(0.5 g) in phosphate buffer (0.1 N, pH 6.50, 100 mL) was added **3e** (5.00 g, 24 mmol). While vigorous stirring was maintained, the pH was kept constant at pH 6.50 by addition of 1 N NaOH from an autoburet. When the appropriate degree of conversion was accomplished [40% for (*R,R*)-**2e**, 28 h], the product was extracted with CH_2Cl_2 (3 × 100 mL). Evaporation of organic solvents and subsequent column chromatography gave 1.24 g (37%) of (*R,R*)-**2e** ($[\alpha]^{20}_D$ −4.2° [c = 2, CH_2Cl_2]) and 2.40 g (48%) of optically enriched (*S,S*)-**3e** ($[\alpha]^{20}_D$ −54.8° [c = 2, CH_2Cl_2]). The latter was submitted to a further 33% conversion as described above. Subsequent workup yielded 1.90 g (38%) of (*S,S*)-**3e** ($[\alpha]^{20}_D$ −78.7° [c = 2, CH_2Cl_2]). From that, 1.17 g (35%) of (*S,S*)-**2e** ($[\alpha]^{20}_D$ +4.2° [c = 2, CH_2Cl_2]) was obtained by methanolysis with catalytic amounts of NaOMe, in 30% yield.

The other enzymatic resolutions were carried out in the same way. Results including ee's are shown in Table I.

Acknowledgment. We thank Carina Illaszewicz for measuring many of the NMR spectra. This work was supported by the Fonds zur Förderung der wissenschaftlichen Forschung, Vienna (Projects P6893C and P6257C).

Registry No. **1a**, 122922-40-1; **1b**, 77549-73-6; **1c**, 62137-90-0; **1d**, 67253-49-0; **1e**, 36611-94-6; **1f**, 124718-82-7; **1g**, 124718-83-8; **2a**, 124718-84-9; (*R*)-**2a**, 124817-02-3; (*S*)-**2a**, 124817-01-2; **2b**, 124718-85-0; (*R*)-**2b**, 124817-04-5; (*S*)-**2b**, 124817-03-4; **2c**, 124718-86-1; (*R*)-**2c**, 124817-05-6; **2d**, 124718-87-2; (*S*)-**2d**, 124817-06-7; **2e**, 124718-88-3; (*R,R*)-**2e**, 124817-07-8; **2f**, 124718-89-4; (3*R*,4*S*)-**2f**, 124817-08-9; **2g**, 124718-90-7; (3*R*,4*S*)-**2g**, 124817-09-0; **3a**, 124718-94-1; (*R*)-**3a**, 124817-11-4; **3b**, 124718-95-2; (*R*)-**3b**, 124817-12-5; (*S*)-**3b**, 124817-13-6; **3c**, 124718-96-3; (*S*)-**3c**, 124817-14-7; **3d**, 124718-97-4; (*R*)-**3d**, 124817-15-8; **3e**, 124718-98-5; (*S,S*)-**3e**, 124817-16-9; **3f**, 124718-99-6; (3*S*,4*R*)-**3f**, 124817-17-0; **3g**, 124719-00-2; (3*S*,4*R*)-**3g**, 124817-18-1; lipase, 9001-62-1; butyric anhydride, 106-31-0; (±)-2-azido-2-phenylethanol, 124718-93-0; (±)-2-azido-1-octanol, 124718-92-9; (±)-2-1-hexanol, 124718-91-8.

Oxidative Cyclization of Acyclic Aryl-Substituted *N*-Vinylurethanes

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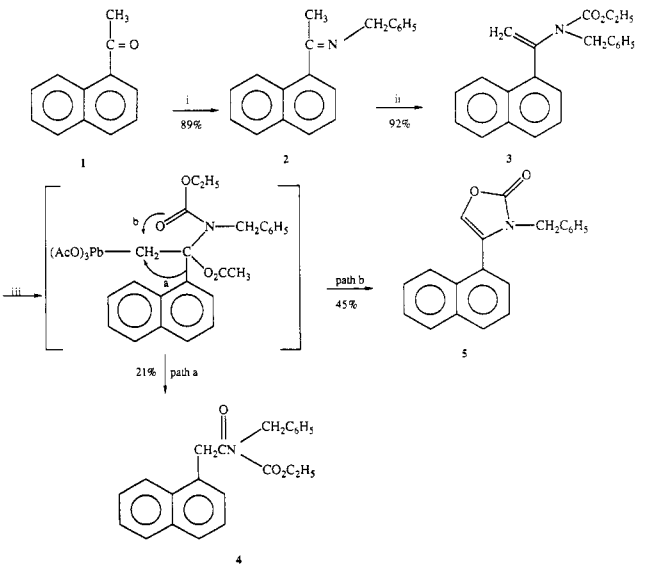
Oxidation of the acyclic *N*-(1-(1-naphthyl)vinyl)urethane (**3**) with lead tetraacetate (LTA) forms a naphthyloxazolone as the major product, accompanied by the product of rearrangement, *N*-(ethoxycarbonyl)-1-naphthylacetamide. When the naphthyl group is replaced by alkoxy-substituted aromatic rings, the *N*-vinylurethane undergoes three successive oxidations by LTA leading to novel substituted nitrogen containing cyclic anhydrides, oxazolidine-2,5-diones. The structure of this unusual oxidation product was proven by X-ray analysis. The mechanism of the oxidation is discussed in terms of known enamide oxidations, and the intermediacy of an oxazolone is demonstrated.

The photochemistry of enamides, *N*-vinylamides and urethanes, leads to a variety of interesting and useful reactions,[1,2] which have been extensively used in natural product synthesis.[3] We have been interested in extending the uses of these types of compounds and have investigated their reactivity toward various oxidizing agents,[4] particularly lead tetraacetate (LTA).[5] Simple enamides readily undergo bis-acetoxylation across the double bond, and the resultant bis-acetates can then undergo subsequent reactions.[6] In the isoquinoline enamides, where the enamide double bond is contained in a 1-benzylidene group, LTA introduces a β-acetoxy group onto the double bond in the *N*-aroyl series, while oxazolone formation is observed with the urethanes.[4] However, with the isoquinoline 1-methylene enamides, LTA causes an oxidative ring expansion, in which the aromatic ring migrates from the α position of enamide double bond to the β position, forming benzazepinones.[7] When the isoquinoline enamide double bond is dialkyl substituted, LTA oxidation causes an oxidative cyclization to form hydroxyoxazolidinones.[8] Since the isoquinoline enamides may be considered as rigid systems, we have extended the LTA oxidation studies to the acyclic case to determine the effects of conformational flexibility on the reaction pathways. The results reported here for the urethane series led to a surprising example of a triple oxidation but did, however, indicate the primary pathway that acyclic *N*-vinylurethanes prefer to take

Scheme I[a]



[a] Reagents: (i) benzylamine, 5-Å molecular sieves; (ii) diethyl pyrocarbonate, toluene, Δ; (iii) lead tetraacetate, acetic acid.

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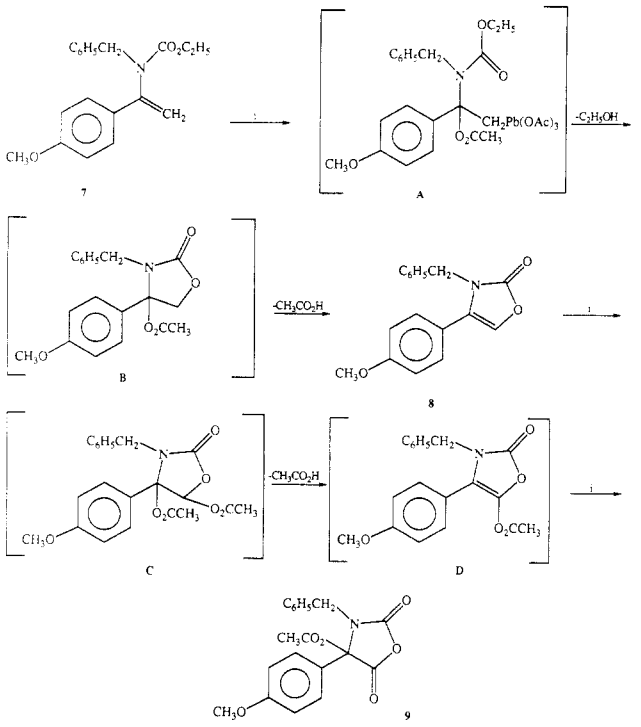
(1) Campbell, A. L.; Lenz, G. R. *Synthesis* **1987**, 421–52.

0022-3263/90/1955-1753$02.50/0

Scheme II[a]



[a] Reagent: (i) lead tetraacetate.

barring conformational restraints.

The urethane (**3**) was synthesized from the imine (**2**), derived from 1-acetylnaphthalene (**1**) and benzylamine,[9] by heating with diethyl pyrocarbonate in toluene (Scheme I). Oxidation with lead tetraacetate in acetic acid led to two products which were separated chromatographically. The major product (**5**), isolated as a crystalline solid in 45% yield, was readily identified as an oxazolone (path b), based on its spectral characteristics. The IR spectrum of **5** showed an absorption at 1757 cm^{-1}, indicative of an oxazolone ring,[4] while its NMR spectrum showed the loss of the ethoxy group in **3** and appearance of the oxazolone ring proton at δ 6.90. In addition, the base peak is the parent peak in the mass spectrum of compound **5**. The second product **4**, an oil, isolated in 21% yield, was identified as the product of an oxidative rearrangement of compound **3** (path a).[7] The structure was confirmed by a high-resolution mass spectrum, which possessed a fragmentation pattern consistent with the assigned structure. The NMR spectrum of **4** demonstrated the retention of the protons in **3**, with the exception of the vinyl protons, and the appearance of a methylene group signal at δ 5.01.

In contrast to the products observed from the oxidation of the naphthalene derivative **3**, oxidation of vinylurethanes containing electron-releasing alkoxy aromatic substitution resulted in a completely different product. For instance, oxidation of the *p*-methoxyphenyl derivative

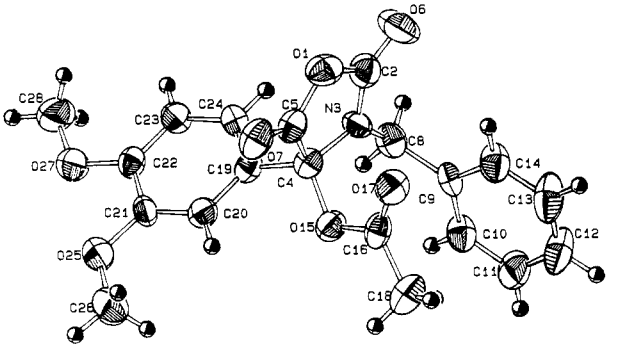
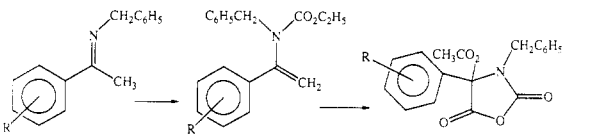


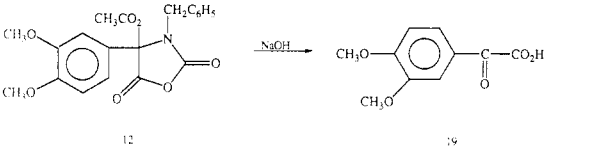
Figure 1. An ORTEP representation of 4-acetoxy-3-benzyl-4-(3′,4′-dimethoxyphenyl)oxazolidine-2,5-dione (**12**).

Table I



imine	substitution	vinylurethane	product
6 (99%)	4-CH_3O	**7** (90%)	**9** (53%)
10 (96%)	3,4-$(CH_3O)_2$	**11** (93%)	**12** (47%)
13 (92%)	3,4,5-$(CH_3O)_3$	**14** (95%)	**15** (54%)
16 (82%)	3,4-(OCH_2O)	**17** (93%)	**18** (57%)

7 (Scheme II), in the presence of an excess of LTA, led to a single major crystalline product **9** in 53% yield, together with several minor products which were not investigated.[10] The spectral characteristics of **9** indicated that significant changes had occurred; the IR spectrum indicated an anhydride (1852 and 1784 cm^{-1}) and an acetoxy group (1755 cm^{-1}). The NMR spectrum showed the loss of the ethoxy group in **7** and the presence of the acetoxy methyl group. Because of these observations, a single-crystal X-ray structural analysis was performed on compound **12**, which confirmed the structure of the oxidation product as the unusual cyclic nitrogen-containing anhydride, 4-acetoxy-3-benzyl-4-(3′,4′-dimethoxyphenyl)oxazolidine-2,5-dione (Figure 1). The compounds studied are collected in Table I. The oxidation products are remarkably stable and can be chromatographed on silica and recovered unchanged. Hydrolysis of the oxidation product **12** with aqueous base slowly yielded the known dimethoxyphenylglyoxylic acid **19**.[11] Isolation of the oxazolone **5** in the naphthalene case,



together with the mechanism postulated in Scheme II, indicated that the oxazolone **8** could be an intermediate in the formation of **9**. Accordingly, when the known oxazolone **8**[12] was oxidized with LTA in the same manner as the vinylurethane **7**, the same oxidation product **9** was obtained in 75% yield.

The mechanism of the oxidation of the acyclic vinylurethanes involves three consecutive LTA oxidations

(2) Lenz, G. R. *Synthesis* **1978**, 489–518.
(3) Ninomiya, I.; Naito, T. *Alkaloids (N.Y.)* **1983**, *22*, 189–280.
(4) See: Lenz, G. R.; Costanza, C. *J. Org. Chem.* **1988**, *53*, 1176–1183, for a sumary of the oxidations of enamides by various reagents.
(5) For a review of LTA oxidations, see: Mihailovic, M. L.; Cekovic, Z.; Lorenc, L. *Org. Synth. Oxid. Met. Compds.* **1986**, 741–816. Rubottom, G. M. *Org. Chem. (N.Y.)* **1982**, *5* (Oxid. Org. Chem., Part D), 1–145.
(6) Boar, R. H.; McGhie, J. F.; Robinson, M.; Barton, D. H. R. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1242–4.
(7) Lenz, G. R. *J. Org. Chem.* **1988**, *53*, 5791–3.
(8) Lenz, G. R. *J. Chem. Soc., Perkin Trans. 1*, in press.
(9) Couture, A.; Grandclaudon, P. *Synthesis* **1986**, 576–8. Kyba, E. P. *Org. Prep. Proced.* **1970**, *2*, 149–56. Taguchi, K.; Westheimer, F. H. *J. Org. Chem.* **1971**, *36*, 1570–2.

(10) Oxidation with lesser amounts of LTA resulted in the same product, but with incomplete consumption of starting material.
(11) Mauthner, F. *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 188–95. Tiemann, F.; Matsmoto, U. *Ber. Dtsch. Chem. Ges.* **1878**, *11*, 141–5.
(12) Saettone, M. F. *J. Org. Chem.* **1966**, *31*, 1959–62. Knapp, S.; Kukkola, P. J.; Sharma, S.; Pietranico, S. *Tetrahedron Lett.* **1987**, *28*, 5399–5402.

leading to the observed oxazolidine-2,5-dione. Oxidation of the vinylurethane double bond by LTA involves the addition of an acetoxy group to the α-vinyl carbon, and the formation of the equivalent of a positive charge at the β-carbon, intermediate A in Scheme II.[4,7] Trapping of the positive charge by the carbonyl of the urethane leads to the acetoxyoxazolidinone B which can undergo elimination to the oxazolone 8. The oxazolone 8 apparently reacts faster than the starting material forming the bis-acetoxy derivative C, which eliminates acetic acid to form the acetoxyoxazolone D.[13] The acetoxyoxazolone is again rapidly oxidized to the bis-acetoxy compound, analogous to C, which hydrolyzes to the observed product **9**. This last oxidation, that of the acetoxylated oxazolone, has previously been observed in the sequential oxidation of oxyprotoberberines.[14]

The results from this study of the LTA oxidation of acyclic vinylurethanes, the isolation and demonstrated intermediacy of oxazolones, indicates that the preferred oxidative pathway is trapping of the incipient positive charge (cf. path b in Schemes I and II) by the urethane carbonyl group. The oxidative rearrangement observed with the rigid isoquinoline enamides (cf. path a in Scheme I) appears to be a less efficient reaction pathway in the acyclic series.

Experimental Section

General Methods. Melting points were obtained using a Thomas-Hoover Unimelt capillary apparatus and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer 683 or, alternatively, an FT-IR was obtained using a Digilab FTS-60 FT-IR spectrometer. NMR spectra were recorded on an IBM AF-270 spectrometer and were run in deuteriochloroform with tetramethylsilane as an internal standard. HPLC was performed on a Waters Delta Prep. Electron impact mass spectra were obtained on an AEI MS-30. The X-ray analysis was obtained with a Rigaku AFC 5S Diffractometer. Microanalyses were determined by the BOC Group Technical Center Microanalytical Service, under the direction of Allan Ellgren.

Imine (2) from 1-Acetylnaphthalene (1) and Benzylamine. 1-Acetylnaphthalene (17 g, 0.10 mol), was placed in a 500-mL flask along with benzylamine (12.9 g, 0.12 mol), anhydrous diethyl ether (40 mL), and 5-Å molecular sieves (40 g). The reaction was stirred magnetically under nitrogen for 3 days. Methylene chloride (40 mL) was added, and the reaction mixture was filtered through sodium sulfate, which was then washed with 200 mL of methylene chloride. The solvent was removed to yield a viscous, yellow oil. The residual benzylamine and 1-acetylnaphthalene were distilled off under reduced pressure. The remaining material was distilled (Kugelrohr) to yield the imine (**2**) as a yellow oil (23.0 g, 88.8 mmol, 89%): bp 158 °C (0.60 mmHg); IR 1642, 1602, 1600, 1595, 1500, 1496 cm^{-1}; MS 259 (M, 89), 258 (M - 1, 98), 244 (M - CH_3, 41), 127 (naphthalene ring, 32), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 8). Anal. Calcd for $C_{19}H_{17}N$; C, 87.99; H, 6.61; N, 5.40. Found: C, 87.86; H, 6.66; N, 5.43.

Imine (6) from 4'-Methoxyacetophenone and Benzylamine. To anhydrous diethyl ether (60 mL), under nitrogen, 4'-methoxyacetophenone (15.0 g, 0.10 mol) was added along with benzylamine (12.9 g, 0.12 mol). The reaction mixture was stirred vigorously, and 5-Å molecular sieves (40 g) were added. After stirring for ca. 24 h, the material in the flask was washed with methylene chloride (3 × 100 mL) and filtered through a Büchner funnel containing sodium sulfate/Celite, and the solvent was evaporated to give a white solid (23.9 g, 99.8 mmol, 99.8%): mp 55.0–56.8 °C; IR 1632, 1603, 1468, 1452 cm^{-1}; NMR δ 7.82–7.92 (m, 2 H), 7.21–7.44 (m, 5 H), 6.87–6.95 (m, 2 H), 4.72 (s, 2 H), 3.83 (s, 3 H), 2.29 (s, 3 H); MS *m/z* (relative intensity) 239 (M, 17), 238 (M - 1, 25), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 12). Anal. Calcd for $C_{16}H_{17}NO$: C, 80.29; H, 7.17; N, 5.85. Found: C, 80.06; H, 6.92; N, 6.01.

The 3',4'-dimethoxy derivative 10 (96% yield) was similarly synthesized from 3',4'-dimethoxyacetophenone (18.0 g, 0.10 mol), benzylamine (12.9 g, 0.12 mol) and molecular sieves (40 g): mp 104–106 °C; IR 2819, 1623, 1600, 1462, 1450 cm^{-1}; NMR δ 7.62 (d, 1 H), 7.25–7.43 (m, 6 H), 6.84–6.88 (d, 1 H), 4.74 (s, 2 H), 3.94 (s, 3 H), 3.92 (s, 3 H); MS *m/z* (relative intensity) 269 (m, 29), 268 (M - 1, 28), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 14). Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.80; H, 7.12; N, 5.20. Found: C, 75.58; H, 7.33; N, 4.94.

The 3',4',5'-trimethoxy derivative 13 (92%) was similarly synthesized from 3',4',5'-trimethoxyacetophenone (20 g, 0.095 mol) and benzylamine (12.3 g, 0.12 mol) with 5-Å molecular sieve (40 g): mp 78–80 °C; IR 1625, 1600, 1468, 1449 cm^{-1}; NMR δ 7.23–7.44 (m, 5 H), 7.15 (s, 2 H), 4.76 (s, 2 H), 3.93 (s, 6 H), 3.89 (s, 3 H), 2.33 (s, 3 H); MS *m/z* (relative intensity) 299 (M, 39), 298 (M - 1, 30), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 10). Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.20; H, 7.08; N, 4.68. Found: C, 72.41; H, 7.14; N, 4.97.

The 3',4'-methylenedioxy derivative 16 (82%) was similarly prepared from 3',4'-(methylenedioxy)acetophenone (21.3 g, 0.13 mol) and benzylamine (16.1 g, 0.15 mol) with 5-Å molecular sieves (40 g): mp 60–62 °C (ether/hexane); IR 1655, 1608, 1605, 1450 cm^{-1}; NMR δ 7.26–7.51 (m, 7 H), 6.81 (d, 1 H), 5.99 (s, 2 H), 4.72 (s, 2 H), 2.29 (s, 3 H); MS *m/z* (relative intensity) 253 (M, 57), 252 (M - 1, 66), 162 (M - $CH_2C_6H_5$, 3), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 6). Anal. Calcd for $C_{16}H_{15}NO_2$; C, 75.86; H, 5.98; N, 5.53. Found: C, 76.04; H, 5.83; N, 5.53.

The imines slowly decomposed upon storage and should be freshly prepared prior to use.

Ethyl *N*-Benzyl-*N*-(1-(1-naphthyl)vinyl)urethane (3). Imine **2** (5 g, 19.3 mmol) was placed in a 200-mL flask together with dry toluene (40 mL) and diethyl pyrocarbonate (7.75 g, 47.8 mmol). The reaction mixture was stirred magnetically, under nitrogen, for 72 h. The solvent was then removed, and the remaining diethyl pyrocarbonate was distilled under reduced pressure. The residual material was distilled (Kugelrohr) to yield a yellow oil (5.8 g, 17.5 mmol, 91%): bp 225 °C (0.70 mmHg); IR 1700, 1628 cm^{-1}; NMR δ 8.12–8.15 (m, 1 H), 7.78–7.85 (m, 2 H), 7.25–7.48 (m, 9 H), 5.40 (s, 1 H), 5.18 (s, 1 H), 4.63 (s, 2 H), 4.07 (q, J = 7 Hz, 2 H), 0.94 (t, J = 7 Hz, 3 H); MS *m/z* (relative intensity) 331 (M, 81), 330 (M - 1, 22), 258 (M - $CO_2CH_2CH_3$, 26), 240 (M - $CH_2C_6H_5$, 51), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 9). Anal. Calcd for $C_{22}H_{21}NO_3 \cdot 0.25H_2O$: C, 78.65; H, 6.46; N, 4.17. Found: C, 78.66; H, 6.27; N, 4.10.

Ethyl *N*-Benzyl-*N*-(1-(4-methoxyphenyl)vinyl)urethane (7). To a magnetically stirred mixture of imine **6** (10 g, 41.9 mmol) and dry toluene (200 mL), under nitrogen, was added diethyl pyrocarbonate (13.5 g, 83.3 mmol). After refluxing for 18 h, the reaction mixture was dried with sodium sulfate, and the solvent was evaporated to give a yellowish oil. The crude oil was flash chromatographed using 1:10 ethyl acetate/hexane to give **7** (11.7 g, 37.7 mmol, 90%) as a colorless oil: bp 166 °C (0.21 mmHg); IR 3018, 2820, 1701, 1625, 1600, 1249 cm^{-1}; NMR δ 7.25–7.34 (m, 7 H), 6.84 (m, 2 H), 5.34 (s, 1 H), 4.91 (s, 1 H), 4.68 (s, 2 H), 4.14 (q, J = 7 Hz, 2 H), 3.82 (s, 3 H), 1.12 (t, J = 7 Hz, 3 H); MS *m/z* (relative intensity) 311 (M, 4), 310 (M - 1, 4), 238 (M - $CO_2CH_2CH_3$, 11), 133 (M - $CO_2CH_2CH_3NCH_2C_6H_5$, 10), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 14), 29 (CH_2CH_3, 62). Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.28; H, 6.81; N, 4.50. Found: C, 73.05; H, 6.76; N, 4.43.

Ethyl *N*-benzyl-*N*-(1-(3,4-dimethoxyphenyl)vinyl)urethane (11) was similarly prepared in 93% yield from imine **10** (10 g, 37.1 mmol) and diethyl pyrocarbonate (12.0 g, 74 mmol) in dry toluene (210 mL): bp 205 °C (0.60 mmHg); IR 3045, 3032, 3018, 2819, 1705, 1629 cm^{-1}; NMR δ 7.24–7.35 (m, 5 H), 6.71–6.92 (m, 3 H), 5.36 (s, 1 H), 4.96 (s, 1 H), 4.70 (s, 2 H), 4.12 (q, J = 7 Hz, 2 H), 3.88 (s, 3 H), 3.78 (s, 3 H), 1.09 (t, J = 7 Hz, 3 H); MS *m/z* (relative intensity) 341 (M, 15), 268 (M - $CO_2CH_2CH_3$, 10), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 10), 29 (CH_2CH_3, 39). Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.35; H, 6.80; N, 4.10. Found: C, 70.09; H, 6.92; N, 4.10.

Ethyl *N*-benzyl-*N*-(1-(3,4,5-trimethoxyphenyl)vinyl)urethane (14) was similarly prepared in 92% yield from imine

(13) Oxidation of benzylidene isoquinoline enamides with LTA in benzene leads to these bisacetoxy derivatives which can be converted to the acetoxy enamides, cf. ref 4 and Lenz, G. R. *J. Org. Chem.* **1988**, *53*, 4447–52.

(14) Dorn, C. R.; Koszyk, F. J.; Lenz, G. R. *J. Org. Chem.* **1984**, *49*, 2642–4.

13 (10 g, 33.4 mmol) and diethyl pyrocarbonate (6.6 g, 40.7 mmol) by refluxing in dry toluene (50 mL) for 3 h. Isolation of 14 was by distillation (Kugelrohr): bp 223 °C (0.4 mmHg); IR 2830, 1701, 1621, 1581, 1128 cm^{-1}; NMR δ 7.27–7.43 (m, 5 H), 6.40 (s, 2 H), 5.38 (s, 1 H), 5.05 (s, 1 H), 4.73 (s, 2 H), 4.11 (q, J = 7 Hz, 2 H), 3.83 (s, 3 H), 3.75 (s, 6 H), 1.07 (t, J = 7 Hz, 3 H). Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.90; H, 6.80; N, 3.77. Found: C, 68.09; H, 6.91; N, 3.48.

Ethyl *N*-benzyl-*N*-(1-(3,4-(methylenedioxy)phenyl)-vinyl)urethane (17) was prepared in 82% yield similarly to compound 14 from imine 16 (10.0 g, 39.5 mmol) and diethyl pyrocarbonate (9.1 g, 56 mmol) in dry toluene (25 mL): bp 205 °C (0.10 mmHg); IR 2975, 1699, 1625, 1601, 1244 cm^{-1}; NMR δ 7.27–7.31 (m, 5 H), 6.74–6.84 (m, 3 H), 5.98 (s, 2 H), 5.31 (s, 1 H), 4.89 (s, 1 H), 4.66 (s, 2 H), 4.14 (q, J = 7 Hz, 2 H), 1.14 (t, J = 7 Hz, 3 H). Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.13; H, 5.90; N, 4.31. Found: C, 69.96; H, 5.97; N, 4.02.

Oxidation of the (Naphthylvinyl)urethane 3 with Lead Tetraacetate. The (naphthylvinyl)urethane 3 (1.00 g, 3.02 mmol) was dissolved in acetic acid (40 mL). Lead tetraacetate (1.70 g, 3.76 mmol) was added, and the mixture was stirred under nitrogen at room temperature for 24 h. After 24 h, additional lead tetraacetate (0.2 g, 0.45 mmol) was added and stirring was continued for an additional 7 h. The reaction was quenched with glycerol (0.1 mL) and stirred for 30 min. The reaction mixture was diluted with methylene chloride (200 mL) and washed with water (200 mL). The aqueous phase was extracted with methylene chloride (2 × 30 mL). The combined organic phases were then washed with water (200 mL) and then with saturated aqueous sodium bicarbonate solution (200 mL). The organic phase was dried over sodium sulfate, filtered, and evaporated to a yellow oil (1.1 g). The oil was chromatographed on silica gel and eluted with 20% ethyl acetate in hexane. The first product eluted was the naphthylacetamide 4, obtained as an oil (223 mg, 21% yield): IR (cm^{-1}) 1734, 1701, 1377, 1350, 1207, 1186, 1024, 775; NMR δ 7.8–8.0 (m, 3 H), 7.25–7.6 (m, 9 H), 5.01 (s, 2 H), 4.75 (s, 2 H), 4.29 (q, J = 7 Hz, 2 H), 1.29 (t, J = 7 Hz, 3 H); MS m/z (relative intensity) 347 (M, 89), 168 ($C_{10}H_7CHCO$, 100), 141 ($C_{10}H_7CH_2$, 69), 115 ($CH_3CH_2OCONCO$, 34), 91 (39); high-resolution MS calcd for $C_{22}H_{21}NO_3$ 347.1521, obsd 347.1523.

Further elution afforded the oxazolone 5 (403 mg, 45%): mp 95–98 °C (methylene chloride/hexane); IR 3152, 1757, 1753, 1491, 1384, 1057, 1036 cm^{-1}; NMR δ 6.7–8.0 (m, 12 H), 6.90 (s, 1 H), 4.55 (s, 2 H); MS m/z (relative intensity) 301 (M, 100), 210 (M – $CH_2C_6H_5$, 100), 91 ($CH_2C_6H_5$, 83). Anal. Calcd for $C_{20}H_{15}NO_2$: C, 79.72; H, 5.02; N, 4.65. Found: C, 79.71; N, 5.05; N, 4.68.

Oxidation of the (1-(3,4-Dimethoxyphenyl)vinyl)urethane 11 to the Oxazolidine-2,5-dione (12). To a magnetically stirred solution of vinyl urethane 11 (5.0 g, 14.7 mmol), in glacial acetic acid (175 mL), under nitrogen, was added lead tetraacetate (22.8 g, 51.5 mmol). After 5 h, the reaction was quenched with glycerol and then diluted with water to give a yellow solution. The aqueous mixture was extracted with methylene chloride (3 × 60 mL), and the combined organics were washed twice with 10% sodium bicarbonate solution and dried with sodium sulfate, and the solvent was evaporated to give a yellow oil. The oil was triturated with anhydrous diethyl ether and a little hexane to give the oxazolidine-2,5-dione 12 as a white solid (2.63 g, 6.82 mmol, 47%): mp 122–123 °C; IR 1852, 1784, 1755, 1238, 1044, 1024 cm^{-1}; NMR δ 7.22–7.37 (m, 5 H), 6.85–7.05 (m, 3 H), 5.05 (d, J = 15 Hz, 1 H), 3.94 (d, J = 15 Hz, 1 H), 3.94 (s, 3 H), 3.90 (s, 3 H), 1.53 (s, 3 H); MS m/z (relative intensity) 385 (M, 6), 326 (M – CH_3CO_2, 11), 137 ($(CH_3O)_2C_6H_3$, 7), 91 ($CH_2C_6H_5$, 100), 43 ($COCH_3$, 23); see Molecular Structure and X-ray data at the end of this section. Anal. Calcd for $C_{20}H_{19}NO_7$: C, 62.32; H, 4.98; N, 3.64. Found: C, 62.54; H, 5.08; N, 3.72.

4-Acetoxy-3-benzyl-4-(4′-methoxyphenyl)oxazolidine-2,5-dione (9) was similarly prepared from the ((methoxyphenyl)-vinyl)urethane 7 (2.50 g, 8.03 mmol) by oxidation with lead tetraacetate (12.5 g, 28.1 mmol) in glacial acetic acid (100 mL). Flash chromatography (1:5 ethyl acetate/hexane) afforded the oxazolidine-2,5-dione 9 (1.51 g, 4.25 mmol, 53%): mp 113–6 °C (ether/hexane); IR 2800, 1853, 1791, 1749, 1605, 1030 cm^{-1}; NMR δ 7.21–7.38 (m, 7 H), 6.99–7.02 (m, 2 H), 5.06 (d, J = 15 Hz, 1 H), 3.86 (d, J = 15 Hz, 1 H), 3.86 (s, 3 H), 1.48 (s, 3 H); MS m/z (relative intensity) 355 (M, 6), 296 (M – O_2CCH_3, 13), 107 ($C_6H_4OCH_3$, 10), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5, 19), 43 ($COCH_3$, 48). Anal. Calcd for $C_{19}H_{17}NO_6$: C, 64.21; H, 4.83; N, 3.94. Found: C, 63.96; H, 5.08; N, 3.71.

4-Acetoxy-3-benzyl-4-(3′,4′,5′-trimethoxyphenyl)oxazolidine-2,5-dione (15) was similarly prepared from the ((trimethoxyphenyl)vinyl)urethane 14 (5.00 g, 13.5 mmol) by oxidation with lead tetraacetate (20.9 g, 47.1 mmol) in glacial acetic acid (150 mL). After workup as above, the oxazolidine-2,5-dione 15 was isolated by crystallization of the residue from ether (3.05 g, 73.4 mmol, 54%): mp 129.5–130.8 °C; IR 2830, 1855, 1788, 1768, 1591, 1238, 1126, 1080, 1020 cm^{-1}; NMR δ 7.23–7.35 (m, 5 H), 6.59 (s, 2 H), 5.00 (d, J = 15 Hz, 1 H), 4.00 (d, J = 15 Hz, 1 H), 3.89 (s, 3 H), 3.87 (s, 6 H), 1.58 (s, 3 H). Anal. Calcd for $C_{21}H_{21}NO_8$: C, 60.71; H, 5.11; N, 3.37. Found: C, 60.83; H, 5.03; N, 3.09.

4-Acetoxy-3-benzyl-4-(3′,4′-(methylenedioxy)phenyl)oxazolidine-2,5-dione (18) was similarly prepared from the (((methylenedioxy)phenyl)vinyl)urethane 17 (5.00 g, 15.4 mmol) by oxidation with lead tetraacetate (23.8 g, 53 mmol) in glacial acetic acid (150 mL). After workup as above, the oxazolidine-2,5-dione was crystallized from the crude residue with ether to yield 18 (3.25 g, 8.8 mmol, 57%): mp 119–122 °C; IR 1854, 1788, 1740, 1700, 1600, 1242, 1125, 1039, 1024 cm^{-1}; NMR δ 7.23–7.34 (m, 4 H), 6.92 (s, 2 H), 6.08 (s, 2 H), 5.08 (d, J = 15 Hz, 1 H), 3.90 (d, J = 15 Hz, 1 H), 2.19 (s, 2 H), 1.49 (s, 3 H); MS m/z (relative intensity) 369 (M, 4), 310 (M – O_2CCH_3, 4), 121 ($CH_2O_2C_6H_3$, 10), 91 ($CH_2C_6H_5$, 100), 77 (C_6H_5), 43 ($COCH_3$, 41). Anal. Calcd for $C_{19}H_{15}NO_7$: C, 61.78; H, 4.16; N, 3.51. Found: C, 61.80; H, 4.16; N, 3.51.

Oxidation of the Oxazolone 8 with Lead Tetraacetate to the Oxazolidine-2,5-dione 9. To a magnetically stirred suspension of lead tetraacetate (3.5 g, 8.0 mmol) in glacial acetic acid (40 mL), under nitrogen, was added the oxazolone (8) (1.0 g, 3.55 mmol).[12] The reaction mixture turned a light brown after ca. 3 h, and TLC, using 30% ethyl acetate/hexane, showed a single product with only a small amount of starting material remaining. An additional 800 mg (1.8 mmol) of lead tetraacetate was added at this stage to the reaction mixture to oxidize the remaining starting material. After stirring overnight, the reaction was quenched with glycerol, diluted with water, and extracted three times with methylene chloride, and the organics were washed twice with saturated sodium bicarbonate solution. The organics were dried with sodium sulfate and filtered, and the solvent was removed to give a yellow solid (1.00 g). The crude material was triturated with anhydrous diethyl ether to give the oxazolidine-2,5-dione 9 as a white solid (946 mg, 2.66 mmol, 75%).

Hydrolysis of the Oxazolidine-2,5-dione 12 to (3′,4′-Dimethoxyphenyl)glyoxylic Acid (19). The oxazolidine-2,5-dione 12 (0.50 g, 1.30 mmol) was dissolved in dioxane (20 mL) and a 20% sodium hydroxide solution (5 mL). After being stirred for 2 days, the mixture was poured into water, acidified with 10% HCl solution, and extracted twice with methylene chloride. After drying with sodium sulfate, the solvent was removed to yield an oil which crystallized upon standing overnight. After trituration with ether and hexanes, the known keto acid[11] 19 (140 mg, 0.67 mmol, 51%) was obtained: mp 134–6 °C (lit.[11] mp 138–9 °C); IR 3290, 1735, 1670, 1587, 1516 cm^{-1}; NMR δ 8.20 (dd, J = 8.6, 2 Hz, 1 H), 7.80 (d, J = 2 Hz, 1 H), 6.95 (d, J = 8.6 Hz, 1 H), 4.00 (s, 3 H), 3.96 (s, 3 H); MS m/z (relative intensity) 210 (M, 22), 165 (M – CO_2H, 100) 137 (M – CO – CO_2H, 18).

Crystal data: $C_{20}H_{19}N_1O_7$, M = 385.37. Orthorhombic, a = 18.061 (7) Å, b = 16.732 (8) Å, c = 12.642 (8) Å, V = 3821 (3) $Å^3$ (by least-squares refinement on diffractometer angles for 20 automatically centered reflections with 18.7° < θ < 24.5°, λ = 1.541 78 Å), space group *Pbca* (No. 61), Z = 8, D_x = 1.34 g/cm^3. Clear parallelepiped. Crystal dimensions 0.25 × 0.25 × 0.25 mm, μ = 8.72 cm^{-1}.

Data Collection and Processing. Data was collected on a Rigaku AFC5S diffractometer, using graphite monochromated Cu Kα radiation, in $\omega/2\theta$ mode, with ω scan width = 1.207 + 0.300 tan θ and ω scan speed 4–16 deg min^{-1}. A total of 3306 reflections were measured (0° < 2θ < 120°, $+h,+k,+l$), all of which were unique, giving 1133 with $I > 3\sigma(I)$, which were used for the final refinement. Three standards were monitored every 150 reflections. An absorption correction (max, min transmission factors = 1.00, 0.91) was applied. A linear and approximately isotropic crystal decay of ca. 2.9% was corrected during processing.

Structure Analysis and Refinement. The structure was determined by direct methods and Fourier difference methods. Full-matrix least-squares refinement was done of the position and anisotropic temperature factors of all non-hydrogen atoms (254 variables). The hydrogens were assigned calculated positions. The hydrogens were assigned calculated isotropic temperature factors 1.2 times the equivalent isotropic temperature factor of the associated non-hydrogen atom. Calculated parameters were updated every two refinement cycles. The weighting scheme $W = 1/[\sigma^2(F_o) + 0.000625F_o^2]$ with $\sigma(F_o)$ from counting statistics gave satisfactory agreement between F_o and F_c, with GOF = 1.26. The final R and R_w values were 0.045 and 0.056, respectively. The programs and computers used and sources of scattering factor data are given in ref 15.

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Supplementary Material Available: Details of the data collection and structural analysis, as well as atomic coordinates, positional and thermal parameters, bond lengths and bond angles, and torsional angles for oxidation product **12** (9 pages). Ordering information is given on any current masthead page.

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The Chemistry of 2′-Amino Analogues of 2′-Hydroxychalcone and Its Derivatives

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The cyclization of 2′-aminochalcone (**2a**) and its side-chain additives has been studied for the development of syntheses of 2-aryl-4-quinolones. **2a** and its 2′-acetamido **2b** and 2′-benzenesulfonamido **2c** derivatives underwent acid- or base-catalyzed cyclization to 1,2,3,4-tetrahydro-4-quinolones. The α,β-dibromides of **2b** and **2c** cyclized to *cis*-3-bromo-4-quinolones as did the corresponding α-bromochalcones and the α-bromo-β-methoxy additive of **2c**. 2′-Acetamido-α-bromochalcone was cyclized by acid to 1,4-dihydro-2-phenyl-4-quinolone. 2′-Aminochalcone formed a stable epoxide which, with acid, gave *cis*-3-hydroxy-1,2,3,4-tetrahydro-3-phenyl-4-quinolone. 2′-Aminochalcones **2a-c** and their additives, such as dibromide and epoxide, are useful, readily available precursors of various 2-aryl-4-quinolones.

Introduction

In 1945, de Diesbach and Kramer[1] noted the similarity between 2-aryl-1,2,3,4-tetrahydro-4-quinolones **1** and flavanones **3**. Yet, except for the base-catalyzed isomerization of 2′-aminochalcone[2] (**2a**) and its *N*-acetyl[3] **2b** and *N*-tosyl[1] **2c** derivatives to the corresponding tetrahydro-4-quinolones **1a-c**, little is known[1-4] of the potential of 2′-aminochalcone (**2a**) and its dihydro derivatives **4** to serve as precursors for 2-aryl-4-quinolones **1**. These 2-aryl-substituted quinolones are difficult to synthesize[5,6] by the usual procedure[6,7] of thermally cyclizing acrylates obtained from the reaction of arylamines with β-keto esters. The opportunity was taken to compare the reactions of 2′-aminochalcone (**2a**) and its derivatives with those of 2′-hydroxychalcone and its corresponding derivatives.

Results and Discussion

2′-Aminochalcone (**2a**), which was conveniently prepared by Murphy and Watanasin's[8] method of aldol condensation, was cyclized by orthophosphoric acid in acetic acid to 1,2,3,4-tetrahydro-2-phenyl-4-quinolone (**1a**), an isomerization analogous to that observed[9] in the synthesis of flavanone **3** from 2′-hydroxychalcone. The same product **1a** was obtained from 2′-acetamidochalcone (**2b**). The *N*-acetyl-4-quinolone **1b** was prepared instead by the reaction of 1,2,3,4-tetrahydro-2-phenyl-4-quinolone (**1a**) with acetic anhydride. 4-Acetoxy-1-acetyl-1,2-dihydro-2-phenylquinoline (**5**) was obtained as a minor product, but, in the presence of sodium acetate, this acetate **5** was the major of the two acetylation products.

2′-(Benzenesulfonamido)chalcone (**2c**) was isomerized to the 1-(phenylsulfonyl)-4-quinolone **1c** by aqueous ethanolic sodium hydroxide. Under similar conditions, 2′-(benzenesulfonamido)-3′,5′-dibromochalcone (**2d**) did not cyclize, probably because of the steric difficulty of accommodating an 8-bromo and a 1-benzenesulfonyl group in a 4-quinolone **1d**.

One of the more effective methods of flavone synthesis is that of Emilewicz and von Kostanecki,[10] in which a 2′-hydroxychalcone dibromide is cyclized by base. For the analogous 4-quinolone synthesis, the *N*-benzenesulfonyl derivative **2c** of 2′-aminochalcone was employed to prevent nuclear halogenation during side-chain bromination and to ensure the availability for cyclization of an ionisable NH function at the 2′-position. Bromination of this chalcone **2c** gave 2′-(benzenesulfonamido)chalcone dibromide (**4a**), which, on reaction with aqueous ethanolic potassium hydroxide, under typical Emilewicz-von Kostanecki reaction

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