As to the position of 1,4-dinitrobenzene (4) in the observed sequence, although the rate-depressing effect deriving from the conjugative effect is absent here, the low reactivity may derive from a substantially large resonance energy of the benzenoid ring of this compound.

The influence of the leaving group and other structural effects will be the object of further investigations.

Acknowledgment. The authors are grateful to Dr. Roberto Mosca (University of Trieste) for the elemental analyses.

Registry No.—**1,** 56350-95-9; **2,** 826-03-9; **3,** 59434-05-8; **4,** 100-25-4; 5-nitrofuran-2-carboxylic acid, 645-12-5; 1-methyl-2-nitro-5-piperidinopyrrole, 56350-96-0; piperidine, 110-89-4; 2-nitro-5-piperidinofuran, 4818-49-9; 2-nitro-5-piperidinothiophene, 19991-84-5; 1-nitro-4-piperidinobenzene, 6574-15-8.

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Pyrrole Chemistry. The Cyanovinyl Aldehyde Protecting Groups†

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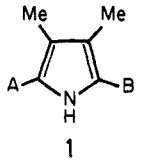
Protection of pyrrolic aldehyde groups with either methyl or ethyl cyanoacetate or malononitrile gives the corresponding cyanovinyl derivatives which are stable toward a variety of acids, oxidants, and reductants. Removal of the protecting groups with aqueous base regenerates the parent aldehyde.

The aldehyde function is one of great importance in the chemistry of pyrroles.[2] Alone, its electron-withdrawing properties can confer considerable stability on an otherwise sensitive system. 2-Formylpyrroles condense readily with 2-unsubstituted pyrroles in the presence of acid to form the very stable and synthetically useful 2,2′-dipyrromethene salts.[3] This reaction forms the basis for several well-known routes to porphyrins,[4] including the regiospecific synthesis of Johnson et al.[5] It is often convenient, given the nature of the readily available pyrrollic starting materials (usually 5-methylpyrrole-2-carboxylate esters), to introduce the formyl group several steps before it is required in the dipyrromethene synthesis. Although 2-formylpyrroles are resistant to autoxidation or Cannizzaro disproportionation, they are very susceptible to decomposition under acidic conditions and in the presence of many of the reagents commonly used in pyrrole syntheses (bromine, sulfuryl chloride, lead tetraacetate).

We report here further applications of the cyanovinyl protecting groups which were first employed by Fisher[6] in, for example, the synthesis of 2,5-diformyl-3,4-dimethylpyrrole (**1a**), and later by Woodward[7] in the synthesis of chlorophyll. Similar use of these protecting groups has been made by Davies,[8] and by Badger[9] in an unsuccessful assault on porphyrin a.

Cyanovinyl derivatives are prepared from the Knoevenagel reaction of 2-formylpyrroles with malononitrile or esters of



1

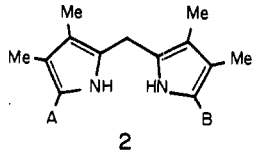
	A	B
a	OHC	CHO
b	H	CH=C(CN)CO_2Me
c	H	CHO
d	Me	CH=C(CN)CO_2Me
e	ClH$_2$C	CH=C(CN)CO_2Me
f	BrH$_2$C	CH=C(CN)CO_2Me
g	MeCO$_2$CH$_2$	CH=C(CN)CO_2Me
h	MeOH$_2$C	CH=C(CN)CO_2Me
i	Me	CO_2Et
j	Me	CHO
k	H	CH=C(CN)$_2$
l	Me	H
m	Me	CH=$\overset{+}{N}$Me$_2$Cl$^-$
n	Me	CH=C(CN)$_2$
o	ClH$_2$C	CH=C(CN)$_2$

† Dedicated to Professor H. H. Inhoffen on the anniversary of his 70th birthday.

cyanoacetic acid, in the presence of a basic catalyst, usually a primary or secondary amine. The reaction conditions required to generate the protected aldehyde vary with the substitution pattern of the pyrrole. Thus 2-formyl-5-pyrrole carboxylate esters tend to give quantitative yields in a few seconds, while trialkylpyrrole aldehydes and 2-formylpyrrole-3,5-dicarboxylate esters[10] require prolonged treatment especially when cyanoacetates rather than malononitrile are used. These compounds generally crystallize well and fluoresce in the solid state, under ultraviolet light, with yellow, orange, or greenish-yellow emission. They are usually higher melting and less soluble than the aldehydes from which they are derived. Indeed the choice as to which protecting group to use is in part dictated by solubility considerations: malononitrile gives the least soluble derivatives, and its use should be avoided in systems of inherently low solubility, such as derivatives of 3,4-dimethylpyrrole. In addition to conferring solubility the cyanoacrylates are also less deactivated toward electrophilic substitution than are the dicyanovinylpyrroles; for example, Fischer[6] was able to Gattermann-formylate **1b** while **1k** under the same conditions gave only unchanged starting material.

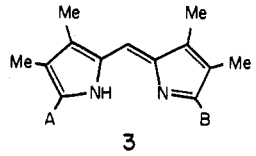
Cis–trans isomerization was observed with the cyanoacrylates, and while one configuration usually predominated the ratio of isomers varied as a series of transformations was effected. Regeneration of the aldehyde function was achieved by heating with strong aqueous caustic alkali; this limits the usefulness of these protecting groups to pyrroles bearing substituents which are base inert or else are reparable such as esters. Further possible limitations, as yet unexplored, would be that certain 2,2′-dipyrrylmethane-3-carboxylate esters, and their polypyrrolic homologues, are known to cyclize to dipyrrolopyridones[11] in alkali. In addition, acetic ester substituents might decarboxylate, under the strongly basic conditions, especially when adjacent to the protecting group.

Our interest in these protecting groups arose while seeking a satisfactory synthesis of the difficultly soluble 5,5′-diformyl-3,3′,4,4′-tetramethyl-2,2′-dipyrromethane (**2e**). Johnson et al.[12] had started with the readily available dipyrrylmethane diester **2a** and converted it via the unstable diacid



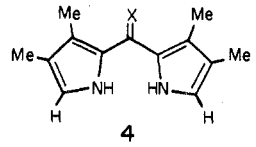
2

a A = B = CO_2Et
b A = B = CO_2H
c A = B = H
d A = B ▪ $CH=\overset{+}{N}Me_2Cl^-$
e A = B = CHO
f A = B = $CH(OMe)_2$
g A = B = $CH=C(CN)CO_2Me$
h A = $CH=C(CN)_2$; B = CH▪$C(CN)CO_2Me$



3

a A = B = Me(HBr)
b A ▪ B = $CHBr_2$(HBr)
c A = B = $CH(OMe)_2$



4

a X = S
b X = O

2b to the even less stable 5,5′-unsubstituted pyrromethane **2c.** Vilsmeier formylation with phosphorus oxychloride in dimethylformamide followed by incomplete hydrolysis gave a very unsatisfactory preparation of **2e.** An adaptation of MacDonald's[13] procedure, involving a tetrabromination of **3a** to give **3b,** followed by **2e** via **3c** and **2f,** proved unsatisfactory owing to incomplete bromination at the beginning. Clezy's[14] preparation, involving formylation with benzoyl chloride in dimethylformamide, on pure **2c** derived from dipyrryl ketone **4b** and dipyrrylthione **4a,** was not known to us at the time our work was in progress.

Our aim was to find a direct synthesis of the dipyrromethane dialdehyde **2e,** protected as the biscyanovinyl derivative **2g,** from monopyrrolic precursors. The protected intermediate **1d** was synthesized by traditional means, and reacted cleanly with 1 equiv of sulfuryl chloride, bromine, or lead tetraacetate to give the corresponding monosubstituted compounds **1e, 1f,** and **1g** in good yield. The two halomethyl derivatives proved to be indefinitely stable to the atmosphere in the solid state, unlike their monoester pyrrole analogues, which rapidly deliquesced and decomposed under similar conditions. This stability was one of the many evidences of the strong deactivation engendered by the cyanovinyl substituent.

Solvolysis of any of the compounds **1e–g,** in aqueous acidic methanol, conditions which usually convert alkoxycarbonylpyrrolylmethyl carbonium ion sources to the symmetrical pyrromethane, gave in this case mostly the methoxymethyl derivative **1h,** with only traces of the dipyrromethane. This observation was consistent with the strongly electron-withdrawing cyanovinyl group increasing both the activation energy for carbonium ion formation, as well as for electrophilic attack on the pyrrolic nucleus, with the result that most of the pyrrylmethyl carbonium ion was trapped by solvent. The equivalent reaction of the 2-unsubstituted compound **1b** with formaldehyde gave back mostly unreacted starting material, with only traces of the dipyrromethane. Prolonged reaction times led to extensive decomposition.

It was then decided to attempt the synthesis in a nonnucleophilic solvent, to prevent the trapping of the intermediate carbonium ion and its diversion to compounds such as **1h,** and also to allow the use of more vigorous conditions by employing a soluble Lewis acid (Friedel–Crafts) catalyst.

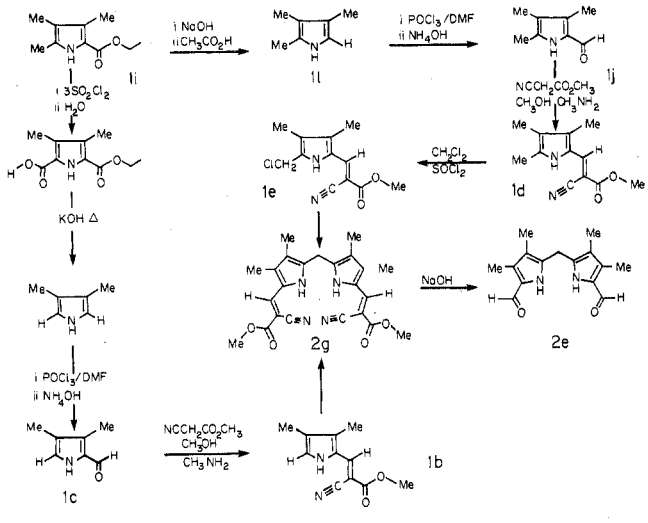
Chloromethylpyrrole **1e** and the 2-unsubstituted pyrrole **1b** were dissolved in dry methylene chloride; no reaction ensued, even though under these conditions, pyrrole monoesters react spontaneously with evolution of hydrogen chloride. However, as soon as some anhydrous stannic chloride was added to the above solution (this being our first choice of catalyst; we have never needed to try anything else since), a deep green color set in accompanied by evolution of hydrogen chloride. Workup followed by crystallization gave a yield of greater than 90% of the desired product **2g.**

When dipyrromethane **2g** was subjected to alkaline hydrolysis, the solution, unlike that of monopyrrolic analogues, initially turned a deep green, due, we assume, to the abstraction of a proton from the methane bridge which would generate a fully conjugated delocalized anion. The color soon faded, as the desired dialdehyde **2e** precipitated out of solution in nearly pure form. The overall synthesis of **2e** is outlined in Scheme I.

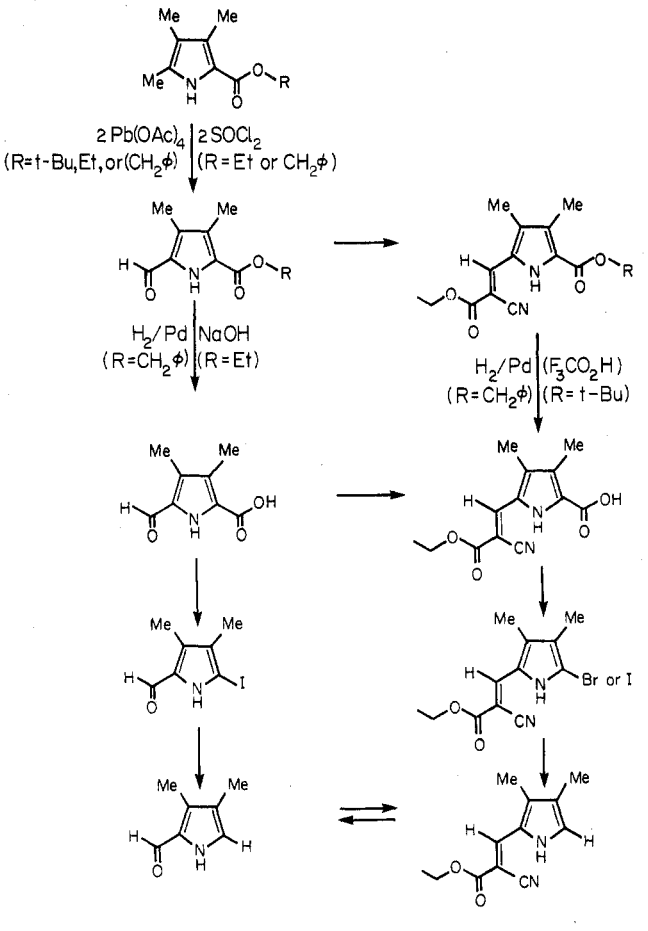
In the above synthesis the 2-unsubstituted pyrrole was prepared from 3,4-dimethylpyrrole. The sequence was both long and wasteful in that both α substituents of the starting material, 2-ethoxycarbonyl-3,4,5-trimethylpyrrole (**1i**), were removed, only to replace one of them at a later stage. In addition if this sequence were to be carried out on a pyrrole containing two different β substituents then an elaborate separation of isomers would be required.[15] A reaction sequence overcoming these limitations is outlined in Scheme II. This route required an ester function which could be removed under nonbasic conditions. Benzyl esters,[16] removable by catalytic hydrogenation, and *tert*-butyl esters,[17,18] removable with acid, have both found considerable use in pyrrole chemistry, and we can now add further testimony to their versatility.

Benzyl esters of pyrrylcarboxylic acids are readily available, in high yield, from the base-catalyzed transesterification of

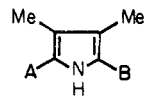
Scheme I



Scheme II



the ethyl esters, whenever a direct Knorr synthesis of the benzyl esters is not available. Reaction of the pyrrole aldehyde **5b** with either the methyl or ethyl ester (it is important to use the same alcohol as the ester alkoxy group; otherwise partial transesterification, presumably via the intermediacy of cyanoketene, will occur under the reaction conditions) of cyanoacetic acid or with malononitrile gave products (**5c, d,** or **e**) so insoluble in the alcohols used as solvent for their preparation that the products were isolated in greater than 95% yield after a reaction time of only a few minutes. In fact, it proved convenient to scavenge mother liquors of the aldehyde with these nitriles to maximize yields in the preparation of the aldehyde. The benzyl esters thus obtained which are so poorly



	A	B
a	Me	$CO_2CH_2\phi$
b	OHC	$CO_2CH_2\phi$
c	MeOCO(CN)C=CH	$CO_2CH_2\phi$
d	EtOCO(CN)C=CH	$CO_2CH_2\phi$
e	$(NC)_2C=CH$	$CO_2CH_2\phi$
f	Me	CO_2t-Bu
g	OHC	CO_2t-Bu
h	EtOCO(CN)C=CH	CO_2t-Bu
i	$(NC)_2C=CH$	CO_2t-Bu
j	EtOCO(CN)C=CH	CO_2H
k	EtOCO(CN)C=CH	Br
l	EtOCO(CN)C=CH	I
m	EtOCO(CN)C=CH	H
n	Me	CO_2CH_2-(p-OMe-C_6H_4)
o	OCH	CO_2CH_2-(p-OMe-C_6H_4)
p	$(NC)_2C=CH$	CO_2CH_2-(p-OMe-C_6H_4)
q	Me	$CO_2CH\phi_2$
r	OHC	$CO_2CH\phi_2$
s	$(NC)_2C=CH$	$CO_2CH\phi_2$
t	$(NC)_2C=CH$	CO_2H

soluble in alcohols dissolve readily in tetrahydrofuran, and catalytic hydrogenation over palladized charcoal produced the required carboxylic acid. The protecting group resisted hydrogenation during the hydrogenolysis and only slowly reduced during prolonged periods of time. Attempted decarboxylative iodination of these acids in aqueous solution proceeded poorly as Badger[8] had already found. However, bromination in warm acetic acid afforded the corresponding α-bromopyrrole **5k** in good yield.

It then became apparent that the use of the corresponding *tert*-butyl esters might avoid some of the problems associated with the benzyl esters, namely the possible overreduction by hydrogen, and the insolubility of the product carboxylic acid. The required 5-formyl-2-*tert*-butoxycarbonylpyrroles had not been reported, but proved readily available via lead tetraacetate oxidation of the 5-methyl derivative. After protection in the usual manner the cyanovinyl derivatives were found to be rather more soluble that their benzyl analogues. It was hoped that a thermal route would be found to generate the α-free pyrrole directly from the *tert*-butyl esters, but all such attempts lead to dark tars. Neat trifluoroacetic acid dissolved the *tert*-butyl esters readily, and the carboxylic acid precipitated out on warming, but their thermal decarboxylations also failed. However, the reaction of an excess of bromine on the *tert*-butyl esters, in hot acetic acid, gave the bromopyrrole directly. Iodine chloride[19] under the same conditions gave only the carboxylic acids.

Since the by-product, isobutylene, interfered with the halogenation, a stepwise procedure was investigated. The *tert*-butyl ester (**5h** or **i**) was dissolved in a hot chlorocarbon followed by the addition of trifluoroacetic acid. Heating was continued until no further solid appeared, at which time the product was collected, by filtration, in greater than 90% yield.

The resulting carboxylic acids (**5j,t**) were lemon yellow crystalline solids, which were stable in air over prolonged periods. Further evidence of the deactivating nature of the cyanovinyl group was indicated by extreme reluctance of the carboxylic acids to undergo thermal decarboxylation; indeed a strong parent ion appeared in the mass spectrum.

The bromination of the free carboxylic acids proceeded in better overall yield than the direct reaction of the *tert*-butyl esters. Similarly iodine chloride, in the absence of isobutylene, reacted in hot acetic acid to give the iodopyrrole, but even in the presence of excess reagent the conversion was incomplete. It was found that the solubility of carboxylic acids, in acetic acid, was markedly improved by the addition of an excess of sodium acetate and acetic anhydride, when the addition of iodine chloride gave the iodopyrrole (**5l**) in high yield.

Hydrogenation over palladized carbon converted both the bromo- and iodopyrroles **5k** and **l** to the 2-unsubstituted pyrroles (**5m**) in high yield. Deprotection at this stage leads to 5-unsubstituted 2-formylpyrroles, of use in pyrromethene synthesis. Unfortunately, the reactions with *tert*-butyl esters are limited to those pyrroles which are readily available from *tert*-butyl acetoacetate. Otherwise one must use the benzyl esters, which are available directly from the Knorr reaction or transesterification, since *tert*-butyl esters are not available by direct transesterification.

An ester group was sought which would be available via a transesterification, and which could be removed with trifluoroacetic acid. Transesterifications were carried out with 2-ethoxycarbonyl-3,4,5-trimethylpyrrole (**1i**) using both *p*-anisyl and benzhydryl alcohols. The resulting esters (**5n,q**) were both oxidized cleanly to the aldehydes (**5o,r**), but their dicyanovinyl derivatives (**5p,s**) were unreactive toward trifluoroacetic acid.

A complete dipyrromethane dialdehyde synthesis was then carried out with the more soluble 3,4-diethylpyrroles, using the most deactivating dicyanovinyl protecting groups as outlined in Scheme III. The resulting tetraethylpyrromethane dialdehyde (**7f**) was also prepared via Clezy's method, and found to be identical in every respect. Only conversion of the benzyl ester (**6i**) to the bromopyrrole (**6k**) via the free acid (**6j**) proceeded in less than excellent yields almost certainly owing to overhydrogenation of the benzyl ester, and the routes outlined in Schemes I and II provide a convenient route, with obvious modifications, to both symmetrically and unsymmetrically substituted 5,5′-diformyldipyrromethanes.

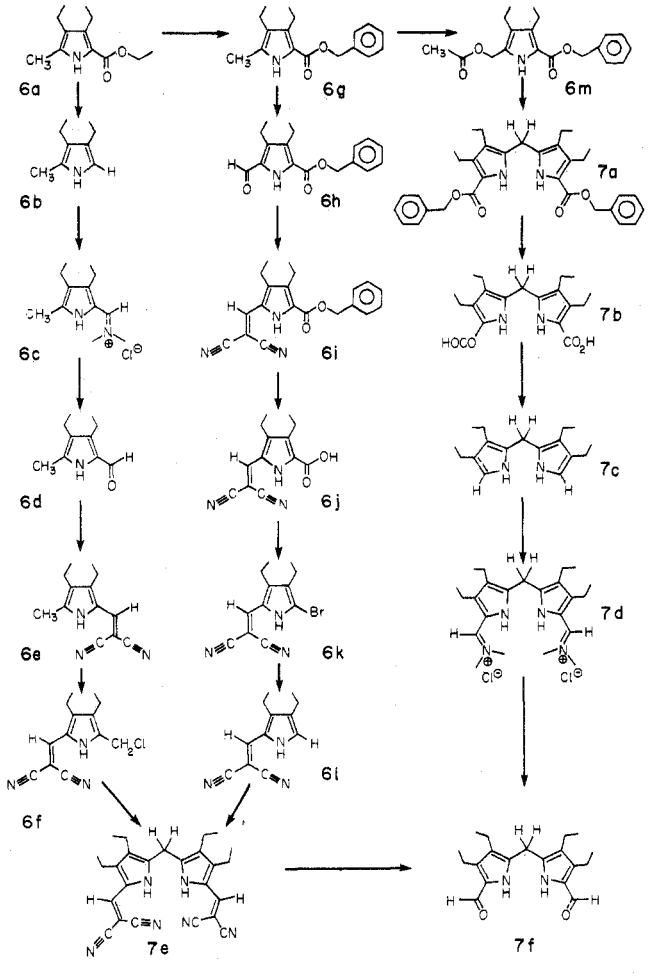
To show that an unsymmetrical pyrromethane was available from our reaction, and in order to assess the susceptibility of pyrromethane "rearrangement" under the reaction conditions, a pyrromethane bearing identical β substituents (methyl) but differing protecting groups was synthesized.

2-Formyl-3,4-5-trimethylpyrrole (**1j**) was protected with malononitrile, and the resulting Knoevenagel adduct (**1n**) chlorinated with sulfuryl chloride. The chloromethylpyrrole (**1o**) reacted with the same α-free dimethylpyrrolecyanoacrylate **1b** as above to give a high yield of the unsymmetrical pyrromethane **2h.** Finally it should be noted that the dicyanovinyl derivatives of 3,4-dimethylpyrrole-2-carboxylic esters can pose technical problems owing to their low solubility. This was particularly true of the free carboxylic acid (**5t**) which proved to be difficult to halogenate as it formed an insoluble adduct with its bromo- or iodopyrrole derivative which precipitated from the reaction mixture before halogenative decarboxylation could proceed to completion. Such problems did not arise when the more soluble 3-methyl-4-ethyl- or 3,4-diethylpyrrole analogues were used.

Experimental Section[20]

2-Formyl-3,4,5-trimethylpyrrole (1j).[21,22] **Method A.** 2-Ethoxycarbonyl-3,4,5-trimethylpyrrole (**1i**) was heated to boiling in a minimal volume of 95% ethanol on the steam bath, and a concentrated aqueous solution of sodium hydroxide (2 equiv) was added. The heating was continued until the mixture became completely water soluble (approximately 2 h), and then the alcohol was evaporated in vacuo. The residue was dissolved in water, neutralized with 1.95 equiv of acetic acid, and steam distilled until no more oily 2,3,4-trimethylpyrrole (**1l**) appeared in the condensate. The distillate was collected in ice water to minimize volatilization, and sodium bicarbonate was added as a preservative.

Scheme III



The 2,3,4-trimethylpyrrole (**1l**), a compound of characteristic benzene odor, solidified on cooling, with entrainment of water; it was dried, in methylene chloride solution, over anhydrous potassium carbonate. The solvent was removed, and the pyrrole was diluted with several volumes of dry *N,N*-dimethylformamide (DMF).

Phosphorus oxychloride (1 ml/g of the theoretical is a convenient excess) was added dropwise to three volumes of ice-cooled DMF. To this, with continued ice cooling, was slowly added the pyrrole solution. The mixture warmed up, became dark red, and eventually became viscous.

After several hours, the mixture was cautiously poured onto crushed ice and water (2 l./mol). Anhydrous sodium carbonate was added slowly until the solution remained only slightly acid (pH 5–6). The solution was then filtered through Celite to remove the dark tars, and the filtrates were made alkaline with aqueous ammonia and heated on the steam bath until the product had recrystallized in coarse form.

The crystals were washed with water and allowed to dry. Their color varied from orange to dark chocolate brown, but the material was suitable for subsequent reactions without further purification. The overall yield was variable; a 1-mol reaction gave 56%.

A purer sample was prepared by several crystallizations from aqueous methanol, to give light tan, elongated plates: mp 146.5–147.5 °C (lit.[21] 147 °C); ^{1}H NMR 1.90 (s, 3 H), 2.23 (s, 6 H), 9.47 (s, 1 H), 10.83 ppm (bs, 1 H); ir 3200 (NH), 1620 cm^{-1} (C=O).

Method B. 2-*tert*-Butoxycarbonyl-3,4,5-trimethylpyrrole[23] (**5f,** 41.8 g, 0.2 mol) was heated to boiling in *N,N*-dimethylformamide (100 ml). Benzoyl chloride (43 ml, 1.5 ml/g of theory, 80% excess) in DMF

(100 ml) was added over a 2-min period, and the heating was continued for 10 min. The mixture evolved gas, and became very dark.

The imine salt (**1m**) crystallized out when the mixture was allowed to cool for 2 h. The filtered solids were rinsed with DMF, and then diethyl ether, which caused further product, also recovered, to crystallize from the filtrates. Yield of crude salts: first crop, 32.5 g; second crop, 8.3 g.

The crude salts were dissolved in water (300 ml), and filtered through Celite. Aqueous ammonia (30 ml, concentrated) was added to the dark orange-brown filtrates, and the mixture was heated until the product (17.5 g, 64%) recrystallized in granular form.

2-(2-Cyano-2-methoxycarbonylvinyl)-3,4,5-trimethylpyrrole (1d). 2-Formyl-3,4,5-trimethylpyrrole (**1j**, 27.4 g, 0.2 mol), methyl cyanoacetate (40 g, 0.404 mol), methanol (200 ml), and diethylamine (2 ml) were taken down to dryness on the steam bath. Benzene (200 ml) and more diethylamine (2 ml) were added to the residue, and the heating was continued until no more water was observed to be azeotroping with the benzene. On cooling, spectacular orange-red crystals were deposited. The mother liquors were evaporated down to an oil, from which additional solids were recovered by washing with hexane, and then 50% (v/v) aqueous methanol.

The combined solids were dissolved in methylene chloride, filtered, and crystallized from methanol. The yield of beautiful, large chunky crystals was 38.1 g (87.5%); an additional 8.5% could be recovered from the mother liquors. The compound readily entrains minor amounts of colored by-products, so that the color varies from yellow, when pure, to orange-red, with a blue reflex. An analytical sample was recrystallized from methylene chloride–methanol: mp 156.0–157.5 °C; ^{1}H NMR 1.93 (s, 3 H), 2.13 (s, 3 H), 2.29 (s, 3 H), 3.83 (s, 3 H), 7.87 (s, 1 H), 9.54 ppm (bs, 1 H); ir 3300 (NH), 2200 (C≡N), 1710 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.03; H, 6.47; N, 12.84. Found: C, 65.87; H, 6.42; N, 12.93.

5-Chloromethyl-2-(2-cyano-2-methoxycarbonylvinyl)-3,4-dimethylpyrrole (1e). 2-(2-Cyano-2-methoxycarbonylvinyl)-3,4,5-trimethylpyrrole (**1d**, 6.54 g, 0.03 mol), dissolved and filtered in methylene chloride (60 ml), was stirred on a magnetic stirrer/hot plate in an Erlenmeyer flask, and treated dropwise with a solution of sulfuryl chloride (4.25 g, 0.031 mol) in methylene chloride (6 ml), over a 3-min period, at room temperature. Little color change occurred during the addition. The solvent was carefully boiled away and replaced near the end with diethyl ether, as the product crystallized. The yield of lemon-yellow needles was 6.1 g (80.8%). An analytical sample was recrystallized from methylene chloride–diethyl ether: mp 165–168 °C dec; ^{1}H NMR 2.03 (s, 3 H), 2.18 (s, 3 H), 3.87 (s, 3 H), 4.62 (s, 2 H), 7.98 (s, 1 H), 9.73 ppm (bs, 1 H); ir 3270 (NH), 2210 (C≡N), 1710 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_{13}ClN_2O_2$: C, 57.04; H, 5.19; Cl, 14.03; N, 11.09. Found: C, 56.97; H, 5.14; Cl, 14.29; N, 11.15.

5-Bromomethyl-2-(2-cyano-2-methoxycarbonylvinyl)-3,4-dimethylpyrrole (1f). 2-(2-Cyano-2-methoxycarbonylvinyl)-3,4,5-trimethylpyrrole (**1d**, 4.36 g, 0.02 mol) was dissolved in methylene chloride (50 ml) and anhydrous diethyl ether (200 ml) was added, followed by rapid dropwise addition of a solution of bromine (3.4 g, 0.021 mol) in methylene chloride (20 ml). The color darkened from yellow to brown. Left standing overnight, protected from moisture, the solution deposited greenish-yellow flakes of product, which were filtered off and washed with ether and then ligroin, yield 3.72 g (62.6%). An analytical sample was recrystallized from methylene chloride, filtered, and washed with hexane. The sample darkened progressively above 150 °C and melted at 175–179 °C dec: ^{1}H NMR 2.04 (s, 3 H), 2.17 (s, 3 H), 3.88 (s, 3 H), 4.50 (s, 2 H), 7.99 (s, 1 H), 9.62 ppm (bs, 1 H); ir 3280 (NH), 2210 (C≡N), 1720 (C=O), 1590 cm^{-1} (C=C).

Anal. Calcd for $C_{12}H_{13}BrN_2O_2$: C, 48.50; H, 4.41; Br, 26.89; N, 9.43. Found: C, 48.51; H, 4.43; Br, 27.09; N, 9.37.

5,5′-Bis(2-cyano-2-methoxycarbonylvinyl)-3,3′,4,4′-tetramethyl-2,2′-dipyrromethane (2g). 2-(2-Cyano-2-methoxycarbonylvinyl)-3,4-dimethylpyrrole[6] (**1b**, 2.04 g, 0.01 mol) and 5-chloromethyl-2-(2-cyano-2-methoxycarbonylvinyl)-3,4-dimethylpyrrole (**1e**, 2.52 g, 0.01 mol) were dissolved in dry methylene chloride (50 ml). Anhydrous stannic chloride (3 g) in methylene chloride (10 ml) was then added, causing an immediate color change from light orange to dark green. After 1 h at room temperature the catalyst was quenched by addition of concentrated hydrochloric acid, followed by water. The organic phase was rinsed with water, then dried over anhydrous potassium carbonate. The resulting solution was filtered and taken down to small volume on the steam bath. The hot solution was diluted all at once with hexane (50 ml), causing the product to precipitate out after a brief induction period. Most of the dark by-products remained in solution. The solids were collected and washed with hexane, crude yield 3.78 g (90%). The solids were redissolved in methylene chloride and reprecipitated as before, to give 3.48 g (82.9%) of clean, lemon-yellow, fluffy, microcrystalline product. A repetition of the synthesis gave a yield of 3.65 g (86.9%) after recrystallization. An analytical sample was prepared by recrystallization first from methanol and then methylene chloride–methanol: mp 214–221 °C dec; ^{1}H NMR 2.01 (s, 6 H), 2.16 (s, 6 H), 3.83 (s, 6 H, a shoulder appeared on this singlet due presumably to cis–trans isomerization), 4.04 (s, 2 H), 7.93 (s, 2 H), 9.48 ppm (bs, 2 H); ir 3400 (NH), 2200 (C≡N), 1710 (C=O), 1590, 1540 cm^{-1} (C=C); mass spectrum M$^+$ *m/e* 420 (calcd = obsd).

Anal. Calcd for $C_{23}H_{24}N_4O_4$: C, 65.70; H, 5.75; N, 13.33. Found: C, 65.73; H, 5.77; N, 13.61.

5,5′-Diformyl-3,3′,4,4′-tetramethyl-2,2′-dipyrromethane[12,14] (2e). 5,5′-Bis(2-cyano-2-methoxycarbonylvinyl)-3,3′,4,4′-tetramethyl-2,2′-dipyrromethane (**2g**, 1.01 g, 0.0024 mol) was suspended in boiling methanol (100 ml). Potassium hydroxide (10.1 g) in water (20 ml) was added; the solid dissolved with the formation of a dark green color. The green color soon faded, and the methanol was boiled off. The heating was continued on the steam bath for several hours, and a light tan sludge eventually appeared. The extremely insoluble product was periodically filtered off, and the filtrates reheated. The yield of crude, crystalline, light tan material was 403 mg (65%): mp 295–298 °C dec (lit.[14] 293–297 °C); mass spectrum M$^+$ *m/e* 258 (calcd = obsd).

2-Benzyloxycarbonyl-3,4,5-trimethylpyrrole[25] (5a). Method A. Sodium metal (~6 g) was dissolved, under argon, in anhydrous benzyl alcohol (500 ml). 2-Ethoxycarbonyl-3,4,5-trimethylpyrrole (**1i**, 200 g, 1.105 mol) was then added, and the mixture was heated in an oil bath held at 150 °C, under aspirator vacuum, for at least 3 h. On cooling to room temperature overnight, the product crystallized out of the exceedingly viscous solution as a mass of interlocking needles. The mixture was mashed up and slurried with 50% (v/v) aqueous methanol containing enough acetic acid to neutralize the sodium. The product could then be filtered readily, to give nearly colorless, shiny needles, which were rinsed with aqueous methanol.

In order to remove the water the moist filter cake was dissolved in methylene chloride and the organic phase was filtered and boiled down, as hot hexane was added. The product crystallized from the hot solution as snow-white needles, with yields in the range of 200–230 g (74.5–85.5%), mp 117–117.5 °C (lit.[24] 118 °C).

Method B.[25] 2-Benzyloxycarbonyl-3,4,5-trimethylpyrrole (5a) (Direct Knorr Synthesis). Benzyl acetoacetate (1536 g, 8 mol) in acetic acid (1500 ml) was nitrosated with a solution of sodium nitrite (552 g, 8 mol) in water (650 ml). The resulting solution of benzyl oximinoacetoacetate was added, along with a slurry of zinc dust (1600 g, 24.2 mol) in water, to a vigorously stirred solution of 3-methyl-2,4-pentanedione[25] (912 g, 8 mol) in acetic acid (2000 ml), in a 12-l. flask over a 2-h period. More acetic acid (1650 ml) was added as the reaction progressed.

The solution was decanted from the residual zinc and diluted slowly with water to precipitate the product in easily filtered form. After filtration and washing with water, the solids were dissolved in methylene chloride. The organic phase was gravity filtered to remove any remaining zinc, and the methylene chloride was displaced with hexane, from which the product readily crystallized. The pyrrole was collected as several crops, all of which were recrystallized from methylene chloride–(hexane or methanol), to give 866 g (44.5%): mp 116.5–117.5 °C; ^{1}H NMR 1.86 (s, 3 H), 2.08 (s, 3 H), 2.25 (s, 3 H), 5.26 (s, 2 H), 7.29 (s, 5 H), 9.43 ppm (bs, 1 H); ir 3280 (NH), 1650 cm^{-1} (C=O).

2-Benzyloxycarbonyl-5-formyl-3,4-dimethylpyrrole[26] (5b). 2-Benzyloxycarbonyl-3,4,5-trimethylpyrrole (**5a**, 121.5 g, 0.5 mol) was dissolved in acetic acid (500 ml, glacial), and lead tetraacetate (480 g of moist commercial product, 1 mol = 443 g) was added, over a 0.5-h period, as a slurry in acetic acid (300 ml). The first half of the reagent reacted with considerable exotherm, the remainder more sluggishly, and the temperature rose to 78 °C. The mixture was then heated on the steam bath for 1 h, after which the Pb(IV) test, with water, was negative.

Water (500 ml) was added slowly to the hot solution to hydrolyze the diacetate, and the mixture was seeded. After crystallization had set in, the suspension was further diluted with water (2500 ml). The filtered and water-washed solids were dissolved in methylene chloride, and the solution was filtered before being boiled down to a volume of 300 ml and diluted with hexane (500 ml). After a recrystallization from the same solvents, the light tan granular first crop weighed 68.87 g (53.6%). Subsequent crops amounted to 26.34 g (20.5%) for a total yield of 74.1%: mp 119.0–119.5 °C (lit.[26] 119–120 °C); ^{1}H NMR 2.25 (s, 6 H), 5.30 (s, 2 H), 7.34 (s, 5 H), 9.70 (s, 1 H), 9.90 ppm (bs, 1 H); ir 3290 (NH), 1680, 1655 cm^{-1} (C=O).

2-Benzyloxycarbonyl-5-(2-cyano-2-methoxycarbonylvin-

yl)-3,4-dimethylpyrrole (5c). 2-Benzyloxycarbonyl-5-formyl-3,4-dimethylpyrrole (**5b,** 1.35 g, 5.25 mmol) and methyl cyanoacetate (1.0 g, an excess) were heated to boiling in methanol (25 ml). Acetic acid (1 drop) and alcoholic methylamine (several drops) were then added. The product soon crystallized out, and the mixture was allowed to cool before filtration. The brilliant lemon-yellow, fluffy solids were rinsed with methanol, then hexane. The yield was 1.65 g (93%). An analytical sample was recrystallized from methylene chloride–methanol: mp 143.0–145.5 °C, and on remelting 144.0–145.0 °C; ^{1}H NMR 2.13 (s, 3 H), 2.27 (s, 3 H), 3.87 (s, 3 H), 5.35 (s, 2 H), 7.37 (s, 5 H), 7.98 (s, 1 H), 10.15 ppm (bs, 1 H); ir 3400 (NH), 2210 (C≡N), 1730, 1715 (C=O), 1600 cm^{-1} (C=C).

Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28. Found: C, 67.35; H, 5.36; N, 8.27.

2-Benzyloxycarbonyl-5-(2-cyano-2-ethoxycarbonylvinyl)-3,4-dimethylpyrrole (5d) (with R. A. Sawka). 2-Benzyloxycarbonyl-5-formyl-3,4-dimethylpyrrole (**5b,** 1.35 g, 5.25 mmol) was dissolved in hot absolute ethanol (25 ml). Ethyl cyanoacetate (1.0 g, an excess) was added, followed by 1 drop of acetic acid and 5 drops of methylamine in ethanol. After a few seconds a sulfur-yellow flocculent precipitate began to separate and then the mixture became very thick. After cooling to room temperature the product was collected by filtration, washed with a little anhydrous ethanol and then hexane, and air dried to give 1.80 g (97%). An analytical sample was recrystallized from methylene chloride–ethanol: mp 167.5–168 °C; ^{1}H NMR 1.36 (t, 3 H, J = 7 Hz), 2.16 (s, 3 H), 2.28 (s, 3 H), 4.34 (q, 2 H, J = 7 Hz), 5.36 (2 H, s), 7.37 (5 H, m), 8.00 (1 H, s), 10.20 ppm 1 H, bs); ir 3430 (NH), 2205 (C≡N), 1709 cm^{-1} (b, C=O).

Anal. Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.23; H, 5.79; N, 8.11.

2-Carboxy-5-(2-cyano-2-ethoxycarbonylvinyl)-3,4-dimethylpyrrole (5j). Method A. 2-*tert*-Butoxycarbonyl-5-(2-cyano-2-ethoxycarbonylvinyl)-3,4-dimethylpyrrole (**5h,** 29.4 g, 0.0927 mol) was heated to boiling in 1,2-dichloroethane (100 ml) on a steam bath, and filtered, if needed. Trifluoroacetic acid (10 ml) was added, and the heating was continued for 80 min. After 5 min, crystalline product began to appear, and the mixture eventually became thick, as the color of the solution gradually deepened to a bright permanganate purple. After 45 min, additional TFA (10 ml) was added; more solvent was added as needed.

After cooling, the product was filtered off and rinsed with dichloroethane, then hexane. The yield of brilliant lemon-yellow crystals was 23.2 g (95.5%). An analytical sample was recrystallized from tetrahydrofuran—absolute ethanol to give clusters of chunky, transparent, yellow blades: mp 212–213 °C dec; ir 3400 (NH), 3150–2400 (CO_2H), 2215 (C≡N), 1730, 1670 (C=O), 1590 cm^{-1} N (C=C).

Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.53; H, 5.38; N, 10.68. Found: C, 59.38; H, 5.43; N, 10.68.

Method B. 2-Benzyloxycarbonyl-5-(2-cyano-2-ethoxycarbonylvinyl)pyrrole (**5d,** 3.40 g, 0.01 mol) and 10% palladium on charcoal (0.24 g) was added to tetrahydrofuran (100 ml) and reduced under 1 atm with hydrogen. The solution was filtered through Celite, and the filtrate taken down to dryness to give 2.5 g (95%) of product, mp 211–212 °C dec.

2-*tert*-Butoxycarbonyl-3,4,5-trimethylpyrrole[23] (5f). To a solution of *tert*-butyl acetoacetate (632 g, 4 mol) in acetic acid (1000 ml), stirred magnetically and immersed in an ice-filled polyethylene bucket, was added a solution of sodium nitrite (276 g, 4 mol) in water (350 ml), dropwise, so as to maintain a reaction temperature below 40 °C.

The resulting solution of *tert*-butyl oximinoacetoacetate was added slowly to a rapidly stirred solution of 3-methyl-2,4-pentanedione (457 g, 4 mol) in acetic acid (1000 ml), concurrently with a slurry of zinc dust (800 g, 12.3 mol) in a minimal volume of water. The addition of reactants required approximately 135 min, and the temperature reached 104 °C.

The resulting solution was decanted from the unreacted zinc and diluted with an equal volume of water. The product was filtered from the still-warm solution and rinsed with much water. The filter cake was slurried with dilute aqueous ammonia (50 ml of concentrated NH_4OH in 2500 ml of slurry), which served as a preservative from atmospheric oxidation or discoloration until the workup could be resumed.

The product was refiltered, and the filter cake dissolved in methylene chloride and filtered. The organic phase was isolated, refiltered, and reduced in volume as the solvent was replaced by methanol.

The product formed transparent, colorless prisms: first crop, 359.2 g (43%); second crop, 38.05 g (4.6%). Recrystallization of the combined crops gave crops of 332.2 (39.74%) and 52.7 g (6.31%), for a total bottled yield of 46.05%, mp 138.5 °C (lit.[23] 137–138 °C). The ability of this compound to form colorless crystals from the blackest of solutions is quite remarkable; ^{1}H NMR 1.55 (s, 9 H), 1.88 (s, 3 H), 2.17 (s, 3 H), 2.22 (s, 3 H), 9.57 ppm (bs, 1 H); ir 3300 (NH), 1660 cm^{-1} (C=O).

2-*tert*-Butoxycarbonyl-5-formyl-3,4-dimethylpyrrole (5g). 2-*tert*-Butoxycarbonyl-3,4,5-trimethylpyrrole (**5f,** 104.5 g, 0.5 mol) in glacial acetic acid (500 ml) was treated, in several portions, with lead tetraacetate (497 g of commercial material, 1.1 mol). The mixture was swirled after each addition of oxidant; the first equivalent reacted especially exothermically and the temperature reached approximately 60 °C. The addition of the lead tetraacetate required only 20 min; some acetic acid (100 ml) was used to rinse it in. The mixture was then heated on the steam bath for 20–30 min, until the temperature reached 80 °C. Ethylene glycol (~10 ml) was added to destroy any lead dioxide present (dark-colored lead tetraacetate was often used with eminently satisfactory results, provided that the appearance—crystallinity, etc.—was otherwise normal).

The mixture was then slowly diluted with water (3000 ml) and seeded. The resulting solids wgre filtered off, washed with water, and dissolved in methylene chloride. The organic phase was gravity filtered, and the solvent was displaced with hexane on the steam bath. When the volume had been reduced to 250 ml, the solution was allowed to cool and seeded. The coarse, tan crystals were rinsed with hexane, yield 71.5 g (64.1%).

The mother liquors were scavenged with malononitrile, to give a 16.8% yield of the dicyanovinylpyrrole, increasing the total isolable conversion to aldehyde to 80.9%. An analytical sample was crystallized from methylene chloride–hexane: mp 99.8–100.9 °C; ^{1}H NMR 1.59 (s, 9 H), 2.22 (s, 3 H), 2.25 (s, 3 H), 9.75 (s, 1 H), 10.10 ppm (bs, 1 H); ir 3300 (NH), 1680, 1660 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_{17}NO_3$:C, 64.55; H, 7.68; N, 6.27. Found: C, 64.66; H, 7.73; N, 6.27.

2-*tert*-Butoxycarbonyl-5-(2-cyano-2-ethoxycarbonylvinyl)-3,4-dimethylpyrrole (5h). 2-*tert*-Butoxycarbonyl-5-formyl-3,4-dimethylpyrrole (**5g,** 44.6 g, 0.2 mol) and ethyl cyanoacetate (30 g, 32.5% excess) were warmed on the steam bath in ethanol (100 ml, absolute), and methylamine catalyst (2 ml) was added to the hot solution. After a few minutes of heating, the product crystallized out peacefully, and the mixture became thick with solid. After chilling on ice, the product was filtered and rinsed with cold ethanol (60 ml, absolute), then hexane. The first crop weighed 55.8 g (87.8%). An additional 2.86 g (4.5%) was isolated from the mother liquors, for a total yield of 92.3%. An analytical sample was recrystallized from methylene chloride–95% ethanol: mp 172.0–174.0 °C; ^{1}H NMR 1.38 (t, 3 H, J = 7 Hz), 1.61 (s, 9 H), 2.16 (s, 3 H), 2.25 (s, 3 H), 4.33 (q, 2 H, J = 7 Hz), 7.97 (s, 1 H), 10.14 ppm (bs, 1 H); ir 3400 (NH), 2210 (C≡N), 1710 (C=O), 1600 cm^{-1} (C=C).

Anal. Calcd for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.97; N, 8.80. Found: C, 64.21; H, 6.94; N, 8.75.

5-Bromo-2-(2-cyano-2-ethoxycarbonyl)-3,4-dimethylpyrrole (5k). 5-Carboxy-2-(2-cyano-2-ethoxycarbonylvinyl)-3,4-dimethylpyrrole (**5j,** 5.26 g, 0.02 mol) and anhydrous sodium acetate (5.0 g) were warmed to 70 °C in glacial acetic acid (50 ml). A solution of bromine (3.86 g, 0.024 mol) in acetic acid (10 ml) was added dropwise over a 5-min period. The bromine color was discharged as rapidly as it entered the reaction mixture (including the excess bromine which presumably reacted with the sodium acetate). The solution remained a clean brilliant lemon-yellow throughout the reaction, which is not the case if the sodium acetate be absent.

The solution was diluted slowly with water (400 ml), causing precipitation of product, which was filtered off and washed with water. The filter cake was then washed with dilute aqueous ammonia (1:4), which was probably a mistake, as the yellow solids temporarily turned green, and the washings became yellow. The washings remained yellow as long as the ammonia was used to rinse the solids, so that it is likely that the product was being attacked, rather than purified by removal of starting material. What was left of the filter cake was dissolved in methylene chloride, and crystallized from methanol (no transesterification was noted) after removal of any aqueous phase, and filtration, yield 3.51 g (59.1%). An analytical sample was recrystallized from methylene chloride–absolute ethanol to give transparent, brilliant orange-yellow crystals: mp 139.5–141.5 °C; ^{1}H NMR 1.37 (t, 3 H, J = 7.5 Hz), 1.98 (s, 3 H), 2.18 (s, 3 H), 4.32 (q, 2 H, J = 7.5 Hz), 7.85 (s, 1 H), 9.59 ppm (bs, 1 H); ir 3250 (NH), 2210 (C≡N), 1710 (C=O), 1580 cm^{-1} (C=C).

Anal. Calcd for $C_{12}H_{13}BrN_2O_2$: C, 48.50; H, 4.41; Br, 26.89; N, 9.43. Found: C, 48.35; H, 4.46; Br, 26.97; N, 9.36.

2-(2-Cyano-2-ethoxycarbonylvinyl)-5-iodo-3,4-dimethylpyrrole (5l). 5-Carboxy-2-(2-cyano-2-ethoxycarbonylvinyl)-3,4-dimethylpyrrole (**5j,** 13.1 g, 0.05 mol), anhydrous sodium acetate (14 g, 0.17 mol), acetic anhydride (10 ml), and acetic acid (100 ml) were heated on a stirrer–hot plate until the solution became homogeneous (near 105 °C). Addition of a solution of iodine chloride (16.25 g, 0.10

mol) in glacial acid (50 ml) was then started immediately, and completed within 6 min, haste being necessary as the pyrrole solution is unstable at elevated temperatures. The solution was boiled for 5 min, until the purple vapors of free iodine had gone. Water (700 ml) was then slowly added, causing oiling and then crystallization of product.

The solids were filtered off, washed extensively with water, and then dissolved in methylene chloride. The organic phase was filtered, and the solvent displaced with methanol (no transesterification occurred) on the stirrer–hot plate. The solution was concentrated until it became thick with solids at the boiling point. The product was filtered off, after cooling, and washed with a minimum volume of methanol, then hexane. The yield of olive-green, fluffy granules was 13.68 g (79.5%). An analytical sample was recrystallized from methylene chloride charcoal, and then from 95% ethanol: mp 125.0–151 °C (a small amount of solid remained until 151 °C); ^{1}H NMR 1.38 (t, 3 H, J = 7.5 Hz), 1.98 (s, 3 H), 2.19 (s, 3 H), 4.33 (q, 2 H, J = 7.5 Hz), 7.80 (s, 1 H), 9.60 ppm (bs. 1 H); ir 3400 (NH), 2200 (C≡N), 1720, 1675 sh (C=O), 1580 cm^{-1} (C=C).

Anal. Calcd for $C_{12}H_{13}IN_2O_2$: C, 41.88; H, 3.81; I, 36.87; N, 8.14. Found: C, 41.92; H, 3.93; I, 36.89; N, 8.00.

2-(2-Cyano-2-ethoxycarbonylvinyl)-3,4-dimethylpyrrole[6] **(5m).** 2-(2-Cyano-2-ethoxycarbonylvinyl)-5-iodo-3,4-dimethylpyrrole (**5l,** 3.5 g, 0.1 mol), anhydrous sodium acetate (3 g), and 10% palladium on charcoal (0.4 g) were hydrogenated overnight in tetrahydrofuran (100 ml) at room temperature and pressure. The mixture was filtered through Celite and the filtrate taken down to dryness. The residue was crystallized from methanol to give 2.0 g (92%) of bright yellow needles, mp 194–195 °C (lit.[6] 190–191 °C).

2-Benzyloxycarbonyl-3,4-diethyl-5-methylpyrrole (6g). 2-Ethoxycarbonyl-3,4-diethyl-5-methylpyrrole[27] (**6a,** 86.5 g, 0.414 mol) and benzyl alcohol (160 ml) were heated to boiling on a hot plate in an Erlenmeyer flask to drive off any water present. Several milliliters of a stock solution of sodium (8 g) in benzyl alcohol (200 ml) were then added, causing immediate vigorous evolution of ethanol vapors and a considerable temperature drop. A little more catalyst was added when the reaction had subsided, and the heating was resumed until the boiling point of benzyl alcohol, 209 °C, was again reached. The hot reaction mixture was then *immediately* quenched in a solution of acetic acid (10 ml) in methanol (500 ml). The color of the reaction mixture had remained light throughout, and only about 15 min had elapsed from initial addition of the catalyst until the quenching.

Aqueous methanol (1000 ml, 50% v/v) was then added, followed by water (500 ml). The product oiled out at first, but soon crystallized, the benzyl alcohol remaining in solution. On standing, the initially tan solids typically acquired a reddish tinge. The solids were rinsed with 40% methanol–water, then with water, before being dissolved in methanol, filtered, and recrystallized from a volume of 500 ml. A first crop of 77 g and a second crop of 13.1 g or 90.1 g total (80.3%) were recovered. An analytical sample was recrystallized from methanol: mp 72.0–73.0 °C; ^{1}H NMR 1.03 (t, 3 H, J = 7.5 Hz), 1.09 (t, 3 H, J = 7.5 Hz), 2.12 (s, 3 H), 2.34 (q, 2 H, J = 7.5 Hz), 2.52 (q, 2 H, J = 7.5 Hz), 5.24 (s, 2 H), 7.23 (s, 5 H), 10.00 (bs, 1 H).

Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.11; H, 7.74; N, 5.18.

2-*p*-Methoxybenzyloxycarbonyl-3,4,5-trimethylpyrrole (5n). 2-Ethoxycarbonyl-3,4,5-trimethylpyrrole (**1i,** 45.1 g, 0.25 mol) and *p*-anisyl alcohol (40.1 g, 0.29 mol) were heated together on a hot plate in an Erlenmeyer flask. Sodium metal (0.62 g) was warmed in *p*-anisyl alcohol (10 ml), under nitrogen; only part dissolved.

When the temperature of the pyrrole solution had reached 216 °C the sodium alkoxide solution was added, causing considerable evolution of gas (ethanol). The temperature fell to 205 °C, but was raised to 232 °C before the reaction mixture was quenched in a mixture of methanol (300 ml), water (200 ml), and acetic acid (10 ml).

The resulting oily droplets soon solidified. The product was filtered off and rinsed with 60% aqueous methanol (90 ml, v/v). The washed solids were then dissolved in boiling methanol (150 ml), filtered hot, and allowed to crystallize, forming a thick mass of fluffy balls, in a dark red solution. These solids were recrystallized from methanol, giving light cream-colored flakes, 18.2 g (27%). An analytical sample was recrystallized from methanol: mp 106.5–108.0 °C; ^{1}H NMR 1.87 (s, 3 H), 2.11 (s, 3 H), 2.25 (s, 3 H), 3.68 (s, 3 H), 5.22 (s, 2 H), 6.82 and 7.30 (AB q, 4 H, J = 9 Hz), 9.57 ppm (bs, 1 H); ir 3300 (NH), 1650 cm^{-1} (C=O).

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.09; H, 7.12; N, 5.09.

2-Diphenylmethoxycarbonyl-3,4,5-trimethylpyrrole (5q). Benzhydrol (30 g, 0.163 mol) was melted under argon, and sodium metal (0.75 g, 0.0326 g-atom) was added, dissolving rapidly above 140 °C. When the sodium had dissolved, 2-ethoxycarbonyl-3,4,5-trimethylpyrrole (**1i,** 18.1 g, 0.1 mol) was added, and the mixture was heated until the temperature reached 190 °C, care being taken to avoid foaming, as the ethanol was evolved, particularly above 150 °C. The reaction mixture was quenched immediately from 190 °C by pouring it into a mixture of methanol (200 ml), water (40 ml), and acetic acid (10 ml). The product soon crystallized, and after standing for 30 min, it was filtered off and washed with 80% (v/v) aqueous methanol. The solids were dissolved in methylene chloride, filtered, and recrystallized from methanol. The yield, as fluffy needles, was 12.28 g (38.5%). An analytical sample was recrystallized from methanol: mp 155.5–156.3 °C; ^{1}H NMR 1.87 (s, 3 H), 2.00 (s, 3 H), 2.34 (s, 3 H), 7.1–7.45 (m, 11 H), 9.33 ppm (bs, 1 H).

Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.71; H, 6.65; N, 4.34.

5-Formyl-2-*p*-methoxybenzyloxycarbonyl-3,4-dimethylpyrrole (5o). 2-*p*-Methoxybenzyloxycarbonyl-3,4,5-trimethylpyrrole (**5n,** 5.51 g, 0.02 mol) in glacial acetic acid (20 ml) was treated with one portion of lead tetraacetate (19.6 g, 0.044 mol). The mixture warmed up, and then set solid due to the formation of monoacetoxymethylpyrrole. The mixture was then heated on the steam bath until the solids had redissolved, and the Pb(IV) test had become negative. Water was added to the hot solution until it became just opalescent. The solution was then chilled on ice and seeded, being further diluted with water (100 ml in toto) after crystallization had started.

The solids were filtered, washed with water, and recrystallized wet from methanol. The product was redissolved in methanol, filtered, and recrystallized, to give light tan flakes, 3.28 g (57.1%). An analytical sample was recrystallized from methanol: mp 110.0–110.5 °C; ^{1}H NMR 2.23 (s, 6 H), 3.77 (s, 3 H), 5.23 (s, 2 H), 6.86 and 7.32 (AB q, 4 H, J = 8.7 Hz), 9.70 (s, 1 H), 9.98 ppm (bs, 1 H); ir 3280 (NH), 1690, 1650 cm^{-1} (C=O).

Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found: C, 66.64; H, 5.97; N, 4.88.

2-Diphenylmethoxycarbonyl-5-formyl-3,4-dimethylpyrrole (5r). 2-Diphenylmethoxycarbonyl-3,4,5-trimethylpyrrole (**5q,** 6.38 g, 0.02 mol) in glacial acetic acid (50 ml) was treated with one portion of lead tetraacetate (19.6 g, 0.044 mol). After the initial reaction had subsided, the mixture was warmed on the steam bath until Pb(IV) was no longer present. The final solution was a clear light orange.

Water (150 ml) was added slowly to the hot solution, causing crystallization of product. The filtered and washed (water) solids were dissolved in methylene chloride, and the solution was filtered and boiled down as methanol was added. This, one of the less soluble pyrrole aldehydes, crystallized from boiling methanol to give 4.22 g (63.3%) after cooling, filtering, and rinsing with methanol. Only a negligible amount remained in the mother liquors to be scavenged with malononitrile. An analytical sample was recrystallized from methylene chloride–methanol: mp 196.0–198.0 °C; ^{1}H NMR 2.27 (s, 3 H), 2.31 (s, 3 H), 7.11, 7.33, and 7.43 (11 H), 9.73 ppm (s, 1 H); ir 3290 (NH), 1680, 1650 cm^{-1} (C=O).

Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.65; H, 5.74; N, 4.20. Found: C, 75.47; H, 5.73; N, 4.17.

5-(2,2-Dicyanovinyl)-2-*p*-methoxybenzyloxycarbonyl-3,4-dimethylpyrrole (5p). 5-Formyl-2-*p*-methoxybenzyloxycarbonyl-3,4-dimethylpyrrole (**5o,** 1.43 g, 5.0 mmol) and malononitrile (0.80 g, 0.33 g = 1 equiv) were boiled in methanol with a few drops of methylamine catalyst (saturated ethanolic methylamine). The solution was boiled down until the product crystallized, forming orange, granular chunks, 1.14 g (68%). An analytical sample was recrystallized from methylene chloride–methanol: mp 135.5–136.5 °C; ^{1}H NMR 2.13 (s, 3 H), 2.26 (s, 3 H), 3.79 (s, 3 H), 5.29 (s, 2 H), 6.89 and 7.36 (AB q, 4 H, J = 8.5 Hz), 7.53 (s, 1 H), 10.00 ppm (bs, 1 H); ir 3400 (NH), 2220 (C≡N), 1690 (C=O), 1580 cm^{-1} (C=C).

Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 67.99; H, 5.20; N, 12.38.

5-(2,2-Dicyanovinyl)-2-diphenylmethoxycarbonyl-3,4-dimethylpyrrole (5s). 2-Diphenylmethoxycarbonyl-5-formyl-3,4-dimethylpyrrole (**5r,** 1.67 g, 5.0 mmol) and malononitrile (0.81 g, 2.5 equiv) were dissolved in methylene chloride (20 ml). Methanol (25 ml) and methylamine catalyst (several drops) were added and the solution was boiled down until the product crystallized. After cooling, the yellow flat needles were filtered off and rinsed with methanol, to give a yield of 1.75 g (91.8%). An analytical sample was recrystallized from methylene chloride–methanol: mp 204.5–205.0 °C; ^{1}H NMR 2.13 (s, 3 H), 2.32 (s, 3 H), 7.08 (s, 1 H), 7.36 (m, 10 H), 7.53 (s, 1 H), 10.18 ppm (bs, 1 H); ir 3370 (NH), 2210 (C≡N), 1680 (C=O), 1575 cm^{-1} (C=C).

Anal. Calcd for $C_{24}H_{19}N_3O_2$: C, 75.57; H, 5.02; N, 11.02. Found: C, 75.39; H, 5.05; N, 10.96.

2-Benzyloxycarbonyl-3,4-diethyl-5-formylpyrrole (6h). 2-Benzyloxycarbonyl-3,4-diethyl-5-methylpyrrole (**6g,** 27.1 g, 0.1 mol)

in glacial acetic acid (150 ml) was treated with lead tetraacetate (100 g, moist commercial material, 0.23 mol), in several portions over a 10-min period, acetic acid (50 ml) being used to facilitate the addition. The first equivalent of oxidant reacted readily, with noticeable exotherm. The remainder dissolved more slowly, and the mixture had to be warmed to 85–90 °C to complete the reaction.

When the Pb(IV) test was negative, water was slowly added to the clear, light orange solution, until permanent opalescence appeared. The mixture was then chilled on ice and seeded. The addition of water was resumed only after crystals of product had become well established; the mixture was then diluted to at least 1 l. When the oils had thoroughly solidified, the solids were filtered off and washed with water. The product was recrystallized from methanol (150 ml), with seeding, to give a first crop of 18.5 g (64.9%). When scavenged with malononitrile, the mother liquors afforded 7.14 g (21.4%) of the dicyanovinyl derivative, for a total isolable conversion to aldehyde of 86.3%. An analytical sample was recrystallized from methanol: mp 78.5–79.5 °C; ^{1}H NMR 1.12 (t, 3 H, J = 7.5 Hz), 1.18 (t, 3 H, J = 7.5 Hz), 2.70 (q, 2 H, J = 7.5 Hz), 2.73 (q, 2 H, J = 7.5 Hz), 5.31 (s, 2 H), 7.30 (s, 5 H), 9.69 (s, 1 H), 10.21 ppm (bs, 1 H); ir 3260 (NH), 1685, 1655 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.40; H, 6.70; N, 4.89.

2-Benzyloxycarbonyl-5-(2,2-dicyanovinyl)-3,4-diethylpyrrole (6i). The crude water-washed filter cake of 2-benzyloxycarbonyl-3,4-diethyl-5-formylpyrrole (**6h**) prepared from 2-benzyloxycarbonyl-3,4-diethyl-5-methylpyrrole (**6g,** 13.55 g, 0.05 mol), acetic acid (80 ml), and the lead tetraacetate (50 g, moist, 0.11 mol), dissolved and filtered in methylene chloride, then evaporated to dryness, was dissolved in methanol (50 ml) and malononitrile (5.5 g, 0.083 mol) was added. The mixture was heated to boiling on the steam bath, and then treated with methylamine catalyst. The mixture turned orange, and soon went solid with lemon-yellow product. More methanol was added to facilitate the filtration, which was carried out on the chilled solution. The product was rinsed with methanol, and then hexane; yield 10.8 g (64.7%). An analytical sample was recrystallized from methylene chloride–methanol: mp 130.7–131.0 °C; ^{1}H NMR 1.13 (t, 6 H, J = 7.5 Hz), 2.58 (q, 2 H, J = 7.5 Hz), 2.75 (q, 2 H, J = 7.5 Hz), 5.34 (s, 2 H), 7.35 (s, 5 H), 7.52 (s, 1 H), 10.03 (bs, 1 H); ir 3400 (NH), 2220 (C≡N), 1720 (C=O), 1575 cm^{-1} (C=C).

Anal. Calcd for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.61. Found: C, 71.90; H, 5.68; N, 12.61.

5-Bromo-2-(2,2-dicyanovinyl)-3,4-diethylpyrrole (6k). 5-Benzyloxycarbonyl-2-(2,2-dicyanovinyl)-3,4-diethylpyrrole (**6i**), 6.66 g, 0.02 mol) in tetrahydrofuran (150 ml) with 10% palladized charcoal (0.5 g) was stirred overnight at room temperature under 1 atm of hydrogen. (The volume of hydrogen taken up seemed to suggest that some of the dicyanovinyl groups had reduced as well.)

The catalyst was filtered off, and the filtrate evaporated to dryness under vacuum. The resulting solid was dissolved in warm acetic acid (60 ml) and treated with a solution of bromine (6.4 g, 0.04 mol) in acetic acid (10 ml).

Water was added to precipitate the product, and when the oils had solidified, they were filtered off, dissolved in methylene chloride, refiltered, and crystallized from methanol. The yield was 1.76 g (31.6%) of brownish, chunky crystals. An analytical sample was recrystallized from methylene chloride–methanol: mp 142.0–143.0 °C; ^{1}H NMR 1.12 (t, 3 H, J = 7.5 Hz), 1.17 (t, 3 H, J = 7.5 Hz), 2.47 (q, 2 H, J = 7.5 Hz), 2.61 (q, 2 H, J = 7.5 Hz), 7.36 (s, 1 H), 9.54 ppm (bs, 1 H); ir 3250 (NH), 2210 (C≡N), 1580 cm^{-1} (C=C).

Anal. Calcd for $C_{21}H_{12}BrN_3$: C, 51.82; H, 4.35; Br, 28.73; N, 15.11. Found: C, 51.44; H, 4.65; Br, 28.97; N, 15.12.

2-(2,2-Dicyanovinyl)-3,4-diethylpyrrole (6l). 5-Bromo-2-(2,2-dicyanovinyl)-3,4-diethylpyrrole (**6k,** 565.6 mg, 2.03 mmol), anhydrous sodium acetate (2 g), and 10% Pd/C (0.29 g) were hydrogenated overnight in tetrahydrofuran (50 ml) at room temperature and pressure. The solution was filtered to remove catalyst and sodium salts, and evaporated to dryness. The solids were dissolved in methylene chloride, refiltered, and recrystallized from methanol. The product, 164.2 mg (41%), was collected as bright yellow-orange, chunky crystals. An analytical sample was recrystallized from methylene chloride–methanol: mp 146.0–147.5 °C; ^{1}H NMR 1.15 (t, 3 H, J = 7.5 Hz), 1.22 (t, 3 H, J = 7.5 Hz), 2.48 (q, 2 H, J = 7.5 Hz), 2.60 (q, 2 H, J = 7.5 Hz), 7.10 (d, 2 H, J = 4 Hz), 7.44 (s, 1 H), 9.62 ppm (bs, 1 H); ir 3350 (NH), 2210 (C≡N), 1580 cm^{-1} (C=C).

Anal. Calcd for $C_{12}H_{13}N_3$: C, 72.33; H, 6.57; N, 21.09. Found: C, 71.44; H, 6.62; N, 20.85.

3,4-Diethyl-2-formyl-5-methylpyrrole[28] (6d). 2-Ethoxycarbonyl-3,4-diethyl-5-methylpyrrole (**6a,** 62.76 g, 0.3 mol) was dissolved in hot methanol (300 ml) and sodium hydroxide (20 g, 0.5 mol) in water (100 ml) was added. After heating for 3 h on the steam bath, the remaining solvent was evaporated in vacuo.

The sodium salts were dissolved in water, neutralized with a slight deficiency of acetic acid (30 ml), and steam distilled until no further oily 3,4-diethyl-2-methylpyrrole (**6b**) condensed. Sodium carbonate was added to the distillate as a preservative. The oily product was extracted into methylene chloride and dried over anhydrous potassium carbonate. The filtered solution was evaporated under reduced pressure, and the product was diluted with dry *N,N*-dimethylformamide (50 ml).

An excess of phosphorus oxychloride (50 ml) was added to dry, ice-cooled DMF (100 ml) over a 10-min period, followed, over a 15-min period, by the pyrrole solution.

After standing overnight, protected from moisture, the solution was poured onto crushed ice. Solid sodium carbonate was cautiously added, until the solution was almost neutral. After a filtration through Celite to remove minor dark tars, the solution was basified (sodium carbonate or ammonia) and warmed to complete the hydrolysis of the iminium salt (**6c**). The aldehyde product floated to the surface as a dark brown oil, which eventually solidifed. To obtain a light-colored compound, the crude solids were three times recrystallized from aqueous methanol, to give 17.8 g (35.9%) of light tan granules: mp 77.0 –77.5 °C (lit.[28] 74 °C); ^{1}H NMR 1.07 (t, 3 H, J = 7.5 Hz), 1.20 (t, 3 H, J = 7.5 Hz), 2.27 (s, 3 H), 2.38 (q, 2 H, J = 7.5 Hz), 2.69 (q, 2 H, J = 7.5 Hz), 9.42 (s, 1 H), 10.92 ppm (bs, 1 H); ir 3200 (NH), 1610 cm^{-1} (C=O).

Scavenging the mother liquors with malononitrile and methylamine afforded 16.4 g (25.6%) of the dicyanovinylpyrrole, for a total recovered yield of 61.5% of useful products.

2-(2,2-Dicyanovinyl)-3,4-diethyl-5-methylpyrrole (6e). Because of the high solubility of the aldehyde precursor to this compound, it was advantageous in maximizing yields to use the crude aldehyde without purification, or else the mother liquors from the purification of the aldehyde.

3,4-Diethyl-2-formyl-5-methylpyrrole (**6d**) was dissolved in benzene, and an excess of malononitrile was added, followed by methylamine or diethylamine catalyst. The mixture was boiled to drive off the water formed in the reaction, and the boiling was continued until the mixture became thick with crystals. The product was recrystallized from methylene chloride–methanol, giving orange to golden-yellow chunks. An analytical sample was recrystallized from methylene chloride–methanol: mp 160.5–161.4 °C; ^{1}H NMR 1.09 (t, 3 H, J = 7.5 hz), 1.14 (t, 3 H, J = 7.5 Hz), 2.34 (s, 3 H), 2.43 (q, 2 H, J = 7.5 Hz), 2.56 (q, 2 H, J = 7.5 Hz), 7.28 (s, 1 H), 9.38 ppm (bs, 1 H); ir 3300 (NH), 2215 (C≡N), 1590 cm^{-1} (C=C).

Anal. Calcd for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 73.11; H, 7.05; N, 19.94.

2-Chloromethyl-5-(2,2-dicyanovinyl)-3,4-diethylpyrrole (6f). 2-(2,2-Dicyanovinyl)-3,4-diethyl-5-methylpyrrole (**6e,** 2.13 g, 0.01 mol) was dissolved in warm methylene chloride (20 ml). Diethyl ether (10 ml was added, followed at once by the rapid dropwise addition of a solution of sulfuryl chloride (1.4 g, 0.01 mol) in methylene chloride (5 ml) to the magnetically stirred solution, before the starting material could recrystallize. The stirred solution was carefully boiled down, as diethyl ether was slowly added, eventually causing crystallization of the pure product, in a yield of 2.1 g (84.8%). An analytical sample was recrystallized from methylene chloride–ether as shiny yellow needles: mp 138–140.5 °C dec; ^{1}H NMR 1.13 (t, 6 H, J = 7.0 Hz), 2.49 (q, 2 H, J = 7.0 Hz), 2.58 (q, 2 H, J = 7.0 Hz), 4.63 (s, 2 H), 7.44 (s, 1 H), 9.59 ppm (bs, 1 H); ir 3300 (NH), 2210 (C≡N), 1580 cm^{-1} (C=C).

Anal. Calcd for $C_{13}H_{14}ClN_3$: C, 63.03; H, 5.70; Cl, 14.31; N, 16.96. Found: C, 63.13; H, 5.73; Cl, 14.20; N, 16.81.

5,5′-Bis(2,2-dicyanovinyl)-3,3′,4,4′-tetraethyl-2,2′-dipyrromethane (7e). 2-Chloromethyl-5-(2,2-dicyanovinyl)-3,4-diethylpyrrole (**6f,** 136.1 mg, 5.5 mmol) and 2-(2,2-dicyanovinyl)-3,4-diethylpyrrole (**61,** 100.1 mg, 5.03 mmol) were dissolved in methylene chloride (10 ml). Several drops of anhydrous stannic chloride were added, causing a deepening of the color to brown. After a brief warming on the steam bath, the solution was quenched with concentrated HCl (10 ml), followed by water. The organic phase was washed with water, dried over K_2CO_3, and filtered. The solvent was boiled off and replaced with methanol, from which the product, 152.7 mg (74.5%), crystallized. An analytical sample was recrystallized from methylene chloride–methanol: mp 203–209 °C dec; ^{1}H NMR 1.09 (t, 6 H, J = 7.5 Hz), 1.17 (t, 6 H, J = 7.5 Hz), 2.48 (q, 4 H, J = 7.5 Hz), 2.60 (q, 4 H, J = 7.5 Hz), 4.13 (s, 2 H), 7.38 (s, 2 H), 9.38 ppm (s, 2 H); ir 3350 (NH), 2200 (C≡N), 1580 cm^{-1} (C=C); mass spectrum M$^+$ *m/e* 410 (calcd = obsd).

Anal. Calcd for $C_{25}H_{26}N_6$: C, 73.14; H, 6.38; N, 20.47. Found: C, 73.14; H, 6.41; N, 20.48.

5-Acetoxymethyl-2-benzyloxycarbonyl-3,4-diethylpyrrole (6m). 2-Benzyloxycarbonyl-3,4-diethyl-5-methylpyrrole (**6g,** 27.1 g, 0.1 mol) was dissolved in acetic acid (100 ml) containing a little acetic anhydride, and lead tetraacetate (48 g, 0.108 mol) was added in one portion. The mixture was swirled manually, and after a brief induction period, the reagent dissolved, reacting exothermically. The mixture was warmed briefly to 60 °C and then ethylene glycol (5–10 ml) was added to reduce any remaining Pb(IV). Water (400 ml) was next slowly added to precipitate the product in an easily filtered form. The thoroughly washed, filtered solids were dissolved in methylene chloride, separated from the water, refiltered, and crystallized from hexane by displacement of the methylene chloride. The compound crystallized as fine, white needles, 17.6 g (53.4%).

The mother liquors were evaporated, and the residues were dissolved in ethanol (100 ml) and boiled on the steam bath, after addition of concentrated HCl (1 ml), for 1 h. On cooling, the symmetrical dipyrromethane (**7a**), 6.40 g (24.3%), crystallized out, giving an overall yield of useful products of 77.7%. An analytical sample was recrystallized from methylene chloride–hexane: mp 113.5–115.0 °C; ^{1}H NMR 1.10 (t, 3 H, J = 7.5 Hz), 1.13 (t, 3 H, J = 7.5 Hz), 2.00 (s, 3 H), 2.45 (q, 2 H, J = 7.5 Hz), 2.73 (q, 2 H, J = 7.5 Hz), 5.02 (s, 2 H), 5.28 (s, 2 H), 7.32 (s, 5 H), 9.55 ppm (bs, 1 H); ir 3280 (NH), 1730, 1665 cm^{-1} (C=O).

Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.14; H, 7.00; N, 4.25.

5,5′-Bis(benzyloxycarbonyl)-3,3′,4,4′-tetraethyl-2,2′-dipyrromethane (7a). 5-Acetoxymethyl-2-benzyloxycarbonyl-3,4-diethylpyrrole (**6m,** 13.18 g, 0.04 mol) was heated to boiling (steam bath) in 95% ethanol (100 ml). Concentrated hydrochloric acid (1 ml) was added, and the heating was continued for 1 h. The solution was then seeded and allowed to cool. Large masses of colorless, chunky blades crystallized out, first crop 7.05 g (67%). The mother liquors were evaporated to dryness, and the resulting solids recrystallized from methylene chloride–methanol, giving an additional 2.60 g (24.7%) of product. An analytical sample was recrystallized from methylene chloride–methanol: mp 119.5–120.5 °C; ^{1}H NMR 1.05 (t, 6 H, J = 7.5 Hz), 1.12 (t, 6 H, J = 7.5 Hz), 2.44 (q, 4 H, J = 7.5 Hz), 2.72 (q, 4 H, J = 7.5 Hz), 3.77 (s, 2 H), 5.18 (s, 4 H), 7.18 (m, 10 H), 9.89 ppm (bs, 2 H); ir 3320 (NH), 1685, 1650 cm^{-1} (C=O).

Anal. Calcd for $C_{33}H_{38}N_2O_4$: C, 75.25; H, 7.27; N, 5.32. Found: C, 75.22; H, 7.27; N, 5.34.

3,3′,4,4′-Tetraethyl-5,5′-diformyl-2,2′-dipyrromethane (7f). Method A. 5,5′-Bis(benzyloxycarbonyl)-3,3′,4,4′-tetraethyl-2,2′-dipyrromethane (**7a,** 5.26 g, 0.01 mol) in tetrahydrofuran (150 ml) was stirred under hydrogen at atmospheric pressure and room temperature for 3.5 h in the presence of 10% Pd/C (0.42 g) and triethylamine (2 drops). After the catalyst had been filtered off and rinsed with hot THF, the filtrates were evaporated to dryness at reduced pressure, giving greenish-white crystalline crusts of the dicarboxylic acid (**7b**).

The solids were dissolved in *N,N*-dimethylformamide (20 ml) and the resulting solution was heated to boiling under argon. An air-cooled condenser was used to allow the argon stream to carry off the vapors of residual tetrahydrofuran and toluene. The mixture was boiled for 25 min, during which the original greenish color had become a medium brown. The solution was then chilled on ice, and an excess of benzoyl chloride (6.0 g, 5.2 ml, 42.7 mmol) was added dropwise over a 2-min period, causing the color to become an orange-red. Overnight at room temperature, the iminium salt (**7d**) crystallized out. This was filtered off, rinsed with DMF and diethyl ether, and dissolved in water. The aqueous solution was filtered, then warmed on the steam bath and basified with potassium carbonate. A brown oil separated at once, and this soon solidified. The aqueous solution became colorless, and the odor of dimethylamine could be detected. The solids were recovered and recrystallized from 95% ethanol. The yield of this nicely soluble dialdehyde was 1.70 g (54.1%), as light tan, chunky needles. An analytical sample was recrystallized from ethanol containing a trace of triethylamine: mp 179.5–180.5 °C; ^{1}H NMR 1.08 (t, 6 H, J = 7.5 Hz), 1.23 (t, 6 H, J = 7.5 Hz), 2.48 (q, 4 H, J = 7.5 Hz), 2.72 (q, 4 H, J = 7.5 Hz), 3.99 (s, 2 H), 9.53 (s, 2 H), 11.15 ppm (bs, 2 H); ir 3200 (NH), 1610 cm^{-1} (C=O).

Anal. Calcd for $C_{19}H_{26}N_2O_2$: C, 72.58; H, 8.34; N, 8.91. Found: C, 72.47; H, 8.28; N, 8.97.

Method B. 5,5′-Bis(2,2-dicyanovinyl)-3,3′,4,4′-tetraethyl-2,2′-dipyrromethane (**7e,** 0.41 g, 1 mmol) in ethanol (50 ml) was treated with potassium hydroxide (5.0 g) in water (10 ml). The mixture was heated on the steam bath for 3 h and the residue treated with water (150 ml). The product was collected by filtration and crystallized from ethanol to give 0.28 g (89%), mp 178–179.5 °C.

2-Benzyloxycarbonyl-5-(2,2-dicyanovinyl)-3,4-dimethylpyrrole (5e). 2-Benzyloxycarbonyl-5-formyl-3,4-dimethylpyrrole (**5b,** 25.7 g, 0.1 mol) and malononitrile (8 g, 0.1 mol = 6.6 g) were heated to reflux on a steam bath in methanol (250 ml). The solution was removed from the heat source and treated with methylamine stock solution (1 ml, methylamine-saturated ethanol). An orange color formed at once, and the reaction quickly went thick with product. After cooling in an ice bath, the product was recovered by filtration and washed with methanol, then hexane, yield 29 g (95%).

An analytical sample was recrystallized from methylene chloride–methanol: mp 156.0–157.0 °C; ^{1}H NMR 2.13 (3 H, s), 2.28 (3 H, s), 5.35 (2 H, s), 7.36 (5 H, bs), 7.52 (H, s), 9.99 ppm (H, bs); ir 3400 (NH), 2215 (C≡N), 1725 (C=O), 1580 cm^{-1} (C=C).

Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.80; H, 4.95; N, 13.76. Found: C, 70.61; H, 4.97; N, 13.72.

2-*tert*-Butoxycarbonyl-5-(2,2-dicyanovinyl)-3,4-dimethylpyrrole (5i). This was prepared in the manner described above for **5e** from 2-*tert*-butoxycarbonyl-5-formyl-3,4-dimethylpyrrole (**5g**) and malononitrile in methanol with methylamine catalysis and recovered in two crops by crystallization.

An analytical sample was recrystallized from methylene chloride–methanol as beautiful, bright lemon-yellow chunks: mp 142.5–144.0 °C; ^{1}H NMR 1.60 (9 H, s), 2.18 (3 H, s), 2.26 (3 H, s), 7.57 (H, s), 9.46 ppm (H, bs); ir 3400 (NH), 2215 (C≡N), 1690 (C=O), 1570 cm^{-1} (C=C).

Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.32; H, 6.35; N, 15.40.

2-Carboxy-5-(2,2-dicyanovinyl)-3,4-dimethylpyrrole (5t). 2-*tert*-Butoxycarbonyl-5-(2,2-dicyanovinyl)-3,4-dimethylpyrrole (**5i,** 29.09 g, 0.1073 mol) was heated to gentle reflux on a steam bath in 1,2-dichloroethane (105 ml). The solution was filtered hot and treated hot with trifluoroacetic acid (10 ml). The heating was continued for 75 min. The color began to darken with the addition of the acids; within 5 min product began to crystallize, and the mixture eventually became thick.

The lemon-yellow crystals were filtered from the dark greenish-brown solution and rinsed with dichloroethane, methylene chloride, and finally hexane, yield 19.3 g (83.8%).

An analytical sample was recrystallized from tetrahydrofuran–methanol, forming fluffy, lemon-yellow needles: ir 3300 (NH), 3160 (CO_2H), 2230, 2215 (C≡N), 1710 (C=O), 1590 cm^{-1} (C=C); mass spectrum M$^+$ *m/e* 215 (calcd = obsd).

Anal. Calcd for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53. Found: C, 61.30; H, 4.21; N, 19.66.

The compound was too insoluble to make its preparation from the benzyl ester practical.

2-(2,2-Dicyanovinyl)-3,4,5-trimethylpyrrole (1n). 2-Formyl-3,4,5-trimethylpyrrole (1j, 13.7 g, 0.1 mol) and malononitrile (10 g, 0.15 mol) were heated to reflux in methanol (50 ml) on the steam bath. Diethylamine (1 ml) was then added, causing an immediate deepening of color and exothermic boiling. Crystallization began within 2 min. Most of the solvent was allowed to boil away, and displaced with benzene (30 ml). After cooling, the product was recovered by filtration, and rinsed with methanol, then hexane, yield 18.5 g (essentially quantitative) of coarse orange granules.

An analytical sample was recrystallized from methylene chloride–methanol: mp 175.5–177.0 °C; ^{1}H NMR 1.95 (3 H, s), 2.12 (3 H, s), 2.32 (3 H, s), 7.30 (H, s), 9.25 ppm (H, bs); ir 3310 (NH), 2210 cm^{-1} (C≡N).

Anal. Calcd for $C_{11}H_{11}N_3$: C, 71.33; H, 5.99; N, 22.69. Found: C, 71.29; H, 5.99; N, 22.59.

5-Chloromethyl-2-(2,2-Dicyanovinyl)-3,4-dimethylpyrrole (1o). 2-(2,2-Dicyanovinyl)-3,4,5-trimethylpyrrole (**1n,** 3.70 g, 0.02 mol) was dissolved in boiling methylene chloride (45 ml). Dry diethyl ether (40 ml) was added, followed at once, before recrystallization could occur, by the rapid dropwise addition of a solution of sulfuryl chloride (2.80 g, 0.02 mol = 2.70 g) in methylene chloride (7 ml) to the gently swirled solution. The reaction proceeded without any marked change in color, and the product soon crystallized out as bright orange granules. After filtration and ethereal rinse, 2.63 g (59.9%) of product was obtained.

Note: This procedure was only executed once; later experience on analogous compounds suggests that the diethyl ether be omitted until the product is to be isolated.

An analytical sample was recrystallized from methylene chloride–diethyl ether, as yellow needles, material decomposed upon heating: ^{1}H NMR 2.03 (3 H, s), 2.14 (3 H, s), 4.58 (2 H, s), 7.42 (H, s), ca. 9.5 ppm (H, bs); ir 3300 (NH), 2220 (C≡N), 1600 cm^{-1} (C=C).

Anal. Calcd for $C_{11}H_{10}ClN_3$: C, 60.14; H, 4.59; N, 19.13; Cl, 16.14. Found: C, 60.53; H, 4.62; N, 19.00; Cl, 15.87.

5-(2-Cyano-2-methoxycarbonylvinyl)-5′-(2,2-dicyanovin-

yl)-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (2h). 2-Chloromethyl-5-(2,2-dicyanovinyl)-3,4-dimethylpyrrole (**1o,** 1.103 g, 0.005 mol = 1.0975 g) and 2-(2-cyano-2-methoxycarbonylvinyl)-3,4-dimethylpyrrole (**1b,** 1.022 g, 0.005 mol) were dissolved in dry methylene chloride (50 ml) with the exclusion of moisture. Anhydrous stannic chloride (1.3 g) was added, causing an immediate deepening of color to dark brown. After brief warming on the steam bath, the reaction mixture was quenched with concentrated hydrochloric acid, then water. The K_2CO_3-dried, filtered organic phase was boiled down and diluted with methanol, from which the product readily crystallized as yellow flakes, 1.37 g (70.8%).

An analytical sample was recrystallized from methylene chloride–methanol: mp 215–218 °C dec; ^{1}H NMR 2.01 (6 H, s), 2.14, 2.16 (6 H, two overlapping s), 3.82 (3 H, s), 4.03 (2 H, s), 7.33 (H, s), 7.91 (H, s), 9.45 ppm (2 H, bs); ir 3400 (NH), 2220 (C≡N), 1720 (C=O), 1590, 1535 cm^{-1} (C=C).

Anal. Calcd for $C_{22}H_{21}N_5O_2$: C, 68.20; H, 5.46; N, 18.08. Found: C, 67.68; H, 5.37; N, 18.33.

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Registry No.—**1b,** 59434-99-0; **1d,** 59435-00-6; **1e,** 59435-01-7; **1f,** 59435-02-8; **1i,** 2199-46-4; **1j,** 27226-50-2; **1l,** 3855-78-5; **1m,** 59435-03-9; **1n,** 59435-04-0; **1o,** 59435-05-1; **2e,** 21211-62-1; **2g,** 59435-06-2; **2h,** 59435-07-3; **5a,** 4424-76-4; **5b,** 59435-08-4; **5c,** 59435-09-5; **5d,** 59435-10-8; **5e,** 59435-11-9; **5f,** 50634-31-6; **5g,** 59435-12-0; **5h,** 59435-13-1; **5i,** 59435-14-2; **5j,** 59435-15-3; **5k,** 34463-41-7; **5l,** 59435-16-4; **5n,** 59435-17-5; **5o,** 59435-18-6; **5p,** 59435-19-7; **5q,** 59435-20-0; **5r,** 59435-21-1; **5s,** 59435-22-2; **5t,** 59435-23-3; **6a,** 16200-50-3; **6b,** 34874-30-1; **6c,** 59435-24-4; **6d,** 41728-28-3; **6e,** 59435-25-5; **6f,** 59435-26-6; **6g,** 59435-27-7; **6h,** 59435-28-8; **6i,** 59435-29-9; **6k,** 59435-30-2 **6l,** 59435-31-3; **6m,** 59435-32-4; **7a,** 59435-33-5; **7b,** 59435-34-6; **7d,** 59435-35-7; **7e,** 59448-45-2; **7f,** 59435-36-8; methyl cyanoacetate, 105-34-0; benzyl oximinoacetoacetate, 27331-98-2; 3-methyl-2,4-pentanedione, 815-57-6; ethyl cyanoacetate, 105-56-6; *tert*-butyl acetoacetate, 540-88-5; *tert*-butyl oximinoacetoacetate, 14352-65-9; benzyl alcohol, 100-51-6; *p*-anisyl alcohol, 105-13-5; benzhydrol, 91-01-1; malononitrile, 109-77-3.

References and Notes

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Chemistry of 2-(Chloromethyl)furans. Reaction of 2-(Chloromethyl)furans with Aqueous Potassium Cyanide and Other Nucleophiles[1]

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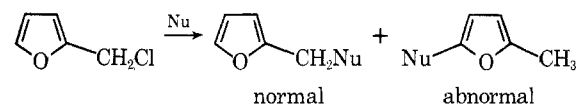
The reaction of 2-(chloromethyl)furan with aqueous cyanide solution was investigated. Experimental evidence is provided for the existence of 5-methylene-2,5-dihydro-2-furonitrile as a reaction intermediate. The effect of temperature, concentration, and solvent on the nature of the products was also examined. Analogous studies were carried out with 4-*tert*-butyl-2-(chloromethyl)furan. A number of 2-(chloromethyl)furans with substituents at various positions of the furan nucleus were synthesized and the reactions of these substituted furans with aqueous cyanide were investigated. The substituents were found to have a noticeable effect on the distribution of the isomeric nitriles obtained. The observed changes could be rationalized in terms of the electronic effects of the substituents. The reactions of 4-*tert*-butyl-2-(chloromethyl)furan with selected nucleophiles were also examined. A mechanism for the nucleophilic displacements of 2-(chloromethyl)furans is proposed.

The reactions of 2-(chloromethyl)furan (**1a**) with various nucleophiles in aqueous and nonaqueous media has generated considerable interest[1,3–20] since Kirner[3] reported the first practical synthesis of the compound more than 45 years ago. An intriguing feature of these reactions is that they often yield 2,5-disubstituted (abnormal) rather than 2-substituted furans (normal).



1a **2a** **3a**

As a result of previous studies, several facts have been established: (1) the so-called rearrangement takes place during