A New Precursor to 3,4-Didehydropyridine, and its Use in the Synthesis of the Antitumour Alkaloid Ellipticine[1]

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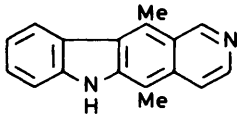
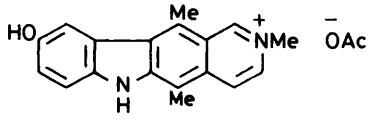
A concise synthesis of the antitumour alkaloid ellipticine (**1**) is reported. The route involves a Diels-Alder reaction between 1,4-dimethylpyrano[3,4-*b*]indol-3-one (**3**), easily prepared in two steps from indole, and 3,4-didehydropyridine (**4**), and for its successful execution required the development of a new thermal, reagent-free precursor to the aryne. This precursor, 3-(3,3-dimethyltriazen-1-yl)pyridine-4-carboxylic acid (**10a**), prepared from 3-aminopyridine-4-carboxylic acid, decomposes in boiling acetonitrile to generate 3,4-didehydropyridine which can be intercepted in Diels-Alder reactions with tetraphenylcyclopentadienone, furan, and 2,5-dimethylfuran. The triazenes (**10b**) and (**10c**) can be prepared and decomposed similarly. The key Diels-Alder reaction between the pyranoindolone (**3**) and 3,4-didehydropyridine (**4**) gives ellipticine (**1**) in 20% yield, together with an equal amount of isoellipticine (**14**).

The pyrido[3,4-*b*]carbazole alkaloid ellipticine (**1**) was first isolated from the tropical evergreen *Ochrosia elliptica* Labill. in 1959,[2] although it was not until 1967 that the antitumour properties of the alkaloid were discovered.[3] Since then ellipticine and its derivatives have been extensively studied as antitumour agents, and *N*-methyl-9-hydroxyellipticinium acetate (**2**) is currently in clinical use for the treatment of some cancers.[4]



(**1**)

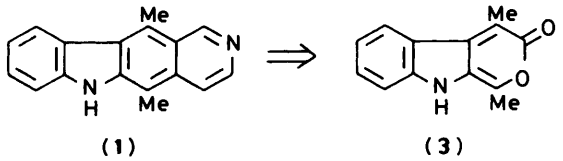


(**2**)

As a result of the biological interest in ellipticine and its derivatives, many synthetic routes to pyrido[3,4-*b*]carbazoles have been developed.[5–8] However, several of these routes are lengthy, and therefore a shorter, simpler synthesis of ellipticine would have obvious advantages. We have developed a concise new synthesis of ellipticine, and we now report our results in detail.

Results and Discussion

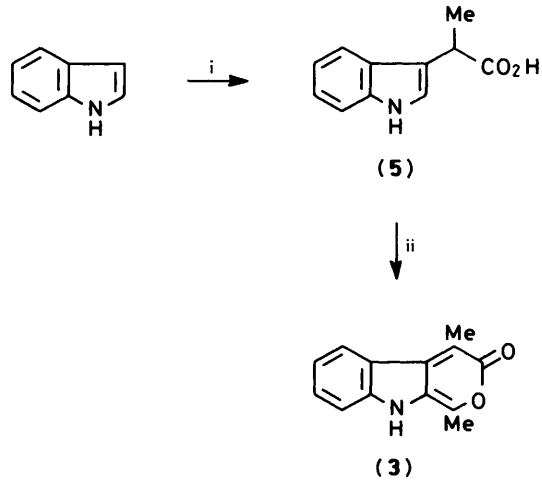
The synthesis is based on the strategy shown in Scheme 1, and involves a Diels-Alder reaction between the pyranoindolone (**3**) and 3,4-didehydropyridine (**4**). Pyrano[3,4-*b*]indol-3-ones are known to undergo Diels-Alder reaction with alkynes, including benzyne, to give carbazoles, after loss of carbon dioxide from the initial adduct.[9] Interestingly, a similar Diels-Alder approach to ellipticine based on the addition of a furo[3,4-*b*]indole to 3,4-didehydropyridine, has been reported by Gribble and co-workers,[10] although their paper appeared after the preliminary account[1] of this work was published.



(**1**) (**3**) + (**4**)

Scheme 1.

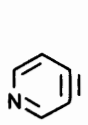
The 'diene,' 1,4-dimethylpyrano[3,4-*b*]indol-3-one (**3**) was prepared from indole in two steps (Scheme 2). Thus reaction of indole with lactic acid in the presence of potassium hydroxide in a sealed vessel at 250 °C following the literature procedure[11] gave 2-indol-3-ylpropionic acid (**5**) (32%) although we were never able to reproduce the literature yield of 80%. Treatment of an acetic anhydride solution of the acid (**5**) with boron trifluoride–diethyl ether gave the pyranoindolone (**3**) in 43% yield.



Scheme 2. *Reagents:* i, lactic acid, KOH, heat; ii, Ac_2O, BF_3–Et_2O

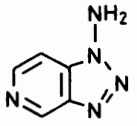
It was clear from earlier experiments on the reaction of pyranoindolones with benzyne that a thermal 'reagent-free' source of 3,4-didehydropyridine would be needed for the required Diels-Alder reaction, and although 3,4-didehydropyridine is the best described of the hetarynes,[12] the heterocyclic analogues of benzyne, the usual methods for its generation were considered inappropriate for the present problem. The most

extensively studied routes to 3,4-didehydropyridine (**4**) involve the base-mediated elimination of hydrogen halide from 3- and 4-halogeno pyridines.[13] Other methods for generation of the aryne include the reaction of 3-bromo-4-chloropyridine (**6**) with lithium amalgam,[14] the reaction of 3-chloro-4-iodopyridine (**7**) with butyl-lithium,[15] and the oxidation of 1-aminotriazolo[4,5-*c*]pyridine (**8**) with lead tetra-acetate.[16,17]

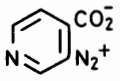


(**4**)

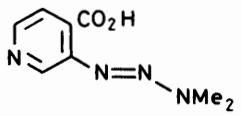
(**6**) X = Br, Y = Cl
(**7**) X = Cl, Y = I



(**8**)



(**9**)

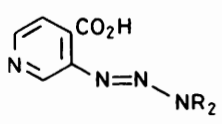


(**10a**)

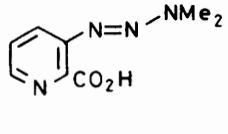
The only thermal precursor to 3,4-didehydropyridine (**4**) reported so far is pyridine-3-diazonium-4-carboxylate (**9**), prepared by diazotisation of 3-aminopyridine-4-carboxylic acid.[18] However, we found that the diazonium carboxylate (**9**) was difficult to prepare, somewhat unstable, and generally unsatisfactory for our purposes. In addition we also found that *in situ* generation of the aryne by aprotic diazotisation of 3-aminopyridine-4-carboxylic acid was unsatisfactory, despite the fact that this reaction is described in a footnote to a short communication,[19] although it has apparently not been reported in full subsequently. Therefore we had to develop a new precursor to 3,4-didehydropyridine, the dimethyltriazenyl pyridine carboxylic acid (**10a**).[20]

The choice of the dimethyltriazenyl moiety as a masked diazonium group was based on the fact that 2-(3,3-dimethyltriazen-1-yl)benzoic acid eliminates dimethylamine, nitrogen, and carbon dioxide on heating in chlorobenzene to generate benzyne.[21] This benzyne precursor is relatively little used, despite the fact that it is commercially available,* presumably because the preparation of benzenediazonium-2-carboxylate is so well described, and easy to carry out.

The pyridyltriazene (**10a**) was prepared by diazotisation of 3-aminopyridine-4-carboxylic acid, obtained from commercially available pyridine-3,4-dicarboxylic acid by the literature procedure,[22] followed by coupling with dimethylamine. The diisopropyl- (**10b**) and pentamethylene-triazene (**10c**) were similarly prepared by coupling the diazonium species to diisopropylamine and piperidine respectively. The hindered amine, 2,2,6,6-tetramethylpiperidine did not undergo the coupling reaction. The triazene (**11**) was similarly prepared by diazotisation of 3-aminopyridine-2-carboxylic acid[23] and coupling with dimethylamine. [CAUTION. The triazenes (**10**) and (**11**) should be regarded as potential carcinogens, and handled accordingly.]



(**10**)

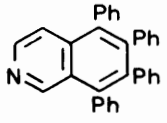


(**11**)

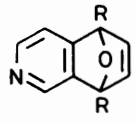
a, R = Me; **b**, R = Pr^i; **c**, RR = $(CH_2)_5$

* Fluka Cat. No. 39882; although not in 1986/87 catalogue.

The triazenes (**10**) are shelf-stable crystalline solids, but decompose on heating in acetonitrile. Thus heating a mixture of the triazene (**10a**) with an excess of tetraphenylcyclopentadienone (tetracyclone) gave 5,6,7,8-tetraphenylisoquinoline (**12**) in 25% yield. The isoquinoline (**12**) is presumably formed by generation of 3,4-didehydropyridine, which is intercepted by the tetracyclone in a Diels-Alder reaction, followed by loss of carbon monoxide from the Diels-Alder adduct. Since the decomposition of 2-(3,3-dimethyltriazen-1-yl)benzoic acid is known to be facilitated by the addition of acid,[21] the decomposition of the triazene (**10a**) was repeated in acetonitrile in the presence of tetracyclone and trifluoroacetic acid. This resulted in an improved (47%) yield of the isoquinoline (**12**). Under these acidic conditions, the triazenes (**10b**) and (**10c**) also gave the isoquinoline (**12**), in 52 and 45% yield respectively, on heating with tetracyclone. The dimethyltriazene (**10a**) was also decomposed photochemically in the presence of tetracyclone, but gave a reduced (18%) yield of the isoquinoline (**12**).



(**12**)



(**13**)

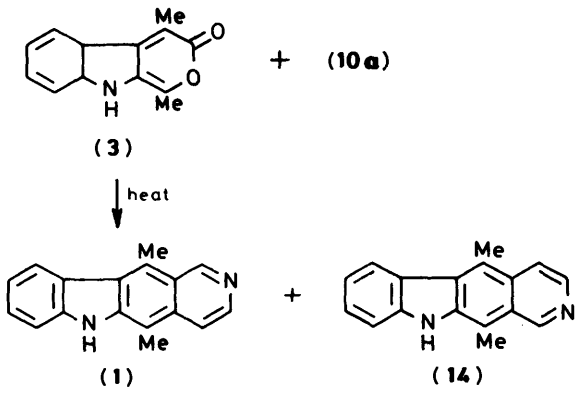
a, R = H
b, R = Me

The triazene (**10a**) was also decomposed in the presence of furan as diene, and gave the dihydroisoquinoline endoxide (**13a**) in 40% yield. Using 2,5-dimethylfuran as diene resulted in formation of the corresponding dimethyl endoxide (**13b**) [26% from triazene (**10a**): 22% from triazene (**10c**)]. No Diels-Alder adducts of 3,4-pyridine were isolated when the triazene (**10a**) was decomposed in the presence of anthracene, cyclopentadiene, methyl furan-2-carboxylate, and acyclic dienes such as 1-acetoxybuta-1,3-diene. This is in line with earlier findings,[12,13] and confirms the view that 3,4-didehydropyridine is less predictable in its dienophilic properties than benzyne.

Although 2,3-didehydropyridine has been generated in the presence of dienes from 2,3-dihalogenopyridines,[24] and from 3-aminotriazolo[4,5-*b*]pyridine,[16] the yields of Diels-Alder adducts are low, since the aryne undergoes facile nucleophilic attack. This is in accord with the predicted greater instability of the 2,3-isomer with respect to the 3,4-isomer.[25,26] 2,3-Didehydropyridine has apparently not been generated thermally in the absence of nucleophiles, and therefore the triazene (**11**) was investigated as a precursor to the aryne. However, decomposition of the triazene (**11**) under various conditions in the presence of a variety of traps, failed to give any products that could have arisen from 2,3-didehydropyridine.

With a convenient new thermal and 'reagent-free' source of 3,4-didehydropyridine now available, attention was turned to its use in the planned ellipticine synthesis (Scheme 1). The key Diels-Alder step was carried out by heating a mixture of the pyranoindolone (**3**) with an excess (2.5 equiv.) of the triazene (**10a**) in acetonitrile, and gave ellipticine (**1**) (20%) together with an equal amount of the isomeric pyridocarbazole (**14**) (isoellipticine) which was easily separated by chromatography.

The complete lack of regioselectivity in the Diels-Alder reaction of the diene (**3**) with 3,4-didehydropyridine was disappointing, since the direction of Diels-Alder additions to pyranoindolones as dienes is usually strongly influenced by the nitrogen line pair,[27] a result supported by Huckel calculations which show that C-1 has a slightly larger coefficient in the HOMO than C-4.[28] In addition, although 3,4-didehydropyridine is considerably less polarised than the 2,3-isomer,



calculations suggest that C-4 has a larger coefficient in the LUMO than C-3,[26] and therefore the Diels-Alder reaction with the diene (**3**) was expected to go largely with the required orientation. However, it is interesting to note that in Gribble's similar approach to ellipticine involving a Diels-Alder reaction of 3,4-didehydropyridine with a furoindole diene, a similar lack of regioselectivity was also observed.[10]

Nevertheless the synthesis of ellipticine described herein is short, being only three steps from indole, easy to carry out, and obviating the protection of the indole nitrogen. The use of the pyranoindolone (**3**) (2 steps from indole) as diene in the Diels-Alder step offers advantages of Gribble's furoindole diene (6 steps from 3-ethylindole or 4 steps from indole-3-carbaldehyde), and the new 3,4-didehydropyridine precursor, the triazene (**10a**), may have wider application.

Experimental

For general points see ref. 29.

Preparation of Triazenes (**CAUTION:** *potential carcinogens*). 3-(3,3-*Dimethyltriazen*-1-*yl*)*pyridine*-4-*carboxylic Acid* (**10a**).—3-Aminopyridine-4-carboxylic acid[22] (1.36 g, 9.85 mmol) was suspended in ethanol (20 ml), and concentrated hydrochloric acid (2.5 ml) was added. The mixture was cooled in ice and treated dropwise with an ice-cold solution of sodium nitrite (1.77 g, 25 mmol) in water (25 ml). After the addition, the mixture was stirred in ice for a further 20 min. The cold diazotisation solution was then added dropwise to an ice-cold mixture of sodium carbonate (3.44 g, 32 mmol) and dimethylamine (26% aqueous solution; 1.73 g, 10 mmol) in water (20 ml). The resulting mixture was stirred in ice for 30 min, acidified to pH 4—5 with concentrated hydrochloric acid, and extracted with chloroform (5 × 25 ml). The combined extracts were dried (Na_2SO_4) and evaporated to give the *title compound* (**10a**) (1.40 g, 73%) as a pale yellow solid, m.p. 134 °C (Found: C, 49.15; H, 5.1; N, 28.5. $C_8H_{10}N_4O_2$ requires C, 49.5; H, 5.2; N, 28.8%); $\nu_{max.}$(Nujol) 3 400—2 600 and 1 700 cm^{-1}; δ(250 MHz; $CDCl_3$) 3.40 (3 H, s), 3.78 (3 H, s), 7.95 (1 H, d), 8.48 (1 H, d), and 8.95 (1 H, s); *m/z* 194 (M^+), 150, 123, 94, and 78.

3-(3,3-*Di-isopropyltriazen*-1-*yl*)*pyridine*-4-*carboxylic Acid* (**10b**).—3-Aminopyridine-4-carboxylic acid (1.38 g, 10 mmol) was diazotised and coupled to di-isopropylamine (1.01 g, 10 mmol) using the above procedure to give the *title compound* (**10b**) (0.87 g, 35%), m.p. 132—134 °C (from ether) (Found: C, 57.5; H, 7.3; N, 22.2. $C_{12}H_{18}N_4O_2$ requires C, 57.6; H, 7.25; N, 22.4%); $\nu_{max.}$(Nujol) 3 400—2 600 and 1 705 cm^{-1}; δ(250 MHz; $CDCl_3$) 1.36 (6 H, d), 1.46 (6 H, d), 4.20 (1 H, m), 4.95 (1 H, m), 7.95 (1 H, d), 8.48 (1 H, d), and 9.01 (1 H, s); *m/z* 250 (M^+), 206, 150, 122, 100 (base), 94, and 86.

3-(3,3-*Pentamethylenetriazen*-1-*yl*)*pyridine*-4-*carboxylic Acid* (**10c**).—3-Aminopyridine-4-carboxylic acid (1.38 g, 10 mmol) was diazotised and coupled to piperidine (0.85 g, 10 mmol) using the above procedure to give the *title compound* (**10c**) (1.10 g, 47%), m.p. 109—111 °C (from ether) (Found: C, 56.4; H, 6.0; N, 24.1. $C_{11}H_{14}N_4O_2$ requires C, 56.4; H, 6.0; N, 23.9%); $\nu_{max.}$(Nujol) 3 080br and 1 730 cm^{-1}; δ(250 MHz; $CDCl_3$) 1.80—2.00 (6 H, m), 3.85 (2 H, t), 4.00 (2 H, t), 8.00 (1 H, d), 8.54 (1 H, d), and 9.04 (1 H, s); *m/z* 234 (M^+), 190, 150, 94, and 84 (base).

3-(3,3-*Dimethyltriazen*-1-*yl*)*pyridine*-2-*carboxylic Acid* (**11**).—3-Aminopyridine-2-carboxylic acid[23] (1.36 g, 9.85 mmol) was diazotised and coupled to dimethylamine (26%; 1.73 g, 10 mmol) using the above procedure to give the *title compound* (**11**) (0.49 g, 26%), m.p. 125—127 °C (from ether–chloroform) (Found: C, 49.6; H, 5.1; N, 28.9. $C_8H_{10}N_4O_2$ requires C, 49.5; H, 5.2; N, 28.8%); $\nu_{max.}$(Nujol) 3 360—2 650 and 1 730 cm^{-1}; δ(250 MHz; $CDCl_3$) 3.34 (3 H, s), 3.73 (3 H, s), 7.38 (1 H, dd), 8.02 (1 H, d), and 8.58 (1 H, d); *m/z* 194 (M^+), 150, 122, and 94.

Decomposition of Triazenes.—(a) *In the presence of tetracyclone. General Procedure.* The triazene (**10**) (0.5 mmol) and tetracyclone (2.5 mmol) were dissolved in dry acetonitrile (20 ml). Trifluoroacetic acid (1 drop) was added, and the mixture was heated under reflux for 6 h. The solvent was evaporated off, and the residue chromatographed to give (i) tetracyclone and (ii) 5,6,7,8-tetraphenylisoquinoline (**12**), m.p. 219—221 °C (lit.,[16] 220—222 °C); δ(250 MHz; $CDCl_3$) 6.85 (8 H, m), 7.25 (12 H, m), 7.45 (1 H, d), 8.45 (1 H, d), and 9.05 (1 H, s); *m/z* 433 (M^+), 356, and 105.

Using the above procedure, the dimethyltriazene (**10a**) (280 mg, 1.44 mmol) gave the isoquinoline (**12**) (293 mg, 47%). In the absence of the trifluoroacetic acid, the yield of isoquinoline (**12**) was 25%.

Using the above procedure, the di-isopropyltriazene (**10b**) (100 mg, 0.4 mmol) gave the isoquinoline (**12**) (90 mg, 52%).

Using the above procedure, the pentamethylenetriazene (**10c**) (250 mg, 1.07 mmol) gave the isoquinoline (**12**) (206 mg, 45%).

(b) *In the presence of tetracyclone under photochemical conditions.* The dimethyltriazene (**10a**) (200 mg, 1.03 mmol) and tetracyclone (1 000 mg, 2.60 mmol) were dissolved in acetonitrile (100 ml). The solution was placed in a pyrex photolysis vessel and irradiated at 300 nm for 96 h. The mixture was evaporated, and the residue chromatographed to give the isoquinoline (**12**) (80 mg, 18%).

(c) *In the presence of furan.* The dimethyltriazene (**10a**) (120 mg, 0.62 mmol) and freshly distilled furan (2.00 g, 29.4 mmol) were dissolved in dry acetonitrile (5 ml), and the mixture was heated at 130 °C for 4 h in a sealed vessel. Evaporation of the solvent and chromatography of the residue gave 5,8-dihydro-5,8-epoxyisoquinoline (**13a**) (36 mg, 40%), δ(90 MHz; $CDCl_3$) 5.90 (1 H, d), 6.00 (1 H, d), 7.10 (2 H, m), 7.30 (1 H, d), 8.30 (1 H, d), and 8.50 (1 H, s); *m/z* 145 (M^+), 119, 103, and 77; picrate, m.p. 177 °C (lit.,[17,18] 178 °C).

(d) *In the presence of* 2,5-*dimethylfuran.* The dimethyltriazene (**10a**) (100 mg, 0.52 mmol) and 2,5-dimethylfuran (500 mg, 5.2 mmol) were dissolved in dry acetonitrile (2 ml), and the mixture was heated under reflux for 14 h. Evaporation of the solvent, and chromatography of the residue gave 5,8-*dihydro*-5,8-*dimethyl*-5,8-*epoxyisoquinoline* (**13b**) (23 mg, 26%) as an oil, $\nu_{max.}$(film) 2 920, 1 600, 1 380, 1 300, 1 130, and 850 cm^{-1}; δ(90 MHz; $CDCl_3$) 1.95 (3 H, s), 2.02 (3 H, s), 6.82 (2 H, q), 7.15 (1 H, d), and 8.30 (2 H, m); *m/z* 173 (M^+), 160, 147, 131, and 77; *picrate* m.p. 159—160 °C (Found: C, 50.8; H, 3.5; N, 13.8. $C_{17}H_{14}N_4O_8$ requires C, 50.7; H, 3.5; N, 13.9%).

Using the above procedure, the pentamethylenetriazene (**10c**) (230 mg, 0.98 mmol) gave the adduct (**13b**) (37 mg, 22%).

1,4-*Dimethylpyrano*[3,4-b]*indol*-3-*one* (**3**).—This was prepared as previously described.[9]

Ellipticine (**1**).—A solution of the pyranoindolone (**3**) (76 mg, 0.36 mmol) and the triazene (**10a**) (180 mg, 0.93 mmol) in dry acetonitrile (15 ml) was heated under reflux for 36 h. The solvent was evaporated and the residue chromatographed on silica gel eluting with chloroform and slowly increasing to 5% methanol in chloroform to give (i) isoellipticine (**14**) (18 mg, 20%), m.p. 244—247 °C (lit.,[30] 243—250 °C), δ(250 MHz; $CDCl_3$) 2.92 (3 H, s), 3.18 (3 H, s), 7.30 (1 H, m), 7.54 (2 H, m), 8.05 (1 H, d, *J* 7 Hz), 8.30 (1 H, m), 8.39 (1 H, d, *J* 7 Hz) 8.49 (1 H, d, *J* 7 Hz), and 9.61 (1 H, s); NH not observed; *m/z* 246 (M^+, base) and 231, and (ii) ellipticine (**1**) (18 mg, 20%), m.p. 312—314 °C (lit.,[31] 311—315 °C); δ(250 MHz; $CDCl_3$) 2.77 (3 H, s), 3.29 (3 H, s), 7.35 (1 H, m), 7.52 (2 H, m), 7.86 (1 H, d, *J* 6 Hz), 8.27 (1 H, br), 8.38 (1 H, d, *J* 7 Hz), 8.49 (1 H, d, *J* 7 Hz), and 9.72 (1 H, s); *m/z* 246 (M^+, base), 245, and 231.

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References

1 Preliminary communication, C. May and C. J. Moody, *J. Chem. Soc., Chem. Commun.*, 1984, 926.
2 S. Goodwin, A. F. Smith, and E. C. Horning, *J. Am. Chem. Soc.*, 1959, **81**, 1903.
3 L. K. Dalton, S. Demerac, B. L. Elmes, J. W. Loder, J. M. Swan, and T. Teitei, *Aust. J. Chem.*, 1967, **20**, 2715.
4 N. Van-Bac, C. Moisand, A. Gouyette, G. Muzard, N. Dat-Xuong, J.-B. Le Pecq, and C. Paoletti, *Cancer Treat. Rep.* 1980, **64**, 879, and references therein.
5 M. Sainsbury, *Synthesis*, 1977, 437.
6 M. J. E. Hewlins, A. M. Oliveira-Campos, and P. V. R. Shannon, *Synthesis*, 1984, 289.
7 G. W. Gribble and M. G. Saulnier, *Heterocycles*, 1985, **23**, 1277.
8 V. K. Kansal and P. Potier, *Tetrahedron*, 1986, **42**, 2389.
9 C. J. Moody, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2505.
10 G. W. Gribble, M. G. Saulnier, M. P. Sibi, and J. A. Obaza-Nutaitis, *J. Org. Chem.*, 1984, **49**, 4518.
11 H. E. Johnson and D. G. Crosby, *J. Org. Chem.*, 1963, **28**, 1246.
12 For a review of hetarynes see M. G. Reinecke, *Tetrahedron*, 1982, **38**, 427.
13 H. C. van der Plas and F. Roeterdink, 'The Chemistry of Triple Bonded Groups, Part 1,' eds. S. Patai and Z. Rappoport, Wiley, New York, 1983, p. 421.
14 T. Kauffmann and F.-P. Boettcher, *Angew. Chem.*, 1961, **73**, 65.
15 G. W. Gribble and M. G. Saulnier, *Tetrahedron Lett.*, 1980, **21**, 4137.
16 G. W. J. Fleet and I. Fleming, *J. Chem. Soc. C*, 1969, 1758.
17 T. Sasaki, K. Kanematsu, and M. Uchide, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 858.
18 T. Kauffmann and F.-P. Boettcher, *Chem. Ber.*, 1962, **95**, 949.
19 L. Friedman and F. M. Logullo, *J. Am. Chem. Soc.*, 1963, **85**, 1549.
20 Preliminary communication, C. May and C. J. Moody, *Tetrahedron Lett.*, 1985, **26**, 2123.
21 J. Nakayama, O. Simamura, and M. Yoshida, *J. Chem. Soc., Chem. Commun.*, 1970, 1222.
22 J. D. Crum and C. H. Fuchsman, *J. Heterocycl. Chem.*, 1966, **3**, 252.
23 C. D. Hurd and V. G. Bethune, *J. Org. Chem.*, 1970, **35**, 1471.
24 R. J. Martens and H. J. den Hartog, *Tetrahedron Lett.*, 1962, 643; M. Mallet, G. Queguiner, and P. Pastour, *C.R. Seances Acad. Sci., Ser. C*, 1972, **274**, 719.
25 W. Adam, A. Grimison, and R. Hoffmann, *J. Am. Chem. Soc.*, 1969, **91**, 2590.
26 I. Fleming, 'Frontier Orbitals and Organic Chemical Reactions,' Wiley, Chichester, 1976, p. 73.
27 C. J. Moody and P. Shah, unpublished results.
28 H. S. Rzepa and P. Shah, unpublished result.
29 M. P. Johnson and C. J. Moody, *J. Chem. Soc., Perkin Trans. 1*, 1985, 71.
30 M. G. Saulnier and G. W. Gribble, *J. Org. Chem.*, 1983, **48**, 2690.
31 M. G. Saulnier and G. W. Gribble, *J. Org. Chem.*, 1982, **47**, 2812.

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