solution was concentrated and distilled in a Kugelrohr apparatus (100 °C pot temperature, 30 mm) to provide 0.342 g (50%) of 2-methylcyclohexanol. Analysis by VPC (10% TCEP, 6 ft × $^1/_8$ in., 110 °C) revealed no observable amounts of the cis isomer. The cis and trans isomers may also be distinguished by the NMR signal of the proton on the carbon adjacent to the oxygen. The cis isomer exhibits a multiplet at 3.7 ppm while the trans isomer exhibits a multiplet at 2.9 ppm. Again, none of the cis isomer could be detected.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Registry No. 1-Methylcyclohexene, 591-49-1; *trans*-2-methylcyclohexanol, 7443-52-9.

Synthesis of 3-Chloro-3-methyl-d_3-diazirine

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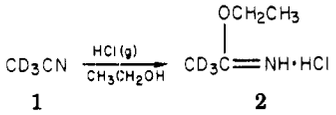
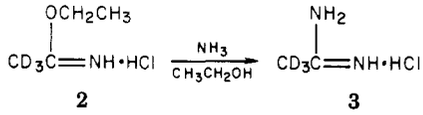
The synthesis of 3-halo-3-methyldiazirines by oxidation of acetamidine precursors has become the standard procedure since Graham's original report.[1] In the study of reactions of hydrogen atoms with 3-chloro-3-methyldiazirine it was crucial to an understanding of the mechanism to prepare the trideuterio compound.[2] This compound is known[3] but no synthetic procedure has been reported. We now report the procedure for the synthesis of the title compound. During preparation, care must be taken to prevent exchange of hydrogen for deuterium.

The deuterated methyl group is derived from acetonitrile-d_3 (1) which was converted to the acetimino ethyl ether (2) with hydrogen chloride in ethanol. Reaction of



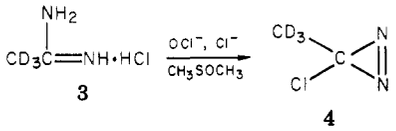
1 2

2 with anhydrous ammonia produced acetamidine hydrochloride (3). As this is hygroscopic it should be kept in



2 3

a desiccator to prevent exchange. 3 was then oxidized to 3-chloro-3-methyl-d_3-diazirine (4) with aqueous sodium hypochlorite. Complete deuteration of 3 was inferred from the proton NMR spectrum and complete deuteration of 4 was found in its mass spectrum.



3 4

Experimental Section

Acetamidine-d_3 Hydrochloride. Anhydrous hydrogen chloride gas was bubbled for 1.5 h at 0 °C into a solution of acetonitrile-d_3 (99 atom % D, 4.4 g, 0.10 mol) in dry ethanol (6 mL, 0.1 mol) in a three-neck flask equipped with drying tubes. The flask was then stoppered and stored for 4 days at 0 °C. Dry diethyl ether (60 mL) was added and the mixture became milky. The solvents were distilled. Acetimine ethyl ether hydrochloride 2 was obtained as a white solid and dried over silica gel in a vacuum desiccator (yield 10.7 g, 85%). Anhydrous ammonia was bubbled for 1 h through dry ethanol (30 mL) at 0 °C in a three-neck flask equipped with a dropping funnel and drying tube. A suspension of 2 (10.7 g) in dry ethanol (50 mL) was added slowly to the stirred ammonia/ethanol solution. The reaction mixture was stirred for 1 h at 0 °C. The precipitated ammonia chloride was filtered out and the solvent evaporated to give acetamidine-d_3 hydrochloride as a white crystalline solid: yield 6.5 g (67%); mp 142–142.5 °C (hygroscopic); IR, (Nujol mull) ν 2380, 2265, 1667, 1441, 1370, 1145, 1081, 1041 cm^{-1}.

3-Chloro-3-methyl-d_3-diazirine (4). Acetamidine-d_3 hydrochloride (3, 2.0 g) was dissolved in 120 mL of dimethyl sulfoxide containing 10 g of lithium chloride in a 500-mL three-neck flask. Aqueous sodium hypochlorite (commercial Javex, 0.78 M, 150 mL) was combined with 150 mL of water containing 50 g of sodium chloride and the resulting solution was added rapidly to the stirred solution of 3. The temperature rose to 55 °C and the gaseous product escaping from solution was dried by passage over 20 g of potassium hydroxide in a U-tube. 3-Chloro-3-methyl-d_3-diazirine (4) was trapped as a liquid at −78 °C. A liquid nitrogen trap was not used because of the hazard of explosion,[4] even though a lower yield results. The liquid diazirine was degassed at −78 °C and expanded into a bulb to give colorless 3-chloro-3-methyl-d_3-diazirine gas (4): yield (P = 120 mm, t = 18 °C, v = 390 cm^3) 2.6 mmol (12%); mass spectrum (70 eV), m/e 65, 58, 30, 28 (100%); mass spectrum (20 eV), m/e 65 (100%), 58, 30; IR (P = 80 mm, t = 22 °C, l = 10 cm) 2975, 1602, 980 cm^{-1}; UV (P = 10 mm, t = 19 °C, l = 9.6 cm) 353 nm (ϵ 130), 348 (40), 344 (69), 342 (54), 366 (90), 333 (41), 328 (42), 325 (34), 320 (34).

Acknowledgment. M.T.H.L. and W.E.J. thank the Natural Sciences and Engineering Research Council of Canada for financial support.

(1) W. H. Graham, *J. Am. Chem. Soc.*, 87, 4396 (1965).
(2) C. D. Burkholder, W. E. Jones, J. S. Wasson, and M. T. H. Liu, *J. Am. Chem. Soc.*, 102, 2847 (1980).
(3) L. C. Robertson and J. A. Merritt, *J. Mol. Spectrosc.*, 42, 403 (1972).
(4) M. T. H. Liu, *Chem. Eng. News*, Sept 9, 3 (1974).

Pyrrole Studies. 22.[1a] [4π + 2π] Cycloaddition Reactions with Vinylpyrroles

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The majority of procedures available for the synthesis of indoles involve ring closure to form the five-membered ring,[2] and relatively few methods start from the pyrrole ring system.[3] Although pyrroles generally react with

(1) (a) Presented in part at the 4th Lakeland Heterocyclic Chemistry Symposium, Grasmere, England, May 1979. Part 21: R. S. Budhram, R. A. Jones, R. O. Jones, and B. C. Uff, *Org. Magn. Reson.* 13, 89 (1980). (b) On leave from the Department of Pharmacy, University of Valencia, Spain.
(2) R. J. Sundberg, "The Chemistry of Indoles", Academic Press, New York, 1970.

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Scheme I

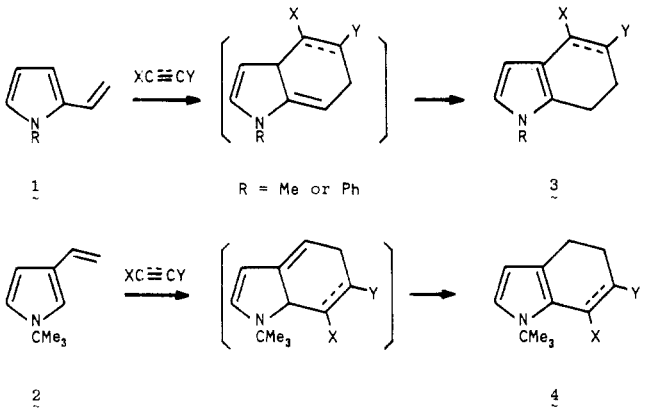


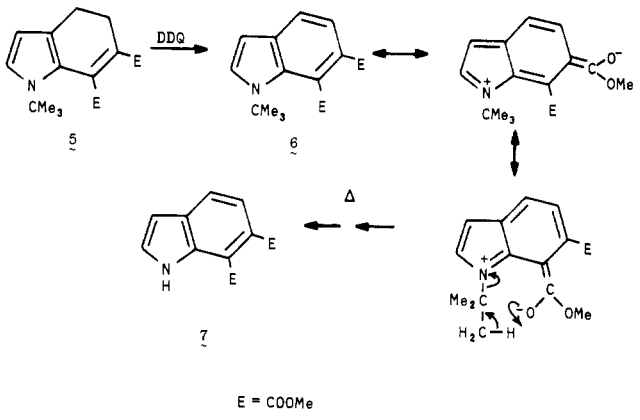
Table I. Reactivity of 1-Methyl-2-vinylpyrrole with Electron-Deficient Dienophiles in $CDCl_3$ at 20 °C

dienophile	10^5k_2, L mol^{-1} s^{-1}
maleic anhydride	>15 000
dimethyl acetylenedicarboxylate[a]	3.23
maleonitrile[b]	2.22
fumaronitrile[c]	0.87
dimethyl maleate	~0.30
methyl acrylate	~0.32
acrylonitrile	~0.31

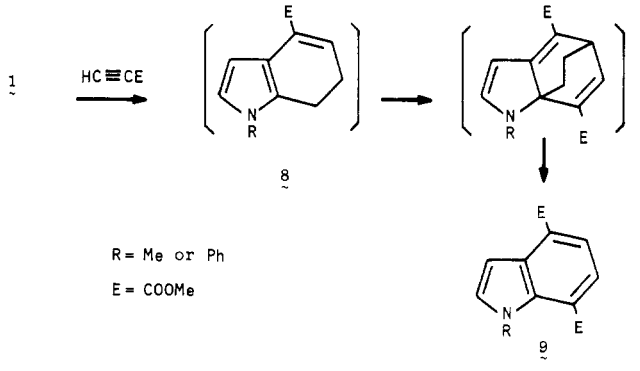
[a] 10^5k at 30 and 40 °C is 6.91 and 14.73 L mol^{-1} s^{-1}; $\Delta H^{\ddagger}_{20\ °C}$ = 55.8 kJ; $\Delta S^{\ddagger}_{20\ °C}$ = −46 J deg^{-1} mol^{-1}. [b] 10^5k at 30 and 40 °C is 3.80 and 8.92 L mol^{-1} s^{-1}; $\Delta H^{\ddagger}_{20\ °C}$ = 50.8 kJ; $\Delta S^{\ddagger}_{20\ °C}$ = −66 J deg^{-1} mol^{-1}. [c] 10^5k at 30 and 40 °C is 2.20 and 3.83 L mol^{-1} s^{-1}; $\Delta H^{\ddagger}_{20\ °C}$ = 54.6 kJ; $\Delta S^{\ddagger}_{20\ °C}$ = −61 J deg^{-1} mol^{-1}.

dienophiles to give Michael adducts or [4π + 2π] cycloadducts across the 2,5-positions of the heterocyclic ring,[4] simple Hückel MO calculations[5] suggest that the [4π + 2π] cycloaddition reaction with vinylpyrroles should yield dihydro- or tetrahydroindoles (cf. the analogous reactions with vinylfurans[6] and vinylthiophenes[7] and the conversion of vinylindoles into carbazole derivatives[8]). This obvious route to indoles has not been studied previously in any detail due to the supposed inaccessibility and/or instability of the requisite vinylpyrroles,[9] although the sequential reaction of α-unsubstituted pyrroles with two molecules of π-electron-deficient alkynes to give indoles via the initial in situ formation of a vinylpyrrole has been reported.[10,11] Vinylpyrroles can be prepared, however, in good yield via a Wittig reaction[12] from formylpyrroles. In this paper we report the facile cycloaddition reactions of 1-substituted-2- and -3-vinylpyrroles **1** and **2** (Scheme I) with electron-deficient dienophiles to produce dihydro- and tetrahydroindoles **3** and **4** in a two-step process, the second step involving a [1,3] sigmatropic hydrogen migration leading to aromatization of the five-membered ring.

Scheme II



Scheme III



The reaction of maleic anhydride with both the 2- and the 3-vinylpyrroles in chloroform (or benzene) was extremely rapid at room temperature, although reactions between the more reactive 1-methyl-2-vinylpyrrole and dimethyl maleate, *cis*- and *trans*-1,2-dicyanoethenes, acrylonitrile, or ethyl acrylate occurred only slowly even at high temperatures. The rate constants for the cycloaddition reactions of 1-methyl-2-vinylpyrrole are given in Table I.[13] In each case the expected tetrahydroindoles were obtained in good yield (54–81%), but all attempts to dehydrogenate the products with quinones or Pd/C failed to give the indoles. The isolation of the isomeric 4,5-dicyanotetrahydroindoles[14] from the reactions of the two 1,2-dicyanoethenes with 1-methyl-2-vinylpyrrole indicates that the cycloadditions are concerted and the regioselectivity of the reactions with the monosubstituted alkenes to give exclusively the 4-substituted tetrahydroindoles[14] is consistent with FMO calculations for the $HOMO_{vinylpyrrole}$–$LUMO_{alkene}$ interactions.[5]

Under milder conditions both the 2- and the 3-vinylpyrroles reacted with dimethyl acetylenedicarboxylate to give, in moderate yields (55–75%), dihydroindoles, which were readily converted into the corresponding indole dicarboxylic esters with 2,3-dichloro-5,6-dicyanoquinone (DDQ). However, in contrast to the stabilities of the indole-4,5-dicarboxylic esters, obtained from the 1-substituted 2-vinylpyrroles, dimethyl 1-*tert*-butylindole-6,7-dicarboxylate (**6**), produced from 1-*tert*-butyl-3-vinylpyrrole, was thermally unstable, and distillation led to the complete

(3) See e.g.: R. E. Ireland, *Chem. Ind. (London)*, 979 (1958); W. Herz and J. Brasch, *J. Org. Chem.*, **23**, 1513 (1958); R. M. Acheson and J. M. Vernon, *J. Chem. Soc.*, 1148 (1962); L. K. Dalton and T. Teitei, *Aust. J. Chem.*, **21**, 2053 (1968); B. Rosen and W. P. Weber, *Tetrahedron Lett.*, 151 (1977).

(4) R. A. Jones and G. P. Bean, "The Chemistry of Pyrroles", Academic Press, London, 1977.

(5) M. T. P. Marriott, Ph.D. Thesis, University of East Anglia, 1979.

(6) R. Paul, *Bull. Soc. Chim. Fr.*, 163 (1943).

(7) J. F. Scully and E. V. Brown, *J. Am. Chem. Soc.*, **75**, 6329 (1953).

(8) See, e.g., W. E. Noland and S. R. Wann, *J. Org. Chem.*, **44**, 4402 (1979), and references cited therein.

(9) R. S. Hosmane, S. P. Hiremath, and S. W. Schneller, *J. Chem. Soc., Perkin Trans. 1*, 2450 (1973).

(10) R. M. Acheson and J. Woolard, *J. Chem. Soc., Perkin Trans. 1*, 446 (1975).

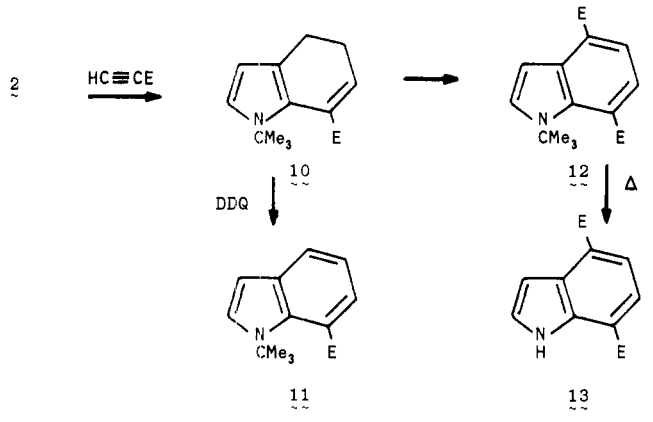
(11) Chang Kiu Lee, Ph.D. Thesis, University of Minnesota, Minneapolis, MN, 1976; *Diss. Abstr. Int. B*, **38**, 1210 (1977); *Chem. Abstr.*, **88**, 120912 (1978).

(12) R. A. Jones and J. A. Lindner, *Aust. J. Chem.*, **18**, 875 (1965).

(13) The reactions of 1-*tert*-butyl-3-vinylpyrrole with the less reactive alkenes were not studied in detail.

(14) The stereo- and regioselectivity of the reactions were confirmed by full spectroscopic analysis of the products.[5]

Scheme IV



extrusion of the *tert*-butyl group to give dimethyl indole-6,7-dicarboxylate (**7**, Scheme II). The ease with which the de-*tert*-butylation occurs appears to result both from steric and electronic factors. In the indole diester **6**, but not in the corresponding dihydroindole **5**, both ester groups can conjugate with the pyrrole ring, thereby aiding the loss of the *tert*-butyl group as 2-methylpropene. This effect is further enhanced by the butressing effect of the two ester groups, which aids the removal of the proton from the *tert*-butyl group by the 7-carboxyl substituent.[15]

The reaction of methyl propiolate with 1-methyl- and 1-phenyl-2-vinylpyrrole leads to the direct formation of the 1-substituted indole-4,7-dicarboxylic esters **9**, via a further $[4\pi + 2\pi]$ cycloaddition to the initially formed 6,7-dihydroindole-4-carboxylic ester **8** by a second molecule of methyl propiolate followed by a retro-Diels–Alder extrusion of ethene (Scheme III). Predictably, maximum yields were obtained with a 2:1 ratio of propiolic ester to vinylpyrrole. It was not possible to isolate either of the intermediate compounds, and, when the reaction was monitored by NMR spectroscopy, signals attributable to the dihydroindole-4-carboxylic ester **8** were of very low intensity and were not well resolved, suggesting that the second and third steps of the reaction sequence were either comparable in rate or faster than the initial cycloaddition step. In contrast, the intermediate 4,5-dihydroindole-7-carboxylic ester **10** could be obtained from the corresponding reaction between methyl propiolate and 1-*tert*-butyl-3-vinylpyrrole. Dehydrogenation of the dihydroindole with DDQ gave methyl 1-*tert*-butylindole-7-carboxylate (**11**, E = COOMe; Scheme IV), which was thermally unstable with the loss of the *tert*-butyl group. Further reaction of **10** with a second molecule of methyl propiolate gave a mixture of dimethyl indole-4,7-dicarboxylate (**13**, E = COOMe) and its 1-*tert*-butyl derivative **12**. The relative thermal stabilities of the three 1-*tert*-butylindole esters **6**, **11**, and **12** confirm that both the mesomeric interaction of the ester groups with the pyrrole ring and steric factors contribute to the facile extrusion of the *tert*-butyl group.

The kinetic measurements, presented in Table I, show that whereas the rate of reaction of 1-methyl-2-vinylpyrrole with maleic anhydride is comparable with that observed[16] for the reaction of cyclopentadiene with maleic anhydride (9340×10^{-5} L mol^{-1} s^{-1}), the vinylpyrrole reacts less readily with other dienophiles. The logarithm of the second-order rate constants for the cycloadditions correlate only approximately with the reciprocal of $E_{HOMO(diene)} - E_{LUMO(dienophile)}$,[17] and the spread of the relative reaction rates is such that the correlation is of little value. It is significant, however, that maleonitrile is approximately 3 times more reactive than fumaronitrile. This contrasts with the almost identical rate constants for the corresponding reaction of cyclopentadiene with the two dinitriles[16] and suggests that there is a favorable secondary orbital interaction between the HOMO of the vinylpyrrole and the LUMO of the *cis*-dinitrile. This effect, which is supported by FMO calculations of the eigenvectors,[5] is reflected in the differences in the activation energies for the two reactions and would also account for the favorable reaction between the vinylpyrroles and maleic anhydride.

2-Vinylpyrrole failed to give $[4\pi + 2\pi]$ cycloadducts with all of the dienophiles used in this study. Spectroscopic analysis of the product mixtures indicated the presence of polymeric compounds resulting from Michael addition reactions.[4] In accord with their lower reactivity, as forecast from FMO calculations of their HOMO energy levels,[5] ethyl *trans*-2-(1-methyl-2-pyrrolyl)acrylate, 1-(1-methyl-2-pyrrolyl)-*trans*-but-1-en-3-one, and 1-methyl-2-styrylpyrrole gave, after prolonged reaction at 80 °C, readily oxidized and thermally unstable products with maleic anhydride and reacted extremely slowly and incompletely with other dienophiles.

Experimental Section

NMR spectra were measured for ca. 1.0 M solutions in $CDCl_3$ at 60 MHz on a Perkin-Elmer R12 instrument and at 100 MHz on a Varian HA-100 spectrometer. Chemical shifts are reported downfield from the internal standard Me_4Si. Infrared spectra were measured as liquid films or Nujol mulls on a Perkin-Elmer 257 spectrometer.[18]

General Synthesis of Vinylpyrroles. Method A. Methyltriphenylphosphonium bromide (40.2 g, 0.67 mol), which had previously been dried over P_2O_5 at 100 °C, was stirred with sodium ethoxide (from 3.65 g of Na) in dry ether (200 mL) for 15 min at 20 °C under nitrogen. The appropriate formylpyrrole (0.61 mol) in dry ether (50 mL) was added dropwise, and the mixture was stirred for 30 min at 20 °C and then heated under reflux for 90 min. The reaction mixture was allowed to stand at 20 °C for 18 h, and the ether was removed under pressure and replaced with dry tetrahydrofuran (200 mL). The solution was refluxed for 2 h, after a further 18 h at 20 °C, the solvent was removed under vacuum, and water (50 mL) was added to the residue. The crude vinylpyrrole was extracted from the aqueous mixture with ether (2×40 mL), and the extracts were washed successively with aqueous sodium metabisulfite (30%, 4×100 mL), aqueous sodium carbonate (20%, 3×100 mL), and water (40 mL). The dried ($MgSO_4$) ethereal extracts were evaporated, and any residual triphenylphosphine oxide was removed by filtration and washed with ether (5–10 mL). Distillation under nitrogen gave the vinylpyrrole.

Method B. Dry methyltriphenylphosphonium bromide (6.3 g, 0.016 mol) was added to sodium hydride (0.45 g) in dry tetrahydrofuran (100 mL) under nitrogen, and the mixture was stirred at 20 °C for 2 h. The appropriate formylpyrrole (0.018 mol) in dry tetrahydrofuran (25 mL) was added to the yellow solution and the mixture stirred for 2 h under reflux. Removal of the solvent gave the crude vinylpyrrole, which was purified by elution from a neutral alumina column with petroleum ether (bp 40–60 °C).

1-Methyl-2-vinylpyrrole (1a): method A, 66%; method B, 53%; bp 64 °C (14 mm) [lit.[12] bp 62–64 °C (16 mm)]; IR 1625

(15) A somewhat similarly assisted N-demethylation of 9-methylcarbazole-1,2,3,4-tetracarboxylic acid by the "ortho" carboxylate group has been reported [W. E. Noland, W. C. Kuryla, and R. F. Lange, *J. Am. Chem. Soc.*, **81**, 6010 (1959)].

(16) B. Blankenburg, H. Fielder, M. Hampel, H. G. Hauthal, G. Just, K. Kahlert, J. Kern, K.-H. Muller, W. Pritzkow, Y. Reinhold, M. Rollig, E. Sauer, D. Schmurpfeil, and G. Zimmerman, *J. Prakt. Chem.*, **316**, 804 (1974).

(17) K.-L. Mok and M. J. Nye, *J. Chem. Soc., Perkin Trans. 1*, 1810 (1975).

(18) Additional details of the spectroscopic data may be obtained from the authors.

cm^{-1} (ν C=C); NMR δ 3.55 (s, 3), 4.50 (dd, 1), 5.42 (dd, 1), 6.05 (m, 1), 6.31 (m, 1), 6.49 (m, 1), 6.55 (dd, 1).

1-Phenyl-2-vinylpyrrole (1b):[19] method A, 92%; method B, 80%; bp 85–86 °C (15 mm); IR 1625 cm^{-1} (ν C=C); NMR δ 4.88 (dd, 1), 5.37 (dd, 1), 6.16 (t, 1), 6.40 (dd, 1), 6.46 (m, 1), 6.68 (t, 1), 7.22 (m, 5).

Anal. Calcd for $C_{12}H_{11}N$: C, 85.2; H, 6.55; N, 8.3. Found: C, 84.6; H, 6.5; N, 8.2.

1-*tert*-Butyl-3-vinylpyrrole (2): method A, 71%; method B, 90%; bp 102–104 °C (14 mm); IR 1635 cm^{-1} (ν C=C); NMR δ 1.46 (s, 9), 4.80 (dd, 1), 5.24 (dd, 1), 6.07 (m, 1), 6.15 (m, 1), 6.45 (dd, 1), 6.60 (m, 1).

Anal. Calcd for $C_{10}H_{15}N$: C, 80.5; H, 10.1; N, 9.4. Found: C, 80.6; H, 10.1; N, 9.3.

Reactions of the 2-Vinylpyrroles with Maleic Anhydride. The appropriate vinylpyrrole (0.003 mol) in chloroform (or benzene, 5 mL) was added dropwise to maleic anhydride (0.294 g, 0.003 mol) in chloroform (or benzene, 5 mL) at ca. 5 °C. After 10 min the solvent was removed under vacuum and the residual oil distilled to give the 4,5,6,7-tetrahydroindole-*cis*-4,5-dicarboxylic anhydride.

For the **1-methyl derivative:** yield 54%; bp 185 °C (2×10^{-3} mm); IR 1860, 1775 cm^{-1} (ν C=O); NMR δ 1.60–2.80 (m, 4), 3.50 (m, 1), 3.45 (s, 3), 4.10 (d, 1), 6.20 (d, 1), 6.60 (d, 1).

Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.4; H, 5.4; N, 6.8. Found: C, 64.6; H, 5.5; N, 6.7.

For the **1-phenyl derivative:** yield 81%; mp 188 °C ($CHCl_3$–petroleum ether); IR 1850, 1780 cm^{-1} (ν C=O); NMR δ 1.60–2.80 (m, 4), 3.50 (m, 1), 4.20 (d, 1), 6.40 (d, 1), 6.80 (d, 1), 7.1–7.5 (m, 5).

Anal. Calcd for $C_{16}H_{13}NO_3$: C, 71.9; H, 4.9; N, 5.2. Found: C, 71.6; H, 5.3; N, 4.9.

1-*tert*-Butyl-4,5,6,7-tetrahydroindole-*cis*-6,7-dicarboxylic Anhydride. Maleic anhydride (0.96 g, 0.01 mol) was added to 1-*tert*-butyl-3-vinylpyrrole (1.5 g, 0.01 mol) in chloroform (5 mL), and the solution was shaken for 5 min and cooled to 20 °C, and petroleum ether (bp 40–60 °C) was added to give the tetrahydroindole (75%) as white needles ($CHCl_3$–petroleum ether): mp 128–129 °C; IR 1840, 1760 cm^{-1} (ν C=O); NMR δ 1.67 (s, 9), 1.1–2.7 (m, 4), 3.45 (m, 1), 4.80 (d, 1), 5.95 (d, 1), 6.90 (d, 1).

Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.0; H, 6.9; N, 5.7. Found: C, 67.9; H, 6.7; N, 5.6.

Dimethyl 1-Methyl-4,5,6,7-tetrahydroindole-*cis*-4,5-dicarboxylate. 1-Methyl-2-vinylpyrrole (0.43 g, 0.004 mol) and dimethyl maleate (2.0 g, 0.014 mol) were heated at 140 °C for 4 days. Unchanged starting material (0.2 g) was removed at 50 °C under reduced pressure (0.01 mm), and the residual oil was distilled to give the tetrahydroindole diester: 0.38 g (70.5%); bp 138–142 °C (0.01 mm); IR 1715 cm^{-1} (ν C=O); NMR δ 2.3–2.8 (m, 4), 3.42 (s, 3), 3.62 (s, 3), 3.5–4.0 (m, 2), 6.05 (d, 1), 6.46 (d, 1).

Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.1; H, 6.8; N, 5.6. Found: C, 61.8; H, 6.5; N, 5.6.

***cis*- and *trans*-4,5-Dicyano-1-methyl-4,5,6,7-tetrahydroindole.** 1-Methyl-2-vinylpyrrole (0.054 g, 0.0005 mol) and maleonitrile[21] (0.039 g, 0.0005 mol) in chloroform (0.5 mL) were kept at 20 °C for 2 days. The solution was cooled to 10 °C to give the *cis*-4,5-dicyanotetrahydroindole: 0.084 g (91%); mp 113–114 °C; IR 2250 cm^{-1} (ν C≡N); NMR δ 2.28 (m, 2), 2.71 (m, 2), 3.20 (m, $J_{4,5}$ = 5.0 Hz, $J_{5,6}$ = 3.75 Hz, $J_{5,6'}$ = 7.5 Hz, 1), 3.40 (s, 3), 4.10 (d, $J_{4,5}$ = 5.0 Hz, 1), 6.00 (d, 1), 6.48 (d, 1).

Anal. Calcd for $C_{11}H_{13}N_3$: C, 71.3; H, 6.0; N, 22.7. Found: C, 71.2; H, 6.0; N, 22.5.

The trans isomer (87%, mp 121–122 °C) was obtained by an analogous procedure from fumaronitrile: IR 2240 cm^{-1} (ν C≡N); NMR δ 2.25 (m, 2), 2.68 (m, 2), 3.16 (m, $J_{4,5}$ = 6.25 Hz, $J_{5,6}$ = 3.5 Hz, $J_{5,6'}$ = 7.25 Hz, 1), 3.43 (s, 3), 4.20 (d, $J_{4,5}$ = 6.25 Hz), 6.00 (d, 1), 6.50 (d, 1).

Anal. Found: C, 70.9; H, 6.0; N, 22.3.

Methyl 1-Methyl-4,5,6,7-tetrahydroindole-4-carboxylate. 1-Methyl-2-vinylpyrrole (0.43 g, 0.004 mol) and methyl acrylate (0.7 g, 0.008 mol) were heated under reflux for 17 h. Excess methyl acrylate was removed under reduced pressure and the residue distilled to give the tetrahydroindole-4-carboxylic ester: 0.61 g (86%); bp 96–98 °C (0.05 mm); IR 1725 cm^{-1} (ν C=O); NMR δ 1.98 (m, 4), 2.49 (m, 2), 3.42 (s, 3), 3.60 (m, 1), 3.66 (s, 3), 5.98 (d, 1), 6.45 (d, 1).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.4; H, 7.8; N, 7.3. Found: C, 68.2; H, 8.3; N, 7.6.

4-Cyano-1-methyl-4,5,6,7-tetrahydroindole. 1-Methyl-2-vinylpyrrole (0.43 g, 0.004 mol) and acrylonitrile (0.6 g, 0.01 mol) were heated under reflux for 8 h. The excess acrylonitrile was removed under reduced pressure and the residual oil distilled to give the 4-cyanotetrahydroindole: 0.39 g (61%); bp 120 °C (0.4 mm); mp 62 °C; IR 2230 cm^{-1} (ν C≡N); NMR δ 1.98 (m, 4), 2.55 (m, 2), 3.42 (s, 3), 3.75 (t, 1), 6.04 (d, 1), 6.48 (d, 1).

Anal. Calcd for $C_{13}H_{12}N_2$: C, 75.0; H, 7.5; N, 17.5. Found: C, 74.1; H, 7.6; N, 17.0.

Reactions of Vinylpyrroles with Dimethyl Acetylenedicarboxylate. The appropriate vinylpyrrole (0.0068 mol), dimethyl acetylenedicarboxylate (0.96 g, 0.0068 mol), and hydroquinone (0.01 g) in chloroform (5 mL) were heated under reflux for 3 h. The volatile material was removed, and the dihydroindole diester was distilled or recrystallized.

Dimethyl 1-methyl-6,7-dihydroindole-4,5-dicarboxylate: yield 67%; bp 132 °C (5×10^{-5} mm); IR 1740, 1720 cm^{-1} (ν C=O); NMR δ 1.0–1.8 (m, 1), 2.70 (s, 3), 3.50 (s, 3), 3.70 (s, 3), 3.80 (s, 3), 6.00 (d, 1), 6.50 (d, 1).[22]

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.6; H, 6.1; N, 5.6. Found: C, 62.4; H, 6.2; N, 5.5.

Dimethyl 1-phenyl-6,7-dihydroindole-4,5-dicarboxylate: yield 75%; mp 115 °C (benzene); IR 1740, 1715 cm^{-1} (ν C=O); NMR δ 1.0–1.8 (m, 1), 2.70 (s, 3), 3.70 (s, 3), 3.85 (s, 3), 6.20 (d, 1), 6.75 (d, 1), 7.30 (m, 5).[22]

Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.4; H, 5.5; N, 4.5. Found: C, 69.5; H, 5.4; N, 4.3.

Dimethyl 1-*tert*-butyl-4,5-dihydroindole-6,7-dicarboxylate: yield 55%; bp 160–165 °C (5×10^{-3} mm); IR 1745, 1715 cm^{-1} (ν C=O); NMR δ 0.8–1.8 (m, 1), 1.57 (s, 9), 2.53 (s, 3), 3.76 (s, 3), 3.86 (s, 3), 5.98 (d, 1), 6.93 (d, 1).[22]

Anal. Calcd for $C_{16}H_{21}NO_4$: C, 66.0; H, 7.3; N, 4.8. Found: C, 65.6; H, 7.2; N, 5.1.

Aromatization of the Dihydroindoles. DDQ (1.25 g, 0.0055 mol) in dry benzene (10 mL) was added to the dihydroindole (0.005 mol) in dry benzene (5 mL) and the solution refluxed for 30 min. The dihydroquinone was removed from the cooled solution and the filtrate evaporated to give the indole.

Dimethyl 1-methylindole-4,5-dicarboxylate: yield 25%; bp 155–160 °C (5×10^{-3} mm); IR 1745, 1715 cm^{-1} (ν C=O); NMR δ 3.69 (s, 3), 3.87 (s, 3), 3.95 (s, 3), 6.57 (d, 1), 7.09 (d, 1), 7.29 (d, 1), 7.70 (d, 1).

Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.3; N, 5.7. Found: C, 62.5; H, 5.4; N, 5.7.

Dimethyl 1-phenylindole-4,5-dicarboxylate: yield 66%; mp 103 °C (purified by elution from a neutral alumina column with diethyl ether); IR 1730 cm^{-1} (ν C=O); NMR δ 3.87 (s, 3), 3.96 (s, 3), 6.75 (d, 1), 7.34 (d, 1), 7.4–7.5 (m, 6), 7.68 (d, 1).

Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.9; H, 4.9; N, 4.5. Found: C, 69.7; H, 5.1; N, 4.4.

Dimethyl 1-*tert*-Butylindole-6,7-dicarboxylate. Chromatographic purification of the crude product, obtained by dehydrogenation of the 4,5-dihydroindole with DDQ, by elution from silica with petroleum ether (bp 40–60 °C)–diethyl ether (2:1) gave dimethyl 1-*tert*-butylindole-6,7-dicarboxylate: yield 83%; mp 58–60 °C dec; IR 1740, 1720 cm^{-1} (ν C=O); NMR δ 1.63 (s, 9), 3.78 (s, 6), 6.38 (d, 1), 7.47 (d, 1), 7.53 (d, 1), 7.67 (d, 1).

(19) 2-Formyl-1-phenylpyrrole had a melting point of 34–34.5 °C [lit.[20] bp 106–109 °C (0.2 mm)]. Anal. Calcd for $C_{11}H_9NO$: C, 77.2; H, 5.3; N, 8.2. Found: C, 77.3; H, 5.3; N, 8.2.

(20) C. F. Candy, R. A. Jones, and P. H. Wright, *J. Chem. Soc. C*, 2563 (1970).

(21) G. E. Ficken, R. P. Linstead, E. Stephen, and M. Whalley, *J. Chem. Soc.*, 3879 (1958).

(22) The NMR signals for the CH_2CH_2 group of the dihydroindoles are part of a characteristic AA'BB'X pattern similar to that observed for 1,2-dihydronaphthalenes.[23] The 1:3 ratio for the two sets of signals would appear to be fortuitous.

(23) M. J. Cook and A. R. Katritzky, F. C. Pennington, and B. M. Semple, *J. Chem. Soc. B*, 523 (1969); M. J. Cook and N. L. Dassanayaka, *J. Chem. Soc., Perkin Trans. 2*, 1901 (1972).

Anal. Calcd for $C_{16}H_{10}NO_4$: C, 66.4; H, 6.6; N, 4.8. Found: C, 66.5; H, 6.7; N, 4.7.

Distillation of the crude dehydrogenation product at 148 °C (5×10^{-4} mm) gave only dimethyl indole-6,7-dicarboxylate: IR 1750 cm^{-1} (ν C=O); NMR δ 3.84 (s, 3), 3.85 (s, 3), 6.50 (dd, 1), 7.22 (d, 1), 7.26 (m, 1), 7.72 (d, 1).

Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.8; H, 4.75; N, 6.0. Found: C, 62.2; H, 5.2; N, 5.6.

Dimethyl 1-Methylindole-4,7-dicarboxylate. 1-Methyl-2-vinylpyrrole (0.43 g, 0.004 mol) in benzene (15 mL) was refluxed with methyl propiolate (0.67 g, 0.008 mol) and hydroquinone (0.01 g) for 2 days. The volume was reduced to 5 mL, and petroleum ether (bp 40–60 °C) was added to give the indole diester: 0.48 g (73%); mp 69–70 °C; IR 1710 cm^{-1} (ν C=O); NMR δ 3.38 (s, 3), 3.88 (s, 6), 6.98 (d, 1), 7.11 (d, 1), 7.48 (d, 1), 7.70 (d, 1).

Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.1; H, 5.3; N, 5.7. Found: C, 63.6; H, 5.6; N, 6.1.

Dimethyl 1-phenylindole-4,7-dicarboxylated (yield 59%; mp 105.5 °C) was prepared by a method analogous to that used for the 1-methyl derivative: IR 1710 cm^{-1} (ν C=O); NMR δ 3.16 (s, 3), 3.98 (s, 3), 7.2–7.5 (m, 7), 7.52 (d, 1), 7.93 (d, 1).

Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.9; H, 4.9; N. 4.5. Found: C, 70.0; H, 4.9; N, 4.5.

Methyl 1-*tert*-Butyl-4,5-dihydroindole-7-carboxylate. 1-*tert*-Butyl-3-vinylpyrrole (1.49 g, 0.01 mol) in benzene (10 mL) was refluxed with methyl propiolate (0.84 g, 0.01 mol) in the presence of hydroquinone (0.05 g) for 3 days. The solvent and unchanged vinylpyrrole (0.5 g) were removed under reduced pressure, and the residue was distilled to give the dihydroindole-7-carboxylic ester (0.65 g, 44% based on reacted unrecovered vinylpyrrole) as a yellow oil: bp 115–116 °C (0.05 mm); IR 1710 cm^{-1} (ν C=O); NMR δ 1.43 (s, 9), 2.0–2.5 (m, 4), 3.71 (s, 3), 5.91 (d, 1), 6.46 (t, 1), 6.73 (d, 1).

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.1; H, 8.2; N, 6.0. Found: C, 71.9; H, 8.2; N, 5.85.

Methyl 1-*tert*-Butylindole-7-carboxylate. Aromatization of the 4,5-dihydroindole-7-carboxylic ester with DDQ gave methyl 1-*tert*-butylindole-7-carboxylate (78%), which was purified by elution from a column of alumina with petroleum ether (bp 40–60 °C)–diethyl ether (4:1): IR 1710 cm^{-1} (ν C=O); NMR δ 1.65 (s, 91), 3.86 (s, 3), 6.45 (d, 1), 6.98 (t, 1), 7.25 (dd, 1), 7.35 (dd, 1), 7.64 (dd, 1).

Anal. Calcd for $C_{14}H_{17}NO_2$: N, 6.1; *m/e* 231.1255 (M^+). Found: N, 6.5; *m/e* 231.1258 (M^+).

Distillation of the ester at 115 °C (0.001 mm) caused partial decomposition with the loss of the *tert*-butyl group.

Dimethyl 1-*tert*-Butylindole-4,7-dicarboxylate. 1-*tert*-Butyl-3-vinylpyrrole (0.45 g, 0.003 mol) and methyl propiolate (0.8 g, 0.01 mol) in benzene (10 mL) were heated under reflux in the presence of hydroquinone (0.05 g) for 4 days. Removal of the solvent and chromatographic purification of the residual oil gave the thermally unstable dimethyl 1-*tert*-butylindole-4,7-dicarboxylate: 0.57 g (66%); NMR δ 1.64 (s, 9), 3.86 (s, 3), 3.88 (s, 3), 6.77 (d, 1), 7.20 (d, 1), 7.45 (d, 1), 7.70 (d, 1).

Anal. Calcd for $C_{16}H_{19}NO_4$ (M^+): *m/e* 289.1314. Found: *m/e* 289.1325.

Distillation of the diester at ca. 150 °C (5×10^{-4} mm) caused considerable decomposition with the loss of the *tert*-butyl group.

Kinetic Measurements. The ^1H NMR spectra of equimolar equivalents of 1-methyl-2-vinylpyrrole and the appropriate dienophile in $CDCl_3$, containing 1,2-dichlorobenzene as a standard, were measured periodically. The average of ten integration values for the vinyl signals at 4.50 and 5.42 ppm and a suitable signal characteristic of the cycloadducts were normalized by comparison with the intensity of the aromatic signals for the standard.

Registry No. 1a, 2540-06-9; **1b**, 74304-92-0; **2**, 74304-93-1; **5**, 74809-21-5; **6**, 74809-22-6; **7**, 74809-23-7; **9** (R = Me), 74825-03-9; **9** (R = Ph), 74809-24-8; **10**, 74809-25-9; **11**, 74809-26-0; **12**, 74809-27-1; 2-formyl-1-methylpyrrole, 1192-58-1; 2-formyl-1-phenylpyrrole, 30186-39-1; 1-*tert*-butyl-3-formylpyrrole, 30186-46-0; maleic anhydride, 108-31-6; 1-methyl-4,5,6,7-tetrahydroindole-*cis*-4,5-dicarboxylic anhydride, 74809-28-2; 1-phenyl-4,5,6,7-tetrahydroindole-*cis*-4,5-dicarboxylic anhydride, 74809-29-3; 1-*tert*-butyl-4,5,6,7-tetrahydroindole-*cis*-6,7-dicarboxylic anhydride, 74809-30-6; dimethyl 1-methyl-4,5,6,7-tetrahydroindole-*cis*-4,5-dicarboxylate, 74809-31-7; dimethyl maleate, 624-48-6; maleonitrile, 928-53-0; *cis*-4,5-dicyano-1-methyl-4,5,6,7-tetrahydroindole, 74809-32-8; *trans*-4,5-dicyano-1-methyl-4,5,6,7-tetrahydroindole, 74809-33-9; fumaronitrile, 764-42-1; methyl 1-methyl-4,5,6,7-tetrahydroindole-4-carboxylate, 74809-34-0; methyl acrylate, 96-33-3; 4-cyano-1-methyl-4,5,6,7-tetrahydroindole, 74809-35-1; acrylonitrile, 107-13-1; dimethyl acetylenedicarboxylate, 762-42-5; dimethyl 1-methyl-6,7-dihydroindole-4,5-dicarboxylate, 74809-36-2; dimethyl 1-phenyl-6,7-dihydroindole-4,5-dicarboxylate, 74809-37-3; dimethyl 1-methylindole-4,5-dicarboxylate, 74809-38-4; dimethyl 1-phenylindole-4,5-dicarboxylate, 74809-39-5; methyl propiolate, 922-67-8; methyl 1-*tert*-butyl-4,5-dihydroindole-7-carboxylate, 74809-25-9.

Facile and Efficient Carboalkoxylation and Carboaryloxylation of Amines

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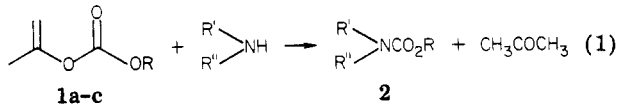
Recently, we demonstrated the synthesis of alkyl and aryl isopropenyl carbonates (1) and their carboalkoxylating and carboaryloxylating capacity in the reaction with amines (eq 1).[1] They react with amines in the absence



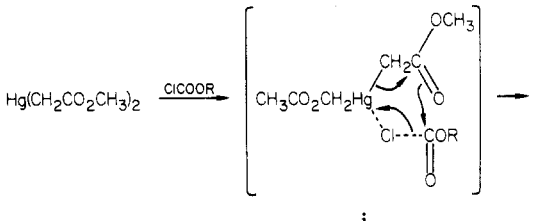
(1)

1a-c 2

a, R = C_2H_5; b, R = CH_3; c, R = C_6H_5

of base or catalyst to give the corresponding N-carboalkoxylated and N-carboaryloxylated compounds (2) in good yields and acetone is the single side product. These characteristics should make them interesting reagents, but their reactivity is not strong enough, especially in the reaction with weakly basic amines. We now report potentially efficient reagents, α-methoxyvinyl carbonates (3), which can react with various types of amines including weakly basic amines in quantitative yields under extremely mild conditions and can be handled under ordinary conditions.[2]

The unknown reagents 3 were prepared by the reaction of bis[(carbomethoxy)methyl]mercury[3] as the enolate equivalent[4] with alkyl and aryl chloroformates (eq 2). The



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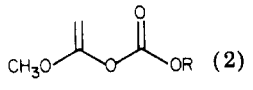

(2)

3a, R = C_2H_5
b, R = CH_3
c, R = C_6H_5

(1) Tamura, Y.; Haruta, J.; Okuyama, S.; Kita, Y. *Tetrahedron Lett.* 1978, 3737.

(2) These reagents are very soluble in common organic solvents and stable enough to be allowed to stand at room temperature for a few weeks or to be stored in the refrigerator for more than several months after the reagent bottle is flushed with nitrogen.

(3) Bis[(carbomethoxy)methyl]mercury was readily prepared by the passage of ketene into mercury(II) oxide and mercury(II) acetate in absolute methanol: Lutsenko, I. F.; Foss, V. L.; Ivanova, N. L. *Dokl. Akad. Nauk SSSR* 1961, *141*, 1107; *Chem. Abstr.* 1961, *56*, 12920*d*.

0022-3263/80/1945-4519$01.00/0