Synthesis of Some Novel 1,3-Dihydro-2*H*-benzimidazol-2-ylidenes

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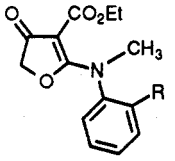
Several years ago,[2,3] we reported the synthesis and biological activity of a series of 2(5*H*)-furanones **2** which were obtained by the rearrangement of 2-(substituted amino)-4,5-dihydro-4-oxo-3-furancarboxylic acids **1**, in the presence of *N,N*-bis(2-oxo-3-oxazolidinyl)phosphorodiamidic chloride (BOP-Cl) and a substituted aromatic amine (Scheme I). During efforts to investigate the scope of this reaction, the preparation of 2-[(2-aminophenyl)amino]-furan-4-one **6a** was required. In the present study, we wish to report our synthetic efforts in this regard which led to the unprecedented formation of certain 2-substituted benzimidazoles (Scheme II).

Chemistry

The 2-[(2-nitrophenyl)amino]furanone **5a** is readily accessible by a base-catalyzed cyclocondensation of ethyl 4-chloroacetoacetate (**4a**) and 2-nitrophenyl isocyanate (**3a**), utilizing a method similar to one previously described.[4] The syntheses of the 5-methyl and 5,5-dimethylfuranones **5b** and **5c** were accomplished by treatment of isocyanate **3a** with ethyl 4-bromo-3-oxopentanoate (**4b**) or ethyl 4-bromo-4-methyl-3-oxopentanoate (**4c**), respectively.[4] The 4-methylphenyl analogue **5d** was similarly prepared from 4-methyl-2-nitrophenyl isocyanate (**3b**) and ethyl 4-chloroacetoacetate (**4a**). *N*-Methyl compound **5f** was obtained by treatment of furanone **5a** with iodomethane and potassium carbonate in DMF.



5f, R = NO_2
6f, R = NH_2

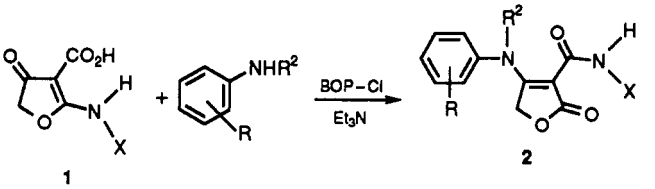
Reduction of the nitro group of **5a** by catalytic transfer hydrogenation (CTH) (10% Pd/C, cyclohexene, EtOH, reflux 2.5 h) afforded benzimidazole **7a** (7%), in addition to the desired **6a** (67%). Extending the reflux period resulted in a gradual increase in **7a** at the expense of **6a** until, after 80 h, 69% of **7a** was obtained.

Reaction conditions were then varied in order to try to increase the rate of the rearrangement, and progress was followed by TLC. The addition of triethylamine increased the rates of both reduction and rearrangement but caused more side reactions. After 24 h, a mixture of **7a** and a new compound, the cyclized 3-(benzimidazol-2-ylidene) lactone **8a**, was obtained. When heating under reflux was continued for another 24 h, none of **7a** remained and **8a** was the major product. Use of the higher boiling hexanol in place of ethanol accelerated not only the rates of reduction and rearrangement but also that of lactonization. For example, after 0.5 h at reflux, a mixture of amine **6a**, benzimidazole **7a**, and lactone **8a** was obtained, while 24 h of heating produced **8a** as the major product along with some **6a** but no intermediate **7a**. Ethanol was the preferred CTH solvent for the rest of the study.

In view of the observed effect of triethylamine on the course of the reaction, it was postulated that both the reduction and the rearrangement steps would be enhanced by substituting the usual 10% Pd/C catalyst with palladium hydroxide. However, when $Pd(OH)_2/C$ (Pearlman's catalyst) was utilized, no change in the rate was noted. Furthermore, when **6a** was heated in refluxing ethanol without palladium catalyst or cyclohexene, **7a** was cleanly produced in 76% yield after 48 h, thus excluding the involvement of palladium in the rearrangement process.

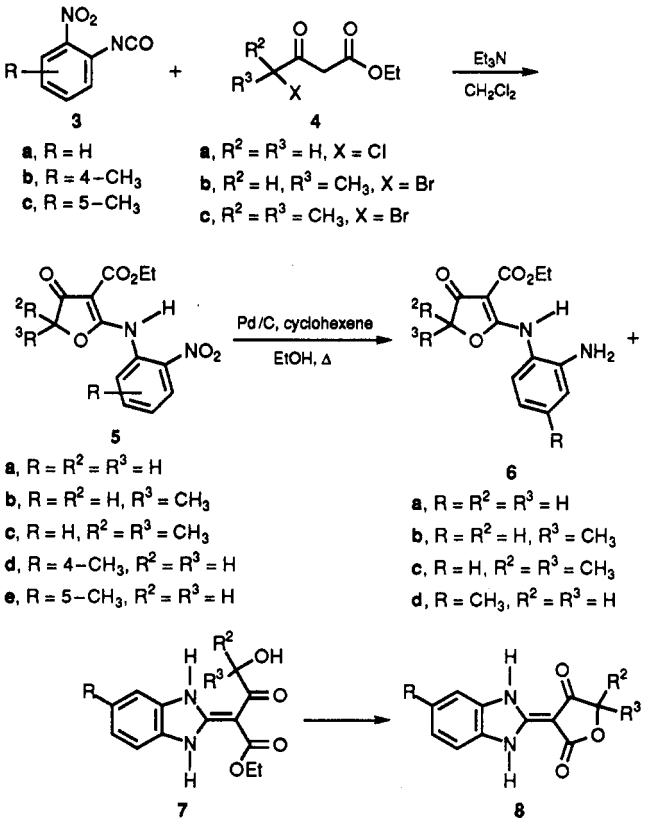
At this point, several other derivatives were made in order to expand the range of the reaction, to examine the effect of structural changes on the course of the rear-

Scheme I



X = substituted Ph or *trans*-2-phenylcyclopropyl

Scheme II



(1) Present address: National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD 20892.
(2) Mack, R. A.; Georgiev, V. St. *J. Org. Chem.* **1987**, *52*, 477.
(3) Georgiev, V. St.; Mack, R. A.; Walter, D. J.; Radov, L. A.; Baer, J. E. *Helv. Chim. Acta* **1987**, *70*, 1526.
(4) Mack, R. A.; Zazulak, W. I.; Radov, L. A.; Baer, J. E.; Stewart, J. D.; Elzer, P. H.; Kinsolving, C. R.; Georgiev, V. St. *J. Med. Chem.* **1988**, *31*, 1910.

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Table I. Benzimidazoles 7 from CTH of Furanones 5

compd	R	R^2	R^3	time of reflux (h)	yield of 7 (%)
5a	H	H	H	80	69
5b	H	H	CH_3	140	27
				70	53[a]
5c	H	CH_3	CH_3	400	b
5d	4-CH_3	H	H	75	58
5e	5-CH_3	H	H	75	69[c]

[a] Doubled cyclohexene amount. [b] Only 8c was produced. [c] Yield of 7d.

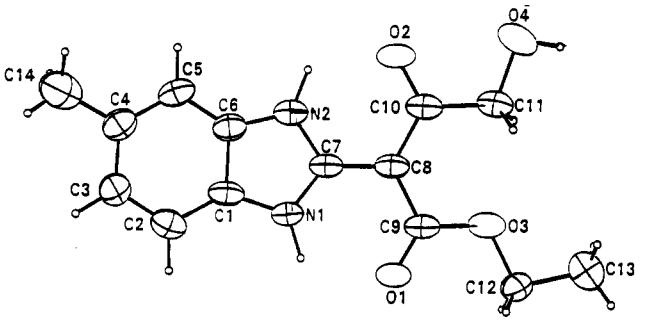
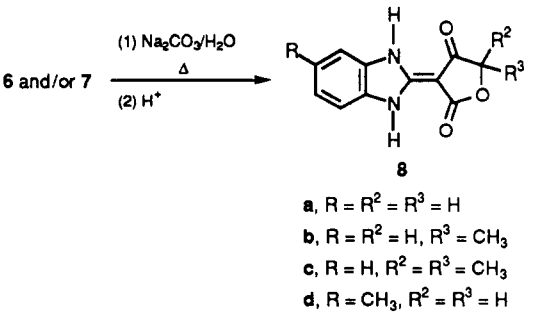


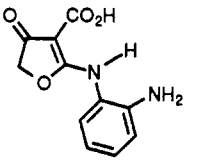
Figure 1. Thermal-ellipsoid plot of 7d.

rangement, and to gain some insight as to the mechanism involved. Each of the nitrophenyl analogues 5 was treated under CTH conditions for 2–6 h to obtain the aminophenyl analogues 6. To prepare the desired benzimidazoles 7 directly from 5, prolonged reflux was necessary and all reactions were monitored by TLC until none of the amine 6 remained. The 5-methyl analogue 5b required 140 h at reflux to complete the reduction and rearrangement but returned only a 27% yield of benzimidazole 7b (Table I). The major product was identified as 8b, which gradually precipitated during reflux. If the amount of cyclohexene was doubled at the start, only 70 h of reflux was required and the yield of 7b increased to 53%. Since the reduction step is so much faster than the rearrangement step, and the latter should not involve cyclohexene in the mechanism, we are uncertain of the reason for this result. The 5,5-dimethyl compound 5c took much longer, needing 17 days to complete the rearrangement, and produced only the cyclized lactone 8c quantitatively. None of the desired open-chain intermediate 7c was ever observed but was assumed to be rapidly cyclized to 8c under the reaction conditions. Reduction of the *N*-methyl analogue 5f required only 6 h to obtain amine 6f. However, prolonged reflux caused decomposition and produced none of the desired benzimidazole 7. Treatment of 5d under CTH conditions required the periodic addition of cyclohexene to drive the reduction step to completion. After 75 h, a 58% yield of the desired benzimidazole 7d was obtained. X-ray crystallography showed the aromatic methyl to be syn to the hydroxymethylcarbonyl side chain; a thermal-ellipsoid plot of 7d is presented in Figure 1. Under similar conditions, 5e (the 5-methyl regioisomer of 5d) also provided 7d in 69% yield (vide infra).

An attempt at hydrolyzing ester 6a in aqueous sodium carbonate solution at reflux for 4 h produced none of the expected carboxylic acid 9. Instead, it readily afforded the lactone 8a in very good yield (Scheme III). Although the open-chain analogue 7a could not be detected, it was shown to be a possible intermediate by conversion to 8a under the same reaction conditions. Similarly, the 5,5-dimethyl analogue 6c gave an 88% yield of 8c. The *N*-methyl compound 6f, however, produced 2-amino-*N*-methylaniline as the sole isolated product, probably via nucleophilic displacement by OH^- at the furan C2.

Scheme III





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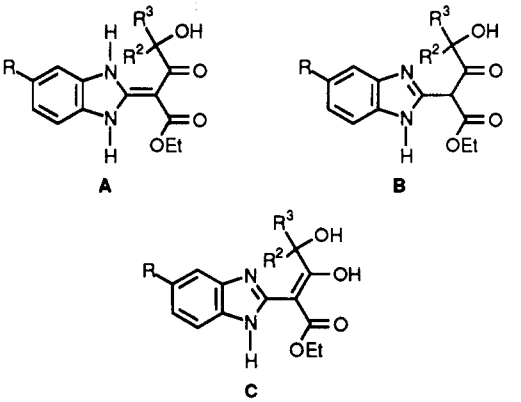
On the basis of these results, a slightly different procedure was used for the synthesis of lactones 8. The nitrophenyl derivatives 5 were first reduced under the usual CTH conditions for 3–72 h, and the resulting mixture of amine 6 and benzimidazole 7 was then heated under reflux in aqueous sodium carbonate solution to provide 8 in 69–81% yield.

Structure

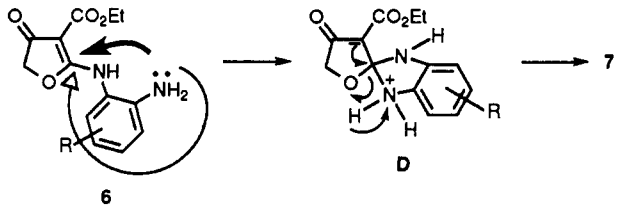
In addition to the X-ray crystal structure determination of 7d, the structures of benzimidazoles 7 were further supported by elemental and spectroscopic analyses. Moreover, since tautomers of the benzimidazole molecule have been known for many years, and spectroscopic methods for distinguishing between them have recently been reported,[5-9] it was felt prudent to compare our results with the currently available data. All ^1H and ^{13}C NMR and IR analyses are in accordance with observed parameters which allow for distinguishing between three possible structures:



Only one set of signals was observed in the NMR spectra of each derivative 7. The absence of an α-methine proton

(5) Huang, Z.-T.; Wang, M.-X. *Tetrahedron* **1992**, *48*, 2325.
(6) Wang, H.-T.; Wang, X.-J.; Huang, Z.-T. *Chem. Ber.* **1990**, *123*, 2141.
(7) Badawey, E. A. M.; Rida, S. M.; Soliman, F. S. G. *J. Heterocycl. Chem.* **1989**, *26*, 405.
(8) Huang, Z.-T.; Liu, Z.-R. *Synthesis* **1987**, 357.
(9) Nardi, D.; Pennini, R.; Tajana, A. J. *Heterocycl. Chem.* **1975**, *12*, 825.

Scheme IV



6 D 7

and the appearance of two NH protons in the ^1H NMR rule out structure **B**. In the ^{13}C NMR, the presence of both ketone and ester carbonyl carbons precludes the enol structure **C**. Due to the combined effects of the two electron-withdrawing carbonyls and two electron-releasing nitrogens, a highly polarized exocyclic double bond results in which the carbon α to the carbonyls has increased electron density. This is evident from the upfield shift of its signal (δ 84) in the ^{13}C spectra.[8] The presence of intramolecular hydrogen bonding between the NH protons and the carbonyls is supported by the large downfield shift of the NH protons (δ 13.28–12.03) in the ^1H spectra.[5] In addition, the conjugation of the carbonyls with the two nitrogens through the double bond as well as hydrogen bonding contributions result in a large bathochromic shift of both carbonyl absorptions in the IR spectra (ketone, 1608–1613; ester 1635–1645 cm^{-1}).[5,9]

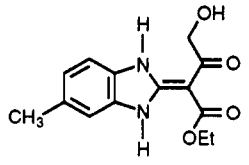
Similar spectroscopic evidence supports a ketene aminal type of structure like **A** for lactones **8**.

Modeling studies[10] demonstrated significantly lower energy for **A** (MOPAC ΔH = −125.27 kcal) vs **B** (MOPAC ΔH = −114.98 kcal) and thus also support **A** as the more favored isomer.

Discussion

It was envisioned that the mechanism of the rearrangement involves the Michael addition of the 2-aminophenyl nitrogen of **6** to the furan C2, leading to a spirobenzimidazole intermediate **D** (Scheme IV) which then undergoes furan ring opening to give **7**.

In the case of the (4-methylphenyl)furanone **6d**, the lack of facial specificity in the attack and/or the possibility of a retro-addition would be expected to result in a scrambling of the aromatic methyl group, producing a mixture of regioisomers **7d** and **7e**. However, **7d** was



7e

isolated exclusively. In order to address the possibility of some unexpected stereocontrol[11] in the mechanism, the reaction was repeated with isomer **5e** in place of **5d**, under identical conditions. Suprisingly, this also provided **7d** as the sole product (Table I).

Extensive 500-MHz ^1H and ^{13}C NMR experiments were then performed in several different solvents and over different temperature ranges to study the behavior of **7d** in solution. At 25–100 °C, no significant changes were noted. However, in THF a gradual broadening of the 2-proton NH peak was seen below 25 °C until at −73 °C four sharp NH peaks appeared as two widely separated doublets (δ 13.28 and 12.54). In addition, the aromatic protons now appeared as two identical overlapping sets of signals. The aromatic carbon signals were also doubled in the ^{13}C spectrum. Comparison of the aromatic proton coupling constants with the NH doublets showed no correlation and therefore ruled out any long-range coupling interactions. Finally, the nuclear magnetic double resonance (NMDR) technique[12] was utilized. When one set of NH doublets was irradiated at 32 dB, its signal collapsed while the other NH doublet was reduced in intensity by about 40%. These results are supportive of a mixture of **7d** and **7e** undergoing rapid NH proton exchange and equilibration via an amidine intermediate (e.g., **B**) at room temperature and resulting in only one set of time-averaged proton signals. At −73 °C, however, the exchange process is slowed sufficiently so that contributions from each of **7d** and **7e** individually are now evident. Such an equilibration route is further evidenced by bond orders, obtained from the MOPAC analysis,[10] which show partial double bond character for both C2–N bonds (the bond order being 1.20 for both bonds), partial single bond character for the exocyclic C2=C2′ bond (the bond order = 1.26), and less than a single bond character for N–H bonds (bond orders being 0.86 and 0.85). It is therefore highly probable that both regioiosmers were produced in solution during the CTH reactions of either **5d** or **5e**. The isolation of **7d** exclusively in both instances can be most easily explained by a preferential equilibrium during crystallization: **7e** ⇌ **B** ⇌ **7d**↓.[13]

The formation of the keto lactones **8** is believed to occur via a thermally driven and base-catalyzed nucleophilic displacement by the terminal hydroxy group at the ester carbonyl. In the absence of added base (CTH conditions), the facility of this cyclization increased with increasing steric bulk at the methylene group (Thorpe–Ingold effect).[14] The structural assignment for **8d**, in particular, was based on that of **7d**. However, since a similar tautomeric equilibrium in solution could be expected for **8d**, one cannot rule out the possibility that the other regioisomer was obtained instead.[15]

In summary, we have presented a useful synthetic entry into benzimidazoles **7** and **8**. A ketene aminal structure has been determined for both series (**7a,b,d** and **8a–d**), and reasonable mechanisms for their formation have been proposed. The notable solution behavior of **7d**, as revealed by NMR studies, suggests that the preparation of other aryl-substituted derivatives may present similar difficulties in structure elucidation.

Experimental Section

General Methods. Melting points were determined in open capillary tubes on a Thomas-Hoover apparatus and are uncor-

(10) Modeling studies were performed using SYBYL molecular modeling software program version 5.41c by Tripos Associates. Tautomeric structures **A** and **B** for compound **7d** were configurationally minimized followed by conformational analysis using SEARCH. The lowest energy conformers thus obtained were further minimized by the MOPAC program, version 5 (QCPE 455).

(11) For example, hydrogen bonding between the ester carbonyl and the secondary amino NH in furanones **5** and **6** is known.[16] In **6d**, such a situation could lock its conformation such that one product would be more favored than the other.

(12) (a) Forsen, S.; Hoffman, R. A. *J. Chem. Phys.* **1963**, *39*, 2892. (b) *Ibid.* **1964**, *40*, 1189.

(13) Using SYBYL the calculated ground-state molecular energies for **7d** and **7e** are 26.670 and 27.056 kcal/mol, respectively.

(14) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; John Wiley & Sons, Inc.: New York, 1965; p 191.

(15) No crystals of **8d** could be obtained for X-ray analysis.

(16) Eichhorn, K.; Fischer, K. F. *Acta Crystallogr.* **1985**, *C41*, 1316.

rected. The following were used for spectral characterization: IR spectra, Nicolet-MX-1-FT spectrometer; NMR spectra, Varian EM-360-A (60 MHz) and Bruker IBM 200 SY Fourier Transform (200 MHz) spectrometers, TMS as an internal standard; mass spectra, Hewlett-Packard HP-5988A. All ^{1}H NMR are 60 MHz, and all ^{13}C spectra are 50 MHz, unless noted otherwise. IR were run in KBr pellets. Anhydrous toluene and DMF were obtained from Aldrich. Absolute ethanol was from U.S. Industrial Chemicals Co. Other solvents were reagent grade obtained from Fisher Scientific. All solvents were used as received. Compounds **4b** and **4c** were prepared according to previously reported procedures.[4]

Preparation of 5-Methyl-2-nitrophenyl Isocyanate (3c). *This reaction should be performed in a well-ventillated fume hood.* While protected by a $CaCl_2$ drying tube, a solution of 2-nitro-5-methylaniline (5 g; 32.86 mmol) in 200 mL of dry toluene was added over 1 h to 25 mL of 20% phosgene in toluene (1.93 M; 48.25 mmol) at −10 to 0 °C (ice/salt bath). The mixture was stirred for 15 min and then heated over 30 min to 95–100 °C and held for 2 h. N_2 was bubbled through for 1 h while cooling. The reaction mixture was concentrated (in the hood) *in vacuo* to dryness. The residue was extracted with hot hexane (200 mL). The hexane was cooled, filtered, and evaporated *in vacuo* to obtain a yellow oil which rapidly solidified upon cooling. Yield: 5 g (85%). IR: 2260 cm^{-1}. MS (CI): *m/z* 179 $(M + H)^+$.

Preparation of 4,5-Dihydro-5-methyl-2-[(2-nitrophenyl)-amino]-4-oxo-3-furancarboxylic Acid Ethyl Ester (5b). Under N_2, triethylamine (29.1 mL; 0.2088 mol) was added rapidly over 5 min to a solution of 2-nitrophenyl isocyanate (**3a**) (30.5 g; 0.1858 mol) in 1.36 L of CH_2Cl_2 at 0–5 °C. Ethyl 4-bromo-3-oxopentanoate (**4b**) (39.5 g; 0.177 mol) in 240 mL of CH_2Cl_2 was then added over 4 h and stirring continued overnight at rt. The solvent was evaporated *in vacuo*, and the yellow residue was stirred in 500 mL of 1 N HCl for 18 h. The solid was filtered off, rinsed with H_2O and petroleum ether, and dried on the filter. Recrystallization from ethyl acetate provided 31.8 g (63%) of product. Mp: 174–176 °C. IR: 3420, 1659, 1600, 1520 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 12.28 (bs, 1H), 8.37–7.07 (m, 4H), 4.79 (q, 1H, J = 7.4 Hz), 4.38 (q, 2H, J = 7.2 Hz), 1.58 (d, 3H, J = 7.4 Hz), 1.39 (t, 3H, J = 7.2 Hz). Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15. Found: C, 54.91; H, 4.68; N, 9.08.

The following compounds were prepared using procedures similar to that used for **5b**:

4,5-Dihydro-2-[(2-nitrophenyl)amino]-4-oxo-3-furancarboxylic Acid Ethyl Ester (5a). Yield: 82%. Mp (toluene): 204–209 °C dec. IR: 1695, 1655, 1569 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 12.28 (br, 1H), 8.48–7.29 (m, 4H), 4.75 (s, 2H), 4.44 (q, 2H, J = 7.5 Hz), 1.41 (t, 3H, J = 7.5 Hz). Anal. Calcd for $C_{13}H_{12}N_2O_6$: C, 53.43; H, 4.14; N, 9.59. Found: C, 53.53; H, 4.19; N, 9.59.

4,5-Dihydro-2-[(4-methyl-2-nitrophenyl)amino]-4-oxo-3-furancarboxylic Acid Ethyl Ester (5d). Yield: 89%. Mp (CH_3CN): dec >220 °C. IR: 3420, 1700, 1662, 1530 cm^{-1}. ^{1}H NMR (200 MHz; $CDCl_3$): δ 12.16 (s, 1H), 8.04 (d, 1H, J_m = 1.4 Hz), 7.88 (d, 1H, J_o = 8.6 Hz), 7.47 (dd, 1H, J_o = 8.6 Hz, J_m = 1.4 Hz), 4.72 (s, 2H), 4.44 (q, 2H, J = 7.1 Hz), 2.45 (s, 3H), 1.40 (t, 3H, J = 7.1 Hz). Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15. Found: C, 54.85; H, 4.65; N, 9.44.

4,5-Dihydro-2-[(5-methyl-2-nitrophenyl)amino]-4-oxo-3-furancarboxylic Acid Ethyl Ester (5e). Yield: 71%. Mp (CH_3CN): 197–198 °C. IR: 1696, 1671, 1593, 1505 cm^{-1}. ^{1}H NMR (200 MHz; $CDCl_3$): δ 12.35 (s, 1H), 8.16 (d, 1H, J = 8.3 Hz), 7.83 (d, 1H, J = 1.4 Hz), 7.14 (dd, 1H, J_o = 8.3 Hz, J_m = 1.4 Hz), 4.76 (s, 2H), 4.45 (q, 2H, J = 7.1 Hz), 2.49 (s, 3H), 1.41 (t, 3H, J = 7.1 Hz). Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15. Found: C, 55.32; H, 4.66; N, 9.40.

4,5-Dihydro-5,5-dimethyl-2-[(2-nitrophenyl)amino]-4-oxo-3-furancarboxylic Acid Ethyl Ester (5c). Purified on the Waters Prep LC/System 500A ($CHCl_3$). Yield: 49%. Mp (*i*-PrOH): 122–124 °C. IR: 1700, 1660, 1515 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 12.23 (br, 1H), 8.33–7.06 (m, 4H), 4.38 (q, 2H, J = 7.4 Hz), 1.53 (s, 6H), 1.41 (t, 3H, J = 7.4 Hz). Anal. Calcd for $C_{15}H_{16}N_2O_6$ + 0.11% H_2O (Karl Fischer titration) + 0.08% $(CH_3)_2CHOH$ (GC analysis): C, 56.14; H, 5.03; N, 8.73. Found: C, 55.75; H, 5.07; N, 8.63.

Preparation of 4,5-Dihydro-2-[(2-nitrophenyl)methyl-amino]-4-oxo-3-furancarboxylic Acid Ethyl Ester (5f). Under N_2, a mixture of **5a** (0.5 g; 1.71 mmol), iodomethane (0.22 mL; 3.53 mmol), and K_2CO_3 (0.3 g; 2.17 mmol) in anhyd DMF (10 mL) was heated at 60–70 °C for 15 min. The solvent was evaporated *in vacuo*, and the residue was partitioned between H_2O and $CHCl_3$. The layers were separated, and the aqueous phase was washed with $CHCl_3$. The combined organic extracts were washed sequentially with H_2O, 1 N HCl, and H_2O. The extracts were then dried over Na_2SO_4 and evaporated *in vacuo* to obtain an orange oil which solidified on standing. The solid was recrystallized from 2-propanol (slow) to obtain 450 mg (86%) of the desired product. Mp: 116–117 °C. IR: 1720, 1714, 1652, 1528 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.23–8.28 (m, 4H), 4.51 (s, 2H), 3.93 (q, 2H, J = 7.0 Hz), 3.51 (s, 3H), 1.14 (t, 3H, J = 7.0 Hz). Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15. Found: C, 54.62; H, 4.71; N, 8.97.

Preparation of 2-[(2-Aminophenyl)amino]-4,5-dihydro-5,5-dimethyl-4-oxo-3-furancarboxylic Acid Ethyl Ester (6c). A mixture of **5c** (22.94 g; 71.62 mmol), cyclohexene (21.1 g; 256.8 mmol), and 1.15 g of 10% Pd/C in 900 mL of absolute EtOH was heated at reflux for 3.5 h. The cooled reaction mass was filtered through Celite, evaporated *in vacuo*, and recrystallized from EtOH. Yield: 18.07 g (88%). Mp: >175 °C dec. IR: 3395, 3320, 1652, 1620 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 9.88 (br, 1H), 7.44–6.54 (m, 4H), 4.32 (q, 2H, J = 7.4 Hz), 3.78 (br, 2H), 1.47 (s, 6H), 1.38 (t, 3H, J = 7.4 Hz). Anal. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.06; H, 6.25; N, 9.65. Found: C, 61.95; H, 6.27; N, 9.59.

The following compounds were prepared by similar methods, from the corresponding nitrophenyl precursors **5**, and were purified by flash chromatography through silica gel:

2-[(2-Aminophenyl)amino]-4,5-dihydro-4-oxo-3-furancarboxylic Acid Ethyl Ester (6a). Eluent: $CHCl_3$/MeOH (95:5). Yield: 67%. Mp (EtOH): 172–174 °C. IR: 3320, 3240, 1686, 1645 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 9.93 (br, 1H), 7.50–6.73 (m, 4H), 4.63 (s, 2H), 4.39 (q, 2H, J = 7.4 Hz), 3.85 (br, 2H), 1.40 (t, 3H, J = 7.4 Hz). Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.54; H, 5.38; N, 10.68. Found: C, 59.68; H, 5.38; N, 10.66.

2-[(2-Aminophenyl)amino]-4,5-dihydro-5-methyl-4-oxo-3-furancarboxylic Acid Ethyl Ester (6b). Eluent: CH_2Cl_2/MeOH (97:3). Yield: 31%. Mp (EtOH): 171–173 °C. IR: 3415, 3335, 3230, 1650, 1625 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 9.93 (s, 1H), 7.62–6.72 (m, 4H), 4.83 (q, 1H, J = 7.0 Hz), 4.46 (q, 2H, J = 7.0 Hz), 3.98 (br, 2H), 1.67 (d, 3H, J = 7.0 Hz), 1.50 (t, 3H, J = 7.0 Hz). Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.65; H, 5.85; N, 10.09.

2-[(2-Amino-4-methylphenyl)amino]-4,5-dihydro-4-oxo-3-furancarboxylic Acid Ethyl Ester (6d). Eluent: same as in **6b**. Yield: 43%. Mp (EtOH): 203–205 °C dec. IR: 3330, 3250, 1660, 1630 cm^{-1}. ^{1}H NMR (200 MHz; $CDCl_3$): δ 9.73 (s, 1H), 7.16 (d, 1H), 6.86–6.66 (m, 2H), 4.60 (s, 2H), 4.26 (q, 2H, J = 7.2 Hz), 2.31 (s, 3H), 1.33 (t, 3H, J = 7.2 Hz). Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.88; H, 5.84; N, 10.12.

4,5-Dihydro-2-[(2-aminophenyl)methylamino]-4-oxo-3-furancarboxylic Acid Ethyl Ester (6f). Eluent: same as in **6b**. Yield: 59%. No analytically pure sample could be obtained, due to instability. IR: 3365, 3320, 3240, 1697 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 8.02–7.70 (m, 1H), 7.48–7.08 (m, 3H), 4.28 (s, 2H), 4.19 (q, 2H, J = 7.0 Hz), 3.77 (s, 3H), 3.20 (s, 2H), 1.28 (t, 3H, J = 7.0 Hz).

The ^{1}H NMR spectra of compounds **7** and **8** were run at 200 MHz.

Preparation of 2-(1,3-Dihydro-2*H*-benzimidazol-2-ylidene)-4-hydroxy-3-oxobutanoic Acid Ethyl Ester (7a). Under N_2, **5a** (10 g; 34.21 mmol) was heated at reflux for 80 h in 500 mL of absolute EtOH containing cyclohexene (5 g; 60.86 mmol) and 10% Pd/C (1 g). The reaction was cooled, diluted with 500 mL of $CHCl_3$, and filtered through Celite. The solvent was evaporated *in vacuo*, and the residue was purified by flash chromatography through silica gel ($CHCl_3$/MeOH (95:5)). Recrystallization of the isolate from EtOH provided 6.15 g (69%) of the desired product. Mp: 196–197 °C dec. IR: 3330, 1635, 1610 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 12.92 (m, 2H), 7.78–7.59 (m, 2H, ArH), 7.42–7.16 (m, 2H, ArH), 4.49 (d, 2H, $-CH_2CO-$), 4.40 (t, 1H, $-OH$), 4.26 (q, 2H, $-CH_2CH_3$), 1.35 (t, 3H, $-CH_2CH_3$). ^{13}C NMR: δ 14.42, 59.33, 66.42, 84.17, 113.08, 123.75, 130.25, 152.33, 168.17, 193.00. MS (thermospray): *m/z* 263 $(M + 1)^+$, 217, 205. Anal.

Calcd for $C_{13}H_{14}N_2O_4$: C, 59.54; H, 5.38; N, 10.68. Found: C, 59.56; H, 5.42; N, 10.69.

The following compounds were prepared by similar procedures, from the appropriate nitrophenyl precursors **5**:

2-(1,3-Dihydro-2*H*-benzimidazol-2-ylidene)-4-hydroxy-3-oxopentanoic Acid Ethyl Ester (7b). Yield: 53%. Mp (EtOH): 176–178 °C dec. IR: 3500, 3275, 3220, 1632, 1613 cm^{-1}. ^1H NMR ($CDCl_3$): δ 12.63 (br, 2H), 7.49–7.68 (m, 4H), 5.22 (q, 1H), 4.34 (dq, 2H), 3.76 (br, 1H), 1.51–1.30 (m, 6H). Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.79; H, 5.81; N, 10.12.

(*E*)-2-(1,3-Dihydro-5-methyl-2*H*-benzimidazol-2-ylidene)-4-hydroxy-3-oxobutanoic Acid Ethyl Ester (7d). Yield: 58%. Mp (EtOH): 162–164 °C. IR: 3410, 3265, 1645, 1608 cm^{-1}. ^1H NMR (DMSO-d_6): δ 12.81 (d, 2H), 7.53 (d, 1H), 7.48 (s, 1H), 7.04 (dd, 1H), 4.61–4.12 (m, 5H), 2.36 (s, 3H), 1.29 (t, 3H). ^{13}C NMR (DMSO-d_6): δ 14.77, 21.27, 59.26, 66.09, 83.86, 112.08, 112.19, 124.35, 127.63, 129.85, 132.52, 151.07, 167.18, 191.61. Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.75; H, 5.87; N, 10.07.

Preparation of 3-(1,3-Dihydro-2*H*-benzimidazol-2-ylidene)-2,4(3*H*,5*H*)-furandione (8a). Method A. A suspension of **6a** (0.5 g; 1.906 mmol) in 6 mL of 7% aqueous Na_2CO_3 solution was refluxed for 4 h, diluted with 50 mL of H_2O, cooled to 0 °C, and acidified to pH 1 with concd HCl. The reaction was stirred for 30 min. The solid was filtered off, rinsed with H_2O, and dried on the filter. Recrystallization from DMF afforded 0.36 g (88%) of product. Mp: >300 °C. IR: 3210, 1713, 1654, 1629, 1614 cm^{-1}. ^1H NMR (DMSO-d_6): δ 12.79 (bs, 2H), 7.66–7.52 (m, 2H), 7.35–7.21 (m, 2H), 4.49 (s, 2H). ^{13}C NMR: δ 71.26, 78.88, 112.66, 123.66, 130.23, 145.59, 173.23, 191.39. MS (EI): *m/z* 216 (M^+), 158. Anal. Calcd for $C_{11}H_8N_2O_3$: C, 61.11; H, 3.73; N, 12.96. Found: C, 60.93; H, 3.87; N, 13.04.

Method B. A method similar to that of method A was used in which **7a** replaced **6a**. Yield: 85%.

Method C. Under N_2, a mixture of **5a** (10 g; 34.21 mmol), cyclohexene (5 g; 60.86 mmol), and 10% Pd/C (1 g) in 500 mL of absolute EtOH was heated under reflux for 3 h. The reaction was cooled to rt, and 300 mL of CH_2Cl_2 was added. The mixture was filtered through Celite and concentrated *in vacuo* to obtain a solid mixture of **6a** and **7a**. The solid was suspended in 200 mL of 7% aqueous Na_2CO_3 solution and boiled for 2 h. The workup and purification was similar to that of method A. Yield: 5.1 g (69%).

The following compounds were prepared by procedures similar to method C from the appropriate nitrophenyl compounds **5**:

3-(1,3-Dihydro-2*H*-benzimidazol-2-ylidene)-5-methyl-2,4-(3*H*,5*H*)-furandione (8b). Yield: 81%. Mp: >300 °C. IR: 3240, 1711, 1634, 1617, 1607 cm^{-1}. ^1H NMR (DMSO-d_6): δ 12.67 (bs, 2H), 7.67–7.54 (m, 2H), 7.36–7.23 (m, 2H), 4.62 (q, 1H, J = 6.8 Hz), 1.35 (d, 3H, J = 6.8 Hz). Anal. Calcd for $C_{12}H_{10}N_2O_3$: C, 62.61; H, 4.38; N, 12.17. Found: C, 62.31; H, 4.48; N, 12.20.

(*E*)-3-(1,3-Dihydro-5-methyl-2*H*-benzimidazol-2-ylidene)-2,4(3*H*,5*H*)-furandione (8d). Yield: 75%. Mp: > 300 °C. IR: 3220, 1714, 1646, 1633, 1615 cm^{-1}. ^1H NMR (DMSO-d_6): δ 12.67 (bs, 2H), 7.48 (d, 1H, J = 7.7 Hz), 7.40 (d, 1H, J = 1.4 Hz), 7.12 (dd, 1H, J_o = 7.7 Hz, J_m = 1.4 Hz), 4.44 (s, 2H), 2.38 (s, 3H). Anal. Calcd for $C_{12}H_{10}N_2O_3$: C, 62.61; H, 4.38; N, 12.17. Found: C, 62.38; H, 4.45; N, 12.16.

Preparation of 3-(1,3-Dihydro-2*H*-benzimidazol-2-ylidene)-5,5-dimethyl-2,4(3*H*,5*H*)-furandione (8c). Under N_2, a mixture of **5c** (0.25 g; 0.7805 mmol), cyclohexene (0.23 g; 2.8 mmol), and 10% Pd/C (20 mg) in 10 mL of absolute EtOH was heated at reflux for 17 d. The reaction was cooled, and 5 mL of CH_2Cl_2 was added. The mixture was filtered through Celite and concentrated *in vacuo*. Recrystallization of the residue from 95% EtOH gave 0.19 g (100%) of the desired product.

More conveniently, **8c** was also prepared from **6c** using a procedure similar to method A. Yield: 88%. Mp: >300 °C. IR: 3240, 1710, 1640, 1615, 1605 cm^{-1}. ^1H NMR (DMSO-d_6): δ 12.74 (bs, 2H), 7.65–7.54 (m, 2H), 7.34–7.23 (m, 2H), 1.36 (s, 6H). Anal. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.93; H, 4.95; N, 11.47. Found: C, 63.88; H, 5.02; N, 11.44.

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Additions and Corrections

Vol. 58, 1993

E. Vedejs,* D. E. Erdman, and D. R. Powell. Cyclic Organotin Lewis Acids.

Page 2842, column 2, lines 31–37. Our recent paper (Vedejs, E.; Erdman, D. E.; Powell, D. R. *J. Org. Chem.* **1993**, *58*, 2840) contains the following statements: "It is known that 5-membered tin alkoxides such as **21** are dimeric in solution ... Complexation with DMSO is also observed ... On the other hand, the 6-membered analog **22** is resistant to coordination and exists in solution as the monomer." The above statements contain errors. Grindley et al. have shown that **21** and also **22** exist in solution as mixtures of oligomers containing hexavalent as well as pentavalent tin: Grindley, T. B.; Thangarasa, R.; Bakshi, P. K.; Cameron, T. S. *Can. J. Chem.* **1992**, *70*, 197. Grindley, T. B.; Thangarasa, R. *J. Am. Chem. Soc.* **1990**, *112*, 1364. References cited therein contain earlier evidence that neither **21** nor **22** is monomeric in solution.

The reported failure of 2,2-dibutyl-1,3,2-dioxastannane (**22**) to form adducts with DMSO (ref 13a in the paper) reflects a disadvantage for monomeric coordination complexes relative to the oligomers, not relative to the tetrahedral monomer **22** in solution. Similarly, the enhanced coordinating ability of **21** (2,2-dibutyl-1,3,2-dioxastannolane) mentioned in footnote 13a is more accurately described as an enhanced preference for monomeric 5-coordinate complexes relative to the mixture of oligomers.