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(4) (a) The structure of this compound is consistent with its ir, nmr, and mass spectra low resolution; (b) C, H, and N combustion analyses within 0.4% of theory were obtained for this substance.

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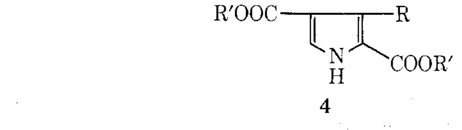
## A Convenient Synthesis of 3-Substituted Pyrrole-2,4-dicarboxylic Acid Esters[1]

*Summary:* Pyrrole compounds **4** were synthesized by the reaction of isocyanoacetates with aldehydes in the presence of DBU in good yields.

*Sir:* In the course of our studies on the synthesis of amino acids and related compounds using isocyano compounds, we have investigated the reaction of isocyanoacetates **2** with aldehydes as a source of 3-substituted pyrrole-2,4-dicarboxylic acids. Schöllkopf, *et al.*, have detected diethyl 3-methylpyrrole-2,4-dicarboxylate from the reaction of acetaldehyde and ethyl isocyanoacetate in the presence of metallic base during the synthesis of ethyl $\alpha$-formylaminoacrylate.[2]

We have carried out the condensation of alkyl isocyanoacetates with a variety of aliphatic and aromatic aldehydes in THF solution, using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base (Table I). Spectral and analytical data confirm the pyrrole structures **4**. The reaction does not require anhydrous conditions.

The reaction presumably involves Michael addition of isocyanoacetate **2** to the $\alpha$-isocyanoacrylate **3**; **4** (R = H; R′ = $CH_3$) was obtained in 60% yield from the condensation of **2** and methyl $\alpha$-isocyanocinnamate.[3] However, the pyrrole was not obtained from the reaction of methyl $\alpha$-formamidocinnamate with **2**.



**Typical Procedure.** To a mixture of methyl isocyanoacetate (1.98 g, 0.02 mol) and DBU (3.0 g, 0.02 mol) dissolved in THF (30 ml) was added dropwise benzaldehyde (1.06 g, 0.01 mol) in THF (10 ml) at 45–50° for a period of 15 min with stirring. After stirring for 5 hr at same temperature, the reaction mixture was neutralized with acetic acid and then the solvent was removed under reduced pressure. The resulting residue was extracted with ethyl acetate and the extract was washed with hydrochloric aicd and water, dried, and then evaporated *in vacuo*. The crystals (1.3 g) recrystallized from aqueous methanol showed mp 183–185°. The mass spectrum of this compound showed the $M^+$ at $m/e$ 259 and the ir spectrum (nujol) showed an NH band at 3370 $cm^{-1}$ and two ester C═O bands at 1735 and 1700 $cm^{-1}$, respectively. The nmr spectrum ($CDCl_3$) indicated the presence of two ester groups ($CH_3$) [$\delta$ 3.58 (s) and 3.51 (s)], NH [12.04 (br)], pyrrole C-5 H [7.52 (d)], and aromatic H [7.25 (s)].

**Table I**
**Preparation of Pyrrole Derivative 4**

| R | R′ | Conditions<br>Temp, °C | Hr | Mp, °C[a,b] | Yield, % |
|---|---|---|---|---|---|
| H | $CH_3$ | 50–55 | 1 | 125–126 | 67 |
| $CH_3$ | $(CH_3)_2CH$ | 50–55 | 1 | 74–76 | 71 |
| $CH_3CH_2$ | $CH_3CH_2$ | 45–50 | 1 | 87–89[c] | 63 |
| Ph | $CH_3$ | 45–50 | 5 | 183–185 | 50 |
| 4-Methoxy Ph | $CH_3$ | 55–60 | 4 | 146–147 | 57 |
| 3,4,5-Trimethoxy Ph | $CH_3$ | 10–15 | 2 | 189–192 | 59 |
| 3-Pyridine | $CH_3$ | 50–55 | 3 | 212–213 | 60 |
| 3-Indole | $CH_3$ | 50–55 | 3 | >250 | 58 |

[a] Recrystallization from aqueous ethanol or methanol. [b] Analyses agreed with the calculated values within ±0.3%. [c] Lit. mp 88.5–89°: R. Grigg, A. W. Johnson, and T. W. F. Wasley, *J. Chem. Soc.*, 359 (1963).

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## Melanin. I. Kinetics of the Oxidative Cyclization of Dopa to Dopachrome

*Summary:* Kinetics of the ring-closure of dopaquinone (**2**) to cyclodopa (**3**) have been studied *via* chronoamperometry of dopa (**1**) in the pH range of 5.0–6.0 and at temperatures of 15, 25, 30, and 37°; the rapidity of the cyclization process is attributed to a very favorable positive activation entropy; at pH 6.6 and above, cyclic voltammetry of dopa clearly demonstrates the formation of 5,6-dihydroxyindole (**5**).

*Sir:* Biogenesis of the important mammalian pigment melanin[1-4] from 3,4-dihydroxyphenylalanine (**1**, dopa) has long been considered to proceed *via* the series of fugitive intermediates illustrated in Scheme I, a pathway originally postulated by Raper[5] and not yet adequately characterized. Mason[6] has estimated the rate constant for decarboxylative rearrangement of dopachrome (**4**) to 5,6-dihy-