (1.37 g, 13 mmol) in a mixture of methanol (30 ml), and water (30 ml) and the reaction mixture was then refluxed for 1 h. The methanol was removed under reduced pressure and the residue was acidified with dilute hydrochloric acid. The acidic aqueous mixture was extracted with chloroform (3 × 30 ml), and the extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give a light brown oil (1.90 g) which was purified by means of preparative h.p.l.c., δ ($CDCl_3$) 2.94 (2 H, t), 4.6 (2 H, t), 7.0—7.55 (9 H, m), and 7.6—7.85 (2 H, m); $\nu_{max.}$ ($CHCl_3$) 1 680, 3 150—3 350 br, and 3 410sh cm^{-1}; *m/z* 241 (M^+), 137, 122, 105, and 77.

O-2-*Phenylethyl*-N-*chlorobenzohydroxamate* (**19**).—*O*-2-phenylethyl benzohydroxamate (0.85 g, 3.5 mmol) was stirred with t-butyl hypochlorite (2.28 g, 2.1 mmol) in dry benzene (40 ml) for 2 h in the dark. Removal of the solvent under reduced pressure at 30 °C left a yellow oil (0.98 g), shown by n.m.r. and i.r. spectroscopy to be *O*-2-phenylethyl *N*-chlorobenzohydroxamate (**19**), δ ($CDCl_3$) 2.83 (2 H, t), 4.25 (2 H, t), 7.0—7.50 (8 H, m), and 7.55—7.8 (2 H, m); $\nu_{max.}$ ($CHCl_3$) 1 720 cm^{-1} [Found: Cl (by iodometry), 11.85%. $C_{15}H_{14}ClNO_2$ requires Cl, 11.85%].

O-3-*Phenylpropyl Benzohydroxamate*.—Potassium benzohydroxamate[19] (6.13 g, 3.5 mmol), 3-phenylpropyl bromide (7.00 g, 3.5 mmol), sodium carbonate (3.71 g, 3.5 mmol), methanol (100 ml), and water (100 ml) were stirred together overnight and then refluxed for 1 h. The methanol was removed under reduced pressure, and the residue, after acidification with dilute hydrochloric acid, was extracted with chloroform (3 × 30 ml), and the extracts were dried (Na_2SO_4), filtered, and concentrated to give an oil (2.02 g). The oil, which solidified slowly with time, was purified by preparative h.p.l.c. to give the *title ester*, δ ($CDCl_3$) 2.01 (2 H, m), 2.69 (2 H, t), 3.98 (2 H, t), 7.05—7.9 (9 H, m), and 8.0—8.25 (2 H, m); $\nu_{max.}$ ($CHCl_3$) 1 690 and 3 410sh cm^{-1} (Found: C, 75.1; H, 6.4; N, 5.45. $C_{16}N_{17}NO_2$ requires C, 75.27; H, 6.71; N, 5.49%).

O-3-*Phenylpropyl*-N-*chlorobenzohydroxamate* (**23**).—*O*-3-Phenylpropyl benzohydroxamate (2.02 g, 8.4 mmol) and t-butyl hypochlorite (2.58 g, 23.8 mmol) were stirred together in dry benzene (40 ml) for 2 h in the dark. Removal of the solvent at 30 °C under reduced pressure gave a low melting yellow solid (2.24 g) consisting of the *N*-chloro adduct as well as the parent hydroxamate (n.m.r.). The mixture was separated by preparative h.p.l.c. to give *O*-3-phenylpropyl *N*-chlorobenzohydroxamate (**23**) (0.93 g), δ ($CDCl_3$) 1.85 (2 H, m), 2.55 (2 H, t), 4.05 (2 H, t), 6.85—7.6 (8 H, m), and 7.61—7.95 (2 H, m); $\nu_{max.}$ ($CHCl_3$) 1 720 cm^{-1} [Found: Cl (by iodometry), 12.2%. $C_{16}H_{16}ClNO_2$ requires Cl, 12.24%].

O-2-*Phenylethyl Acetohydroxamate*.—Potassium acetohydroxamate (3.00 g, 26.5 mmol), synthesised according to standard procedures,[19] 2-phenylethyl bromide (3.00 g, 16.2 mmol), sodium carbonate (2.00 g, 18.9 mmol), methanol (40 ml), and water (15 ml) were stirred together overnight and then refluxed for 1 h. The methanol was distilled off under reduced pressure and the residue remaining was acidified with dilute hydrochloric acid. The acidic, aqueous mixture was extracted with chloroform (3 × 30 ml) and the combined extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give the *title ester* as a white solid (2.22 g) which was recrystallised from benzene as fine needles, m.p. 91—93 °C; δ ($CDCl_3$) 1.87 (3 H, s), 2.92 (2 H, t), 4.05 (2 H, t), 7.22 (5 H, s), and 9.1—9.5 (br); $\nu_{max.}$ ($CHCl_3$) 1 695 and 3 410sh cm^{-1} (Found: C, 67.0; H, 7.3; N, 7.9. $C_{10}H_{13}NO_2$ requires C, 67.02; H, 7.31; N, 7.82%).

O-2-*Phenylethyl*-N-*chloroacetohydroxamate* (**20**).—O-2-Phenylethyl acetohydroxamate (1.00 g, 5.6 mmol) and t-butyl hypochlorite (1.80 g, 16.6 mmol) were stirred together in dry

benzene (25 ml) in the dark for 2 h. Removal of the solvent under reduced pressure at 30 °C yielded a pale yellow oil (1.12 g), $\nu_{max.}$ ($CHCl_3$) 1 735 cm^{-1} [Found: Cl (by iodometry), 15.6%. $C_{10}H_{12}ClNO_2$ requires Cl, 16.59%].

Thermal Reaction of N-*Bromo*-N-*methylbiphenyl*-2-*carboxamide* (**8**).—A solution of *N*-bromo-*N*-methylbiphenyl-2-carboxamide (**8**) (0.32 g, 1.1 mmol) in dry benzene (20 ml) was refluxed in the dark for 2 h. Removal of solvent afforded unchanged *N*-bromo-*N*-methylbiphenyl-2-carboxamide (n.m.r.).

Dark Reaction of N-*Chloro*-N-*methylbiphenyl*-2-*carboxamide* (**7**) *with Silver Tetrafluoroborate*.—*N*-Chloro-*N*-methylbiphenyl-2-carboxamide (**7**) (0.50 g, 2 mmol) was stirred for 3 h in methanol (50 ml) with silver tetrafluoroborate (0.396 g, 2 mmol). The reaction mixture was filtered and the solvent was removed under reduced pressure to leave a brown gum. This was taken up in chloroform (30 ml), the solution was washed with water (50 ml), and the organic phase was separated, dried (Na_2SO_4), and the solvent removed under reduced pressure to leave a light brown gum (0.5 g). Integration of the relative n.m.r. methyl singlets showed the mixture to consist of *N*-chloro-*N*-methylbiphenyl-2-carboxamide (**7**) (90%) and parent amide (*ca.* 10%); this analysis was confirmed by iodometry.

Thermal Reaction of N-*Acetyl*-N-*bromobiphenyl*-2-*carboxamide* (**6**).—A benzene solution (50 ml) of *N*-acetyl-*N*-bromobiphenyl-2-carboxamide (**6**) (1.09 g, 3.4 mmol) and the parent *N*-acetylamide (0.18 g, 0.7 mmol) was refluxed for 14 h in the dark. Concentration under reduced pressure in the dark afforded an oil which, from analysis of the *N*-acetyl methyl resonances in its n.m.r. spectrum, consisted of *N*-acetyl-*N*-bromobiphenyl-2-carboxamide (**6**) (70%) and the parent *N*-acetylbiphenyl-2-carboxamide (30%).

Dark Reaction of N-*Acetyl*-N-*chlorobiphenyl*-2-*carboxamide* (**5**) *with Silver Tetrafluoroborate*.—A mixture of *N*-acetyl-*N*-chlorobiphenyl-2-carboxamide (**5**) (0.82 g, 3 mmol) and the parent amide (0.07 g, 0.3 mmol) in benzene (45 ml) was stirred overnight in the dark with silver tetrafluoroborate (0.79 g, 4.1 mmol). The reaction mixture was filtered and washed with water (3 × 100 ml). The organic fraction was dried (Na_2SO_4) and concentrated under reduced pressure at 30 °C to give a pale amber gum (0.58 g). Analysis (n.m.r.) showed it to contain no cyclised products, the parent amide (54.5%), δ 2.28 (3 H, s), and unchanged *N*-acetyl-*N*-chlorobiphenyl-2-carboxamide (**5**) (45%), δ 2.05 (3 H, s). Iodometry confirmed the percentage residual *N*-chloroamide.

Dark Reaction of N-*Methoxybiphenyl*-2-*carboxamide* (**1**) *in the Presence of t-Butyl Hypoiodite*.—Iodine (2.79 g, 11 mmol) and t-butyl hypochlorite (1.19 g, 11 mmol) were added successively to t-butyl alcohol (50 ml) in a 100 ml Pyrex, round-bottom flask fitted with a sealed mechanical stirrer and cooled in a cooling bath. The reaction mixture was stirred in the dark for 10 min whereupon potassium t-butoxide (1.36 g, 12 mmol) was added and the mixture was stirred for a further 10 min. *N*-Methoxybiphenyl-2-carboxamide (**1**) (0.50 g, 2.2 mmol) was added and the mixture was stirred for 2 h in the dark. The mixture was poured into excess of aqueous sodium thiosulphate, washed, and extracted with chloroform (3 × 20 ml) and the combined extracts were washed with water (3 × 30 ml), dried (Na_2SO_4), and concentrated under reduced pressure below 40 °C to give an oil which was shown (n.m.r.) to consist of methyl biphenyl-2-carboxylate (**10**) (41%), *NN'*-bis(biphenyl-2-carbonyl)-*NN'*-dimethoxyhydrazine (**9**) (13%), and *N*-methoxyphenanthridone (**11**) (31%). Preparative t.l.c. afforded the biphenyl-2-carboxylate (**10**) which was identical with authentic material (t.l.c., analytical h.p.l.c.), $\nu_{max.}$ ($CHCl_3$) 1 720 cm^{-1}; δ ($CDCl_3$) 3.6 (3 H, s, OMe) and 7.2—7.9 (9 H, m, Ar-H); *NN'*-bis(biphenyl-2-carbonyl)-*NN'*-dimethoxyhydrazine (**9**), $\nu_{max.}$ ($CHCl_3$) 1 722 cm^{-1}; δ ($CDCl_3$) 3.10 (6 H, s, 2 OMe) and 7.2—7.6 (18 H, m, ArH); *m/z* ($M^+/2$) 226, 212, 181, and 152 (the compound decomposes at room temperature). The oil was refluxed overnight in benzene (10 ml). Concentration under reduced pressure afforded methyl biphenyl-2-carboxylate (**10**); *N*-methoxyphenanthridone (**11**), m.p. 99—104 °C [needles from benzene–light petroleum (40—60 °C)]; $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1}; (lit.,[8] 1 660 cm^{-1}); δ ($CDCl_3$) 4.10 (3 H, s, OMe) (lit.,[8] δ 4.13), 7.1—7.9 (5 H, m, ArH), 8.1—8.3 (2 H, crude d, *J* 7 Hz, ArH], and 8.4—8.7 (1 H, crude d, *J* 7 Hz, ArH); *m/z* 225 (M^+), 195, 180, and 166 (Found: C, 74.5; H, 5.05; N, 6.1. Calc. for $C_{14}H_{11}NO_2$: C, 74.67; H, 4.92; N, 6.22%).

Reaction of N-*Methoxybiphenyl*-2-*carboxamide* (**1**) *with* t-*Butyl Hypobromite in the Dark*.—Potassium t-butoxide (1.63 g, 14.5 mmol) and bromine (2.11 g, 13.2 mmol) were stirred together in dry benzene (25 ml) in the dark for 15 min in an ice-bath. After the addition of *N*-methoxybiphenyl-2-carboxamide (**1**) (1.00 g, 4.4 mmol) the reaction mixture was stirred in the dark at room temperature for 2 h. The mixture was filtered under suction and the mother liquor was concentrated in the dark, under reduced pressure below 40 °C, to give a gum. Analysis of its n.m.r. spectrum indicated the presence of methyl biphenyl-2-carboxylate (**10**) (56%), δ 3.55 (3 H, s, OMe); *NN'*-bis(biphenyl-2-carbonyl)-*NN'*-dimethoxyhydrazine (**9**) (16%) δ 3.1 (6 H, s, 2 OMe); and *N*-methoxyphenanthridone (**11**) (12%), δ 4.1 (3 H, s, OMe).

Thermal Reaction of N-*Chloro*-N-*methoxybiphenyl*-2-*carboxamide* (**4**).—(*a*) A solution of *N*-chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) (0.24 g, 0.9 mmol) in benzene (25 ml) was refluxed in the dark for 2 h. Concentration of the reaction mixture gave an oil (0.28 g) whose composition was shown by n.m.r. spectroscopy to be *N*-methoxyphenanthridone (**11**) (50%), δ 4.12 (3 H, s) and the parent *N*-methoxybiphenyl-2-carboxamide (**1**) (50%), δ 3.3 (3 H, s).

(*b*) *N*-Chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) was unchanged after 2 h in benzene in the dark.

(c) *In the presence of silver tetrafluoroborate*. *N*-Chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) (0.24 g, 0.9 mmol) and silver tetrafluoroborate (0.196 g, 1 mmol) were stirred in benzene (25 ml) in the dark for 12 h at room temperature. The mixture was filtered under suction, washed with water, dried, and concentrated under reduced pressure below 40 °C to give an oil (0.21 g) which was shown by n.m.r. spectroscopy to be *N*-methoxyphenanthridone (**11**), δ 4.09 (3 H, s). This was confirmed by comparison with authentic material (i.r., t.l.c.).

(d) *In the presence of iodine*. *N*-Chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) (0.24 g, 0.9 mmol) and iodine (0.28 g, 1 mmol) were stirred in benzene (25 ml) overnight in the dark at room temperature. The reaction mixture was poured into excess of aqueous sodium thiosulphate and the mixture was extracted with chloroform (3 × 20 ml), and the combined extracts were dried (Na_2SO_4) and the concentrated under reduced pressure below 40 °C to give a light brown gum (0.26 g) which, from n.m.r. spectroscopy, was shown to comprise *N*-methoxyphenanthridone (**11**) (58%), δ 4.1 (3 H, s) and parent *N*-methoxybiphenyl-2-carboxamide (**1**) (42%), δ 3.3 (3 H, s).

(e) *In the presence of silver tetrafluoroborate and methanol*. *N*-Chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) (0.28 g, 1.1 mmol) was stirred overnight in the dark in methanol (40 ml) with silver tetrafluoroborate (0.196 g, 1 mmol). Methanol was removed under reduced pressure below 40 °C and the residue which remained was taken up into chloroform (30 ml) and the extract was washed with water (50 ml), dried (Na_2SO_4), and

concentrated under reduced pressure to leave a brown gum (0.28 g). N.m.r. analysis showed quantitative conversion into *N*-methoxyphenanthridone (**11**), δ 4.1 (3 H, s).

Irradiation of N-*Chloro*-N-*methoxybiphenyl*-2-*carboxamide* (**4**).—*In the presence of* 3,3-*dimethylbut*-1-*ene*. A solution of *N*-chloro-*N*-methoxybiphenyl-2-carboxamide (**4**) (0.30 g, 1.15 mmol) in benzene (30 ml) was irradiated for 2 h with u.v. light in the presence of 3,3-dimethylbut-1-ene (0.96 g, 11.4 mmol). Work-up afforded a gum (0.28 g) which, from n.m.r. spectroscopy, was seen to consist of methyl biphenyl-2-carboxylate (**10**) (35%) δ 3.6 (3 H, s) and *NN'*-bis(biphenyl-2-carbonyl)-*NN'*-dimethoxyhydrazine (**9**) (32.5%), δ 3.1 (3 H, s) which were isolated by preparative t.l.c. along with 1,2-dichloro-3,3-dimethylbutane and were identical with authentic materials (i.r., n.m.r., t.l.c.).

General Procedure for the Cyclisation of the N-*Chlorohydroxamates* (**19**) (**20**), *and* (**23**).—A solution of the *N*-chlorobenzohydroxamate in dry benzene was stirred overnight in the dark with silver tetrafluoroborate (unless otherwise specified). The reaction mixture was filtered and washed with water (3 × 100 ml). The organic phase was dried (Na_2SO_4), filtered, and concentrated under reduced pressure.

(a) O-2-*Phenylethyl* N-*chlorobenzohydroxamate* (**19**). (i) 2-Phenylethyl *N*-chlorobenzohydroxamate (**19**) (0.78 g, 2.8 mmol) was stirred for 3 h with silver tetrafluoroborate (0.54 g, 2.8 mmol) in benzene (25 ml). Work-up afforded a crystalline brown solid (0.75 g). Preparative h.p.l.c. (chloroform) yielded the parent *O*-2-phenylethyl benzohydroxamate (0.30 g), identical with authentic material (n.m.r., i.r., and t.l.c.), as well as N-*benzoyl*-3,4-*dihydro*-1H-2,1-*benzoxazine* (**21**) (0.45 g) which crystallised from benzene–light petroleum as prisms, m.p. 149—151 °C (Found: C, 75.05; H, 5.45; N 5.9. $C_{15}H_{13}NO_2$ requires C, 75.3; H, 5.48; N, 5.85%); $\nu_{max.}$ ($CHCl_3$) 1 658 (carbonyl) and 1 358s cm^{-1}; δ_H (60 MHz; $CDCl_3$) 2.92 (2 H, t, *J* 6 Hz, benzylic CH_2), 4.1 (2 H, t, *J* 6 Hz, CH_2O), and 7.0—7.9 (9 H, m, ArH); *m/z* 239 (M^+), 105 (M^+ − 134), and 77 (M^+ − 162).

(ii) *With silver perchlorate*. The above experiment was repeated using silver perchlorate (0.58 g, 2.8 mmol). Work-up and isolation yielded the parent hydroxamate (0.19 g) and *N*-benzoyl-3,4-dihydro-1*H*-2,1-benzoxazine (**21**) (0.54 g).

(iii) *With mercury*(II) *oxide*. A solution of *O*-2-phenylethyl *N*-chlorobenzohydroxamate (**19**) (0.50 g, 1.8 mmol) in benzene (30 ml) was stirred together with mercury(II) oxide (0.39 g, 1.8 mmol). Work-up and isolation yielded a brown gum (0.49 g) from which *N*-benzoyl-3,4-dihydro-1*H*-2,1-benzoxazine (**21**) (0.11 g) was isolated by preparative t.l.c.

(iv) *With mercury*(II) *acetate*. The above reaction was repeated using mercury(II) acetate (0.58 g, 1.8 mmol). Work-up and isolation yielded a brown gum (0.36 g) from which *N*-benzoyl-3,4-dihydro-1*H*-2,1-benzoxazine (**21**) (0.08 g) was isolated by preparative t.l.c.

(b) O-2-*Phenylethyl* N-*chloroacetohydroxamate* (**20**). A solution of *O*-2-phenylethyl *N*-chloroacetohydroxamate (**20**) (0.84 g, 3.9 mmol) in benzene (80 ml) was stirred for 4 h in the dark with silver tetrafluoroborate (0.77 g, 3.9 mmol). Work-up yielded a brown oil (0.5 g). Separation by preparative t.l.c. gave the parent acetohydroxamate (0.09 g), identical with authentic material (n.m.r., i.r., t.l.c.), as well as N-*acetyl*-3,4-*dihydro*-1H-2,1-*benzoxazine* (**22**) (0.26 g) which crystallised from benzene–light petroleum as prisms, m.p. 90.5—92 °C (Found: C, 67.6; H, 6.25; N, 7.85. $C_{10}H_{11}NO_2$ requires C, 67.78; H, 6.26; N, 7.9%); $\nu_{max.}$ ($CHCl_3$) 1 671 (carbonyl), 1 380s, and 1 348s cm^{-1}; δ_H (60 MHz; $CDCl_3$) 2.24 (3 H, s, CH_3), 2.94 (2 H, t, *J* 6.5 Hz, benzylic CH_2), 4.27 (2 H, t, *J* 6.5 Hz, CH_2O), 7.0—7.4 (3 H, m), and 7.8—8.05 (1 H, m); *m/z* 177 (M^+, 13%), 135 (M^+ − CH_2CO), 100, and 43 (M^+ − 134).

(c) O-3-*Phenylpropyl* N-*chlorobenzohydroxamate* (**23**). A solution of *O*-3-phenylpropyl *N*-chlorobenzohydroxamate (**23**) (0.84 g, 2.9 mmol) in benzene (25 ml) was stirred with silver tetrafluoroborate (0.62 g, 3.2 mmol). Work-up gave a dark brown oil (0.89 g) which was separated by preparative t.l.c. to give *O*-3-phenylpropyl *N*-phenylbenzohydroxamate (**25**) (0.31 g), δ ($CDCl_3$) 1.75 (2 H, m), 2.49 (2 H, t), 3.82 (2 H, t), and 6.7—7.75 (15 H, m); $\nu_{max.}$ ($CHCl_3$) 1 680 cm^{-1}; *m/z* 331 (M^+), 197, 105, and 77, and N-*benzoyl*-1H,3H-4,5-*dihydro*-2,1-*benzoxazepine* (**24**) (0.26 g) which crystallised from benzene–light petroleum as prisms, m.p. 120 °C (Found: C, 75.9; H, 6.0; N, 5.55. $C_{16}H_{15}NO_2$ requires C, 75.87; H, 5.97; N, 5.53%); $\nu_{max.}$ ($CHCl_3$) 1 660 (carbonyl) and 1 350s cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.6—3.1 (2 H, m, CH_2), 2.9—3.2 (2 H, m, benzylic CH_2), 4.22 (2 H, t, *J* 6 Hz, OCH_2), and 6.8—7.65 (9 H, m); *m/z* 253 (M^+), 105 (M^+ − 148), and 77.

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References

1 P. G. Gassman, *Acc. Chem. Res.*, 1970, **3**, 26.
2 P. G. Gassman, K. Uneyama, and J. L. Hahnfield, *J. Am. Chem. Soc.*, 1977, **99**, 647; M. Mokotoff and R. F. Sprecher, *Tetrahedron*, 1974, **30**, 2623.
3 F. W. Wassmundt and G. T. Babic, *J. Org. Chem.*, 1982, **47**, 3585.
4 J.-M. Surzur in 'Reactive Intermediates,' ed. R. A. Abramovitch, Plenum Press, New York, 1982, vol. 2, p. 168; R. Tadayoni, J. Lacrampe, A. Heumann, R. Furstoss, and B. Waegell, *Tetrahedron Lett.*, 1975, 735; O. E. Edwards, G. Bernath, J. Dixon, J. M. Paton, and D. Vocelle, *Can. J. Chem.*, 1974, **52**, 2123.
5 G. P. Ford and J. D. Scribner, *J. Am. Chem. Soc.*, 1981, **103**, 4281.
6 S. A. Glover and A. Goosen, *Tetrahedron Lett.*, 1980, **21**, 2005.
7 S. A. Glover, A. Goosen, and R. D. Venter, *S. Afr. J. Chem.*, 1978, **31**, 33.
8 A. R. Forrester, E. M. Johansson, and R. H. Thomson, *J. Chem. Soc., Perkin Trans 1*, 1979, 1113.
9 J. H. Cooley, M. W. Mosher, and M. A. Khan, *J. Am. Chem. Soc.*, 1968, **90**, 1867.
10 S. A. Glover, A. Goosen, C. W. McCleland, and J. L. Schoonraad, submitted to *J. Chem. Soc., Perkin Trans. 1*, submitted for publication.
11 M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, 1977, **99**, 4899, 4907; M. J. S. Dewar, M. L. McKee, and H. S. Rzepa, *ibid.*, 1978, **100**, 3607.
12 S. A. Glover and A. Goosen, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2353.
13 S. A. Glover and A. Goosen, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1348.
14 S. A. Glover and A. Goosen, *J. Chem. Soc., Perkin Trans. 1*, 1978, 653.
15 D. Döpp and K. H. Sailer, *Tetrahedron Lett.* 1975, 1129.
16 (*a*) IBM Version: W. Thiel, *QCPE*, 1978, **10**, 353; (*b*) CDC Version: W. Thiel, *QCPE*, 1979, **11**, 379.
17 C. D. Hurd and A. G. Prapas, *J. Org. Chem.*, 1959, **24**, 388.
18 L. W. Jones and C. D. Hurd, *J. Am. Chem. Soc.*, 1921, **43**, 2422.
19 C. R. Hauser and W. B. Renfrow, Jr., *Org. Synth.*, Coll. Vol. 2, 1943, p. 67.

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