assigning configuration and conformation in molecules characterized by the 1,3-diene entity.[10,11]

Experimental Section

Materials. Dienes 1–6 were prepared by the thermolysis of cyclobutenes.[12]

Dienes 7 and 8 are known compounds,[7] but they were prepared as follows: thermolysis of 3-methyl-3-cyanocyclobutene afforded 8. The dehydration of 4-cyano-3-hydroxypent-1-ene, which was obtained from the condensation of acrolein with ethyl cyanide, gave mainly 7, contaminated with 8. The treatment of diene 8 with iodine in benzene at room temperature gave an equilibrium mixture of 7 and 8. Both dienes had 60-MHz NMR spectra identical with those reported.[7] 7: NMR (360 MHz, C_6D_6) δ 6.12 (dd, J = 1, 11 Hz, 1 H), 5.87 (m, small couplings and J = 11, 16.5 Hz, 1 H), 4.93 (d, J = 11 Hz, 1 H), 4.84 (d, J = 16.5 Hz, 1 H), 1.21 (s, 3 H). 8: NMR (360 MHz, C_6D_6) δ 6.63 (m, small couplings and J = 11, 17 Hz, 1 H), 5.73 (d, J = 11 Hz, 1 H), 4.90 (d, J = 17 Hz, 1 H), 4.89 (d, J = 11 Hz, 1 H), 1.25 (s, 3 H).

Diene 9 is already known.[13] However, it was conveniently prepared as a single isomer by hydrolysis of the ethyl ester[14] obtained by condensation of acrolein with ethyl propionate followed by dehydration of the resulting hydroxy ester. The Z isomer, diene 10, was produced by the thermal electrocyclic reaction of 1-methylcyclobut-2-enecarboxylic acid. It is unstable and isomerizes quantitatively to the more stable isomer 9 under acidic conditions. 9: NMR (360 MHz, C_6D_6) δ 7.34 (dd, J = 1, 11.5 Hz, 1 H), 6.26 (m, small couplings and J = 10, 11.5, 17 Hz, 1 H), 5.09 (m, 2 H), 1.73 (s, 3 H). 10: NMR (360 MHz, C_6D_6) δ 7.56 (m, small couplings and J = 11, 17 Hz, 1 H), 6.13 (dd, J = 1, 11 Hz, 1 H), 5.09 (m, 2 H), 1.76 (s, 3 H).

The sodium dienecarboxylate 11 was obtained by dissolving 9 in NaOD solution. Sodium carboxylate 12 was prepared by the thermolysis of sodium 1-methylcyclobut-2-enecarboxylate in D_2O. When the isomerization of 10 to 9 was interrupted with base, a mixture of 11 and 12 was formed. No isomerization of these two salts was observed. 11: NMR (360 MHz, 15% NaOD/D_2O, HDO, δ 4.67, as standard) δ 6.24 (d, J = 11 Hz, 1 H), 6.13 (m small couplings and J = 10, 11, 16 Hz, 1 H), 4.94 (d, J = 16 Hz, 1 H), 4.82 (d, J = 10 Hz, 1 H), 1.30 (s, 3 H). 12: NMR (360 MHz, 15% NaOD/D_2O, HDO, δ 4.67, as standard) δ 6.01 (m, small couplings and J = 11, 17 Hz, 1 H), 5.38 (d, J = 11 Hz, 1 H), 4.53 (d, J = 11 Hz, 1 H), 1.32 (s, 3 H), one proton signal was hidden by the solvent peak.

Diene 13 is known[15] but was readily obtained by acid-catalyzed isomerization of its Z isomer 14. Similarly, the latter is known,[13a] and was prepared, in the present instance, by heating methyl 1-methylcyclobut-2-enecarboxylate in benzene. 13: NMR (360 MHz, C_6D_6) δ 7.30 (d, J = 11 Hz, 1 H), 6.35 (m, small couplings and J = 10, 11, 17 Hz, 1 H), 5.17 (d, J = 17 Hz, 1 H), 5.05 (d, J = 10 Hz, 1 H), 3.40 (s, 3 H), 1.82 (s, 3 H). 14: NMR (360 MHz, C_6D_6) δ 7.71 (m, 1 H), 6.13 (d, J = 11 Hz, 1 H), 5.13 (d, J = 15 Hz, 1 H), 5.12 (d, J = 11.5 Hz, 1 H), 3.33 (s, 3 H), 1.80 (s, 3 H).

Procedure for NOE Difference Spectroscopy. Samples where prepared by dissolving the diene in deuterated benzene or in deuterium oxide containing NaOD in an NMR tube. Degassing to remove oxygen was effected by passing a stream of dry, pure N_2 through the solution for 5 min. Tubes were sealed and examined. The irradiation of protons on substituents invariably caused an NOE enhancement of the signal of the contiguous proton by some 8–23% (Table I).

All the spectra were recorded at 360 MHz on a Bruker AM 360 or WM 360 spectrometer. Depending on the sample, the decoupler power (DP) was selected in the range 22–33 L. The relaxation time was 4–5 times greater than the longest T_1 of the diene. The % NOEs was calculated by using the irradiated inverted peaks as the reference. Error limits were ±2%.

Acknowledgment. We are grateful to Dr. M. Geckle and Mr. A. Pinto for assistance with the NMR measurements and the U.S. and Swiss National Science Foundations for financial support of this research.

(10) To the authors' knowledge, no such use has been reported so far (cf.: Neuhaus, D.; Williamson, M. *The Nuclear Overhauser Effect in Structural and Conformational Analysis*; Verlag Chemie: Weinheim, 1989).

(11) For a recent application to aldoximes and ketoximes, see: Heinish, G.; Holzer, W. *Tetrahedron Lett.* **1990**, *31*, 3109.

(12) Houk, K. N.; Spellmeyer, D. C.; Jefford, C. W.; Rimbault, C. G.; Wang, Y.; Miller, R. D. *J. Org. Chem.* **1988**, *53*, 2125. Jefford, C. W.; Wang, Y.; Houk, K. N., unpublished work.

(13) (a) House, H. O.; Rasmusson, G. H. *J. Org. Chem.* **1961**, *26*, 4278. (b) Bond, F. T.; Ho, C.-Y. *J. Org. Chem.* **1976**, *41*, 1421.

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Synthesis of 3*H*-Pyrrolo[1,2-*c*]imidazole-3,5(2*H*)-diones

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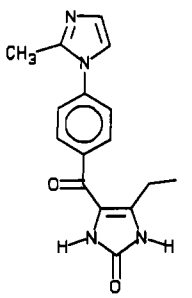
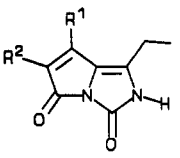
During the course of a program aimed toward the development of nitrogen acylated prodrugs[1] of cardiotonic agent 1,[2] it was noted that acylation by certain anhydrides produced unexpected fluorescent byproducts. These fluorescent compounds were determined to be 3*H*-pyrrolo[1,2-*c*]imidazole-3,5(2*H*)-diones, 2. This heterocyclic system has not been previously reported.[3] Several of the pyrrolo[1,2-*c*]imidazoledione derivatives derived from compounds such as 1 displayed cardiotonic properties similar to the parent [4-(1*H*-imidazol-1-yl)benzoyl]-imidazolones.[4] The synthesis and activities of these analogues will be reported elsewhere. This paper describes a synthetic study of the novel system 2 by the reaction of imidazolones 3 with anhydrides 4 (Scheme I). A ring-opening reaction in which pyrrolo[1,2-*c*]imidazoledione 2d is treated with aqueous NaOH is also reported.



1



2

Imidazolone 3a was prepared in an 87% yield by Friedel–Crafts reaction of 5-ethyl-2-oxoimidazole-4-carboxylic acid with CH_3CO_2H in a manner similar to the reported synthesis of compound 3b.[5] Reactions of 3 with 4 using excess NaH at 0–65 °C in DMF afforded varying mixtures of 2 and 5 (Scheme I). The intermediate N-acylated derivatives 5 could be isolated, or the crude reaction mixtures completely deacylated with $NaOCH_3$ in MeOH to afford

(1) Detailed results will be published elsewhere. For a preliminary review of the chemistry and biology, see: Erhardt, P. W.; Hagedorn, A. A., III. U.S. Patent 4,743,612, 1988.

(2) Hagedorn, A. A., III; Erhardt, P. W.; Lumma, W. C., Jr.; Wohl, R. A.; Cantor, E.; Chou, Y.-L.; Ingebretsen, W. R.; Lampe, J. W.; Pang, D.; Pease, C. A.; Wiggins, J. *J. Med. Chem.* **1987**, *30*, 1342.

(3) The saturated 1*H*-pyrrolo[1,2-*c*]imidazole-3,5-dione ring system has been reported: Butler, D. E.; Leonard, J. D. U.S. Patent 4,582,838, 1986. For a general review of pyrrolo[1,2-*c*]imidazole derivatives, see: Preston, P. N. Condensed Imidazoles, 5-5 Ring Systems. In *The Chemistry of Heterocyclic Compounds*; Wiley: New York, 1986; p 42.

(4) Shaw, K. J. U.S. Patent 4,937,258, 1990.

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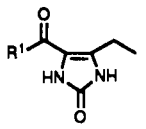
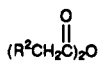
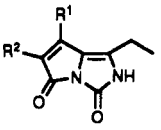
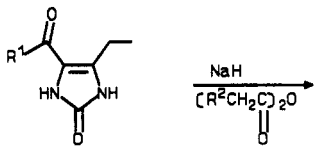
0022-3263/91/1956-0858$02.50/0

Table I. Reaction of Imidazolones 3 with Anhydrides 4

entry	imidazolone	anhydride	product[a]	yield,[b] %
				
1	**3a**: $R^1 = CH_3$	**4b**: $R^2 = CH_3$	**2a**: $R^1 = CH_3$; $R^2 = CH_3$	42
2	**3a**: $R^1 = CH_3$	**4c**: $R^2 = C_6H_5$	**2b**: $R^1 = CH_3$; $R^2 = C_6H_5$	36
3	**3b**: $R^1 = C_6H_5$	**4a**: $R^2 = H$	**2c**: $R^1 = C_6H_5$; $R^2 = H$	6
4	**3b**: $R^1 = C_6H_5$	**4b**: $R^2 = CH_3$	**2d**: $R^1 = C_6H_5$; $R^2 = CH_3$	72
5	**3b**: $R^1 = C_6H_5$	**4c**: $R^2 = C_6H_5$	**2e**: $R^1 = R^2 = C_6H_5$	80

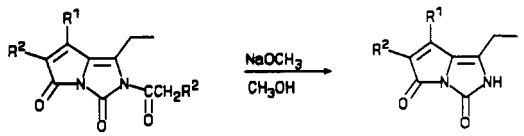
[a] All new compounds have satisfactory analyses and ^1H NMR spectra. [b] Yields are based on pure products isolated by flash chromatography over silica gel, or by recrystallization of crude products.

Scheme I



3a $R^1 = CH_3$
3b $R^1 = C_6H_5$

4a $R^2 = H$
4b $R^2 = CH_3$
4c $R^2 = C_6H_5$

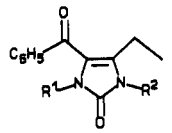


5a-e **2a-e**

a: $R^1 = CH_3$, $R^2 = CH_3$
b: $R^1 = CH_3$, $R^2 = C_6H_5$
c: $R^1 = C_6H_5$, $R^2 = H$
d: $R^1 = C_6H_5$, $R^2 = CH_3$
e: $R^1 = C_6H_5$, $R^2 = C_6H_5$

the pyrrolo[1,2-*c*]imidazolediones **2** in 6–80% yields (Table I). The phenylacetyl moieties of **5b** and **5e** are more labile than the propionyl analogues of **5a** and **5d**. Thus, the ratios of **2**:**5** were higher in these crude reaction mixtures, and deacylation could be carried out using milder conditions (refluxing MeOH). Alternatively, reaction of the isolated monosodium salts of the imidazolones **3** with 1.5 equiv of the anhydrides **4** could be used in some cases to afford the pyrrolo[1,2-*c*]imidazolediones **2** with only minor formation of the N-acylated intermediates. Although lower yields of **2** were obtained, these reaction conditions were useful for the preparation of some base-sensitive analogues.[4]

It appears that the reactions proceed through intermediate formation of a monoacylated or diacylated imidazolone (e.g. **6a** or **6b**, respectively) followed by intramolecular condensation.[6] The intermediacy of the mono-



6a: $R^1 = COCH_2CH_3$, $R^2 = H$
6b: $R^1 = R^2 = COCH_2CH_3$
6c: $R^1 = R^2 = COCH_3$

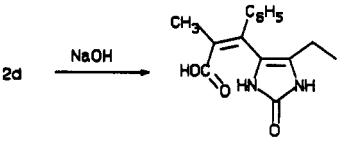
(6) The other monoacylated regioisomer does not form to an appreciable extent and often cannot be detected in the reaction mixture. The unexpected regioselectivity of the monoacylated imidazalones has been explained by a reversible, selective deacylation of the diacylated imidazalone. The structures of the N-1 regioisomers are supported by NMR NOE studies and X-ray crystallographic data.[1]

Table II. Fluorescence Data[a]

compd	fluorescence emission λ_{max}	fluorescence excitation[b] λ_{max}
2a	480	370
2b	510	385
2c	475	390
2d	480	380
2e	520	400

[a] In MeOH. [b] Fluorescence excitation spectra were taken by fixing on the fluorescence emission maximum.

Scheme II



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acylated and diacylated imidazolones can be observed by TLC. In addition, propionylimidazolone **6a** was isolated and subsequently converted to pyrrolo[1,2-*c*]-imidazolediones **2d** by reaction with NaH in DMF. Lower temperatures and shorter reaction times suppress the cyclization and maximize the yields of the acylated imidazolones. For example, imidazolone **6a** was isolated in a 47% yield by the reaction of the monosodium salt of **3b** with 1.5 equiv of propionic anhydride at 40 °C for 18 h. Excess NaH and anhydride can be used to obtain the diacylated imidazolones.

Reactions with acetic anhydride gave poor yields of the pyrrolo[1,2-*c*]imidazolediones. Under the same conditions that were used with propionic anhydride to afford **5d** in a 95% yield, the corresponding acetyl derivative **5c** was isolated in a 9% yield along with 75% of the diacylated imidazolone **6c**. Higher temperatures and longer reaction times led to decomposition products. The sluggish reactivity of acetic anhydride compared to propionic and other substituted anhydrides has been noted previously in the Perkin reaction and has been attributed to the decreased reactivity of the α-methyl compared to the α-methylene.[7]

The 3*H*-pyrrolo[1,2-*c*]imidazole-3,5(2*H*)-diones **2** are stable, yellow crystalline compounds with UV–visible absorption λ_{max} = 245–305 and 370–400 nm. The compounds also display a characteristic fluorescence with λ^{em}_{max} = 475–520, λ^{ex}_{max} = 370–400 nm (Table II). The structure of **2d** is additionally supported by mass spectral analysis, and ^1H and ^{13}C NMR. Assignment of the ^{13}C NMR

(7) Johnson, J. R. *Org. React.* **1942**, *1*, 210–265.

spectrum was aided by APT and HETCOR experiments (Table III). Definitive structural proof was obtained by X-ray crystallographic analysis (Figure 1).[8]

3*H*-Pyrrolo[1,2-*c*]imidazole-3,5(2*H*)-dione (**2d**) was found to be both acid- and base-sensitive. Treatment of **2d** with dilute acid (e.g. 0.1 M HCl) at room temperature resulted in the formation of numerous compounds, whereas basic conditions afforded a single product. Refluxing **2d** with 0.1 M sodium hydroxide afforded a 79% yield of vinylimidazole **7** (Scheme II). The structure of **7** is supported by mass spectral analysis and ^{13}C and ^{1}H NMR. NOE studies are consistent with the *Z* stereochemistry.

Experimental Section

General. Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Elemental analyses were performed by the Berlex Analytical Section, Cedar Knolls, NJ, or Microlit Laboratories, Caldwell, NJ. ^{1}H, ^{13}C, APT, and HETCOR NMR spectra were recorded with a Varian XL-300 (300 MHz) spectrometer. Tetramethylsilane was used as the internal standard in all solvents. FAB mass spectra were recorded on a Kratos MS25 system. Ultraviolet spectra were obtained on a Hewlett-Packard 8450A spectrophotometer. Fluorescence emission spectra and fluorescence excitation spectra were recorded on a Perkin-Elmer 204-A fluorescence spectrophotometer using a xenon power supply.

5-Ethyl-1,3-dihydro-4-(1-oxoethyl)imidazol-2-one (3a). A mixture of 5-ethyl-2-oxoimidazole-4-carboxylic acid[5] (10.0 g, 64.0 mmol) and glacial acetic acid (3.2 g, 53.3 mmol) was stirred in a mixture of polyphosphoric acid (80 g) and methanesulfonic acid (80 g) while the temperature was gradually (ca. 2 h) raised to 85 °C, where it was maintained for 16 h. The reaction mixture was cooled to room temperature, poured onto ice (300 g), and brought to pH = 7 with 50% aqueous NaOH. The suspension was extracted with *n*-BuOH (5 × 150 mL). The combined *n*-BuOH extracts were evaporated under reduced pressure, and the resulting solid was recrystallized from CH_3CN, affording 7.1 g (87%) of **3a** as amber needles: mp 228–230 °C; ^{1}H NMR (DMSO-d_6) δ 1.14 (t, 3 H), 2.26 (s, 3 H), 2.69 (quar, 2 H), 10.3 (br s, 1 H), 10.9 (br s, 1 H). Anal. Calcd for $C_7H_{10}N_2O_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.37; H, 6.46; N, 18.06.

1-Ethyl-6,7-dimethyl-3*H*-pyrrolo[1,2-*c*]imidazole-3,5-(2*H*)-dione (2a). NaH (60% dispersion in mineral oil, 0.65 g, 16.2 mmol) was washed with hexanes and added to a stirred suspension of **3a** (0.50 g, 3.2 mmol) in DMF (75 mL). The temperature was brought to 65 °C, and the reaction mixture was stirred for 1 h. Propionic anhydride (2.1 g, 16.1 mmol) was added neat, and the mixture stirred for 4 h at 65 °C. The DMF was removed in vacuo, and the residue was partitioned between CH_2Cl_2 (100 mL) and 1 M HCl (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), the combined organics were dried (Na_2SO_4) and evaporated, and the residue was dissolved in MeOH (100 mL). Sodium methoxide (0.22 g, 4.0 mmol) was added, and the solution was stirred for 2 h at room temperature. The MeOH was evaporated, and the residue was partitioned between CH_2Cl_2 (100 mL) and 1 M HCl (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 75 mL), the combined organics were dried (Na_2SO_4) and evaporated, and the residue was purified by column chromatography eluting with 4% MeOH/CH_2Cl_2 to afford 0.26 g (42%) of **2a** as a yellow solid. An analytical sample was obtained by recrystallization from CH_3CN: mp 244–254 °C dec; ^{1}H NMR (DMSO-d_6) δ 1.15 (t, 3 H), 1.73 (s, 3 H), 2.08 (s, 3 H), 2.46 (quar, 2 H), 10.46 (br s, 1 H); UV λ_{max} (MeOH) 275 (ϵ 2960), 370 (ϵ 8960). Anal. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.49; H, 6.29; N, 14.57. Found: C, 62.63; H, 6.15; N, 14.56.

1-Ethyl-7-methyl-6-phenyl-3*H*-pyrrolo[1,2-*c*]imidazole-3,5(2*H*)-dione (2b). NaH (60% dispersion in mineral oil, 0.22 g, 5.5 mmol) was washed with hexanes and added to a stirred suspension of **3a** (0.34 g, 2.2 mmol) in DMF (50 mL). After 1 h the reaction mixture was cooled to 0 °C, and then phenylacetic anhydride[9] (1.23 g, 4.8 mmol) in DMF (10 mL) was added over the course of 1 h. The mixture was stirred for an additional 0.5 h at 0 °C and then warmed to room temperature, and the DMF was removed in vacuo (30 °C, 0.1 mm). The residue was partitioned between CH_2Cl_2 (50 mL) and 1 M HCl (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organics were dried (Na_2SO_4) and concentrated. The residue was dissolved in MeOH (50 mL), sodium methoxide (0.06, 1.1 mmol) was added, and the solution was stirred for 30 min at room temperature. The MeOH was evaporated, and the residue was partitioned between CH_2Cl_2 (50 mL) and 1 M HCl (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), the combined organics were dried (Na_2SO_4) and evaporated, and the residue purified by column chromatography eluting with 2% MeOH/CH_2Cl_2 to afford 0.20 g (36%) of **2b** as a yellow solid. An analytical sample was obtained by recrystallization from CH_3CN: mp 237–240 °C; ^{1}H NMR (DMSO-d_6) δ 1.22 (t, 3 H), 2.29 (s, 3 H), 2.58 (quar, 2 H), 7.45 (m, 5 H), 10.8 (br s, 1 H); UV λ_{max} (MeOH) 245 (ϵ 11400), 385 (ϵ 13500). Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found C, 71.01; H, 5.53; N, 11.01.

1-Ethyl-7-phenyl-3*H*-pyrrolo[1,2-*c*]imidazole-3,5(2*H*)-dione (2c). NaH (60% dispersion in mineral oil, 0.92 g, 23 mmol) was washed with hexanes and then added to a mechanically stirred solution of **3b** (1.00 g, 4.6 mmol) in DMF (40 mL). The reaction mixture was heated to 65 °C and stirred for 1 h, acetic anhydride (2.38 g, 23 mmol) was then added neat, and the foamy reaction mixture was stirred at 65 °C for 18 h. The reaction mixture was cooled to room temperature and concentrated by distillation in vacuo. The residue was partitioned between 1 M HCl (50 mL) and CH_2Cl_2 (75 mL). The acid layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organics were dried (Na_2SO_4), evaporated, and purified by column chromatography, eluting with 30–40% Et_2O/hexane to afford 1.04 g (75%) of the diacetylated imidazolone **6c** and 0.12 g (9%) of **5c**.

6c: Off-white plates from Et_2O/hexanes; mp 91–93 °C; ^{1}H NMR ($CDCl_3$) δ 1.07 (t, 3 H), 2.55 (s, 3 H), 2.64 (quar, 2 H), 2.72 (s, 3 H), 7.46 (m, 2 H), 7.58 (m, 1 H), 7.83 (m, 2 H). Anal. Calcd for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 64.42; H, 5.37; N, 9.48.

5c: white colonies from Et_2O/hexanes; mp 168–170 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 (t, 3 H), 2.70 (s, 3 H), 2.82 (quar, 2 H), 6.11 (s, 1 H), 7.50 (m, 5 H). Anal. Calcd for $C_{16}H_{14}N_2O_3 \cdot 0.15H_2O$: C, 67.43; H, 5.06; N, 9.83. Found: C, 67.55; H, 4.97; N, 9.92.

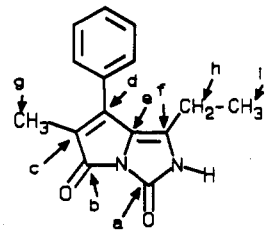
To a suspension of **5c** (100 mg, 0.35 mmol) in MeOH (10 mL) at 0 °C was added $NaOCH_3$ (19 mg, 0.35 mmol). The resulting yellow solution was stirred for 5 min at 0 °C, added to 0.1 M HCl (30 mL), and extracted with CH_2Cl_2 (3 × 25 mL). The combined CH_2Cl_2 extracts were dried (Na_2SO_4), evaporated, and purified by column chromatography eluting with 3% MeOH/CH_2Cl_2 to afford 53 mg (6% overall) of **2c** as a yellow solid. Recrystallization from CH_3CN gave yellow needles: mp 211–213 °C; ^{1}H NMR (DMSO-d_6) δ 1.15 (t, 3 H), 2.42 (quar, 2 H), 6.08 (s, 1 H), 7.54 (m, 5 H), 10.9 (br s, 1 H); UV λ_{max} (MeOH) 285 (ϵ 1460), 380 (ϵ 300). Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.59; H, 5.12; N, 11.43.

1-Ethyl-6-methyl-7-phenyl-3*H*-pyrrolo[1,2-*c*]imidazole-3,5(2*H*)-dione (2d). Method A. In Situ Salt Formation with Excess NaH. NaH (60% dispersion in mineral oil, 4.6 g, 115 mmol) was washed with hexanes and then added to a stirred solution of **3b** (5.0 g, 23 mmol) in DMF (500 mL). The reaction mixture was heated to 65 °C and stirred for 1 h, propionic anhydride (15.0 g, 115 mmol) was then added neat, and the reaction mixture was sitrred at 65 °C for 18 h. The reaction mixture was cooled to room temperature and concentrated by distillation in vacuo. The residue was partitioned between 1 M HCl (500 mL) and CH_2Cl_2 (500 mL). The acid layer was extracted with CH_2Cl_2 (2 × 200 mL), and the combined organics were dried (Na_2SO_4), evaporated, and purified by column chromatography eluting with 10–20% Et_2O/hexane to afford 6.8 g (95%) of **5d** as an orange solid. An analytical sample was obtained by recrystallization from Et_2O/hexanes: mp 86–87 °C; ^{1}H NMR ($CDCl_3$) δ 1.06 (t, 3 H), 1.21 (t, 3 H), 1.95 (s, 3 H), 2.61 (quar, 2 H), 3.10 (quar, 2 H), 7.38

(8) X-ray crystallographic analysis performed by J. C. Huffman, Molecular Structure Center, Indiana University.

(9) Cabre-Castellvi, J.; Palomo-Coll, A.; Palomo-Coll, A. L. *Synthesis* 1981, 616.

Table III. Carbon-Proton Correlation Obtained from HETCOR and APT



carbon	^{13}C chemical shift, ppm	^{1}H chemical shift, ppm
a	147.17	
b	162.87	
c	125.95	
d	141.26	
e	128.85	
f	118.06	
g	9.05	1.83 (s, 3 H)
h	17.93	2.22 (q, 2 H, J = 7.5 Hz)
i	12.26	1.02 (t, 3 H, J = 7.5 Hz)

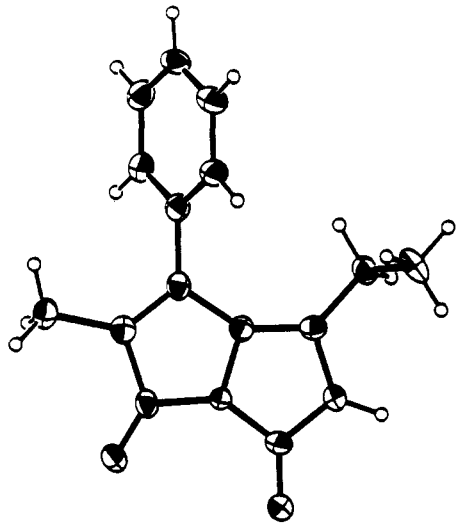


Figure 1. ORTEP drawing of the X-ray structure of compound **2d**.

(m, 2 H), 7.49 (m, 3 H). Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.50; H, 5.84; N, 8.93.

A solution of **5d** (5.50 g, 17.7 mmol) and $NaOCH_3$ (0.96 g, 17.7 mmol) in MeOH (150 mL) was stirred for 1 h. The reaction mixture was added to 0.1 M HCl (300 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined CH_2Cl_2 extracts were dried (Na_2SO_4), evaporated, and recrystallized from CH_3CN to afford 3.41 g (72% overall) of **2d** as yellow needles: mp 253–266 °C dec; ^{1}H NMR (DMSO-d_6) δ 1.02 (t, 3 H), 1.83 (s, 3 H), 2.22 (quar, 2 H), 7.50 (m, 5 H), 10.65 (br s, 1 H); ^{13}C NMR (DMSO-d_6) δ 162.87, 147.17, 141.26, 130.88, 129.50, 128.85, 128.79, 128.38, 125.95, 118.06, 17.93, 12.26, 9.05; MS m/z 255 $(M + H)^+$; UV λ_{max} (MeOH) 304 (ϵ 7350), 380 (ϵ 8660). Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.83; H, 5.50; N, 11.08.

Method B. Isolation and Reaction of Monosodium Salt. $NaOCH_3$ (125 mg, 2.31 mmol) was added to a stirred suspension of **3b** (500 mg, 2.31 mmol) in MeOH (25 mL), and the mixture was refluxed for 1 h. The yellow solution was cooled, the solvent was evaporated, and the yellow solid was dried in vacuo to afford the sodium salt (550 mg, 100%). Propionic anhydride (0.45 g, 3.46 mmol) was added to a stirred suspension of the sodium salt in DMF (20 mL), and the mixture was heated at 50 °C for 40 h. The DMF was removed by distillation in vacuo, and the residue was purified by column chromatography, eluting with 2% $MeOH/CH_2Cl_2$ to afford 188 mg (32%) of **2d** as a yellow solid. The ^{1}H NMR spectrum of **2d** was identical with **2d** isolated above.

1-Ethyl-6,7-diphenyl-3*H*-pyrrolo[1,2-*c*]imidazole-3,5-(2*H*)-dione (2e). NaH (60% dispersion in mineral oil, 0.28 g, 7.0 mmol) was washed with hexanes and added to a stirred suspension of **3b** (0.30 g, 1.4 mmol) in DMF (5 mL). After stirring 0.5 h at room temperature, phenylacetic anhydride (1.78 g, 7.0 mmol) was added neat and the mixture was stirred for 2 h at room temperature, over which time the reaction mixture became a bright red homogeneous solution. The reaction mixture was partitioned between CH_2Cl_2 (25 mL) and 1 M HCl (35 mL). The acid layer was extracted with CH_2Cl_2 (2 × 25 mL), and the combined organics were dried (Na_2SO_4) and evaporated in vacuo. The residue was refluxed for 18 h in MeOH (30 mL), cooled, and evaporated, and the residue was purified by column chromatography, eluting with a 2% $MeOH/CH_2Cl_2$ to afford 0.35 g (80%) of **2e** as a yellow solid. An analytical sample was obtained by recrystallization from $MeOH/Et_2O$/hexanes: mp 249–251 °C; ^{1}H NMR (DMSO-d_6) δ 1.14 (t, 3 H), 2.36 (quar, 2 H), 7.18–7.42 (m, 10 H), 10.00 (br s, 1 H); UV λ_{max} 245 (ϵ 15200), 400 (ϵ 13400). Anal. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86. Found C, 75.54; H, 5.02; N, 8.72.

5-Benzoyl-4-ethyl-1,3-dihydro-1-propionyl-2*H*-imidazol-2-one (6a). $NaOCH_3$ (187 mg, 3.46 mmol) was added to a stirred suspension of **3b** (750 mg, 3.47 mmol), and the mixture was refluxed for 1 h. The yellow solution was cooled, the solvent was evaporated, and the yellow solid was dried in vacuo. Propionic anhydride (0.63 g, 4.84 mmol) was added to a stirred solution of the sodium salt in DMF (30 mL), and the mixture was heated at 40 °C for 18 h. The DMF was removed by distillation in vacuo, and the residue was purified by column chromatography, eluting with 2% $MeOH/CH_2Cl_2$ to afford 0.44 g (47%) of **6a** as an off-white solid. An analytical sample was obtained by recrystallization from CH_3CN: mp 192–194 °C; ^{1}H NMR (DMSO-d_6) δ 0.91 (t, 3 H), 1.06 (t, 3 H), 2.28 (quar, 2 H), 2.88 (quar, 2 H), 7.48 (t, 2 H), 7.57 (m, 1 H), 7.69 (m, 2 H), 11.4 (br s, 1 H). Anal. Cacld for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.09; H, 5.91; N, 10.34.

(*Z*)-3-(5-Ethyl-2,3-dihydro-2-oxo-1*H*-imidazol-4-yl)-2-methyl-3-phenyl-2-propenoic Acid (7). A mixture of **2d** (0.20 g, 0.79 mmol) and 0.1 M NaOH (30 mL) was refluxed for 1 h. The reaction mixture was cooled to room temperature and then brought to pH = 1 with 1 M HCl. The precipitate was filtered and dried to afford 0.17 g (79%) of **7** as an off-white solid. An analytical sample was obtained by recrystallization from $MeOH/CH_3CN$: mp 228–230 °C; ^{1}H NMR ($CDCl_3$) δ 0.97 (t, 3 H), 1.87 (s, 3 H) 2.10 (quar, 2 H), 7.16 (m, 2 H), 7.35 (m, 3 H), 9.39 (s, 1 H), 9.85 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 170.87, 154.05, 138.81, 133.36, 130.56, 129.10, 128.06, 127.72, 121.39, 116.45, 17.51, 17.36, 12.72. MS m/z 273 $(M + H)^+$. An NOE difference experiment with irradiation of the methyl protons showed enhancement of the ortho aromatic protons, indicating a cis relationship between the methyl and phenyl groups. Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.25; H, 5.92; N, 10.62.

X-ray Crystallographic Analysis of 2d. A yellow orthogonal prism crystal of **2d** was obtained by recrystallization from CH_3CN: $C_{15}H_{14}N_2O_2$; space group $P2_1/n$; cell constants a = 8.740 (3) Å, b = 7.779 (3) Å, c + 21.208 (8) Å, B = 117.74 (1) Å, V = 1276.17 Å^3, and D_c = 1.324 g cm^{-3} (Z = 4). A computer controlled Picker four-circle goniostat equipped with a Furnas Monchromator (HOG crystal) and Picker X-ray generator (MoKα radiation, λ = 0.71069 Å) was employed in the study, and the sample was cooled to −155 °C. A total of 1680 unique intensities were observed. Of these, 1329 were observed ($F > 2.3\sigma F$) and corrected for Lorentz and polarization effects. The structure was solved using the MULTAN78 interactive crystallographic program and refined by using a full-matrix least-squares method. The function minimized was $\sum\omega(|F_o| - |F_c|)^2$ with $\omega = 1/(\sigma F)^2$ to give an unweighted residual value of 0.046 and a weighted value of 0.048.

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Supplementary Material Available: Tables containing bond lengths, bond angles, fractional atomic coordinates, and thermal parameters for the X-ray analysis of **2d** (4 pages). Ordering information is given on any current masthead page.