aqueous filtrate: 28.6 mg (45%) yield; mp >300 °C dec; IR (KBr) 3429, 3042, 2920, 2852, 1691, 1613, 1444, 1424, 1210, 818 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.37 (6 H, s, 2,8-dimethyl); MS (EI), m/z 274 (P^+).

Anal. Calcd for $C_{12}H_{10}N_4O_4 \cdot 0.25H_2O$: C, 51.71; H, 3.79; N, 20.09. Found: C, 51.53; H, 3.58; N, 19.92.

Acknowledgment. The research was supported by an award from the National Cancer Institute (PHS#1 R01 CA36876-04).

A Convenient Synthesis of Substituted Quinolines by Thermal Electrocyclic Rearrangement of *o*-Vinyl Anils under Nonacidic Conditions

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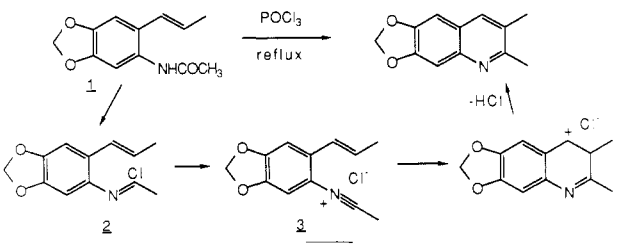
Anils **8a–g** (Table II) underwent smooth rearrangement and oxidation to the quinolines **9a–g** at 155–200 °C via formation of the 2–3 carbon–carbon bond. These cyclizations proceeded in high yields under nonacidic conditions. It was often possible to prepare the quinolines directly in one step from the appropriately substituted aniline and aldehyde. These cyclization conditions eliminate the formation of unwanted byproducts common to some acidic Bischler–Napieralski type quinoline syntheses. The scope and mechanism of the reaction are discussed.

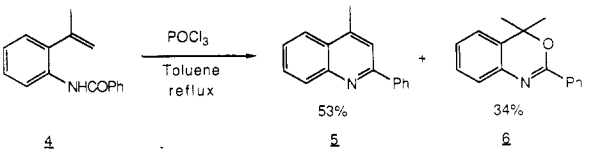
The Bischler–Napieralski synthesis is one of the most useful methods for the synthesis of isoquinolines and has been extensively reviewed.[2] A popular modification of this reaction, introduced by Foulds and Robinson[3] for the synthesis of quinolines, involves treatment of 2-vinylic anilide derivatives **1** with phosphorus oxychloride at reflux. As shown in Scheme I, the reaction involves an electrophilic cyclization of the carbonyl carbon of an amide to an adjoining site of unsaturation. Under these conditions, the cyclization in believed to proceed via the nitrilium ion[4] **3**, which is thought to result from dissociation of the precursor imidoyl chloride **2** upon heating. Other modifications have included phosphorus oxychloride treatment of amidines[5] or ureas,[6] which produce good yields of phenanthrenes and quinolines, respectively.

We have observed cases where the use of acidic reagents such as phosphorus oxychloride results in the formation of substantial amounts of undesired byproducts. For example, cyclization of **4** under the standard conditions resulted in a 53% yield of quinoline **5** and a 34% yield of 4,4-dimethyl-2-phenyl-4*H*-3,1-benzoxazine (**6**), as shown in Scheme II. In an effort to improve the selectivity and yield of this reaction, we sought to develop a convenient nonacidic method for the synthesis of quinolines from 2-aminostyrenes.

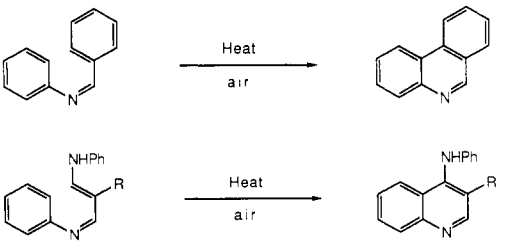
Scheme I



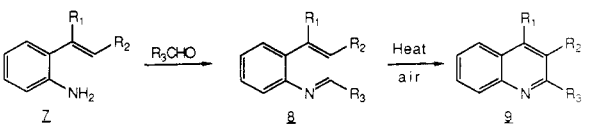
Scheme II



Scheme III



Scheme IV

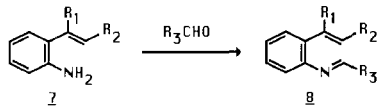


In contrast to the electrophilic cyclizations described above, there have been relatively few reports of the thermal electrocyclic synthesis of quinolines under nonacidic con-

(1) Smith Kline and French Postdoctoral Scientist, 1987.
(2) Whaley, W. M.; Govindachari, T. R. *Org. React.* **1951**, *6*, 74. Kametani, T.; Fukumoto, K. In *Chemistry of Heterocyclic Compounds*; Weissberger, A., Taylor, E. C., Eds.; Wiley: New York, 1981; Vol. 38-1, p 142.
(3) Foulds, R. P.; Robinson, R. *J. Chem. Soc.* **1914**, *105*, 1963. Taylor, T. W. J.; Houbson, P. M. *J. Chem. Soc.* **1936**, 181. For an example of a phenanthrene synthesis, see: Morgan, G. T.; Walls, L. P. *J. Chem. Soc.* **1931**, 2447. Gast, G.; Schmutz, J.; Sorg, D. *Helv. Chim. Acta* **1977**, 1644. Walls, L. P. In *Heterocycl. Comp.* **1952**, *4*, 564. For other quinoline synthesis based on electrophilic reactions of anils, see: Jones, G. in *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: New York, 1984; Vol. 2, p 450.
(4) Jones, G. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: New York, 1984; Vol. 2, pp 410–416.
(5) Cymerman, J.; Short, W. F. *J. Chem. Soc.* **1949**, 703.
(6) Gast, G.; Schmutz, J.; Sorg, D. *Helv. Chim. Acta* **1977**, 1644.

0022-3263/88/1953-4218$01.50/0

Table I



	R_1	R_2	R_3	yield, %	mp, °C
a	CH_3	H	p-$PC_6H_4NO_2$	91	63–63.5
b	CH_3	H	o-$PC_6H_4NO_2$	90	56–57
f	H	CO_2CH_3	p-$PC_6H_4NO_2$	81	138–138.5

ditions. Most reported[7] examples have involved formation of the quinoline 4–4a carbon–carbon bond from vinyl- or phenyl-substituted anils, as shown in Scheme III. These systems required temperatures in excess of 250 °C for efficient cyclization.

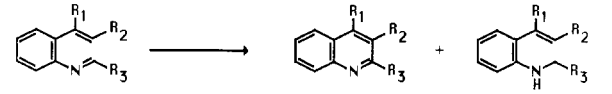
We reasoned that a nonacidic thermal electrocyclic rearrangement of anil 8, shown in Scheme IV, should give rise to the quinoline ring system by formation of the 2–3 carbon–carbon bond. Anils 8 might be prepared easily from the desired 2-aminostyrene derivative 7[8] and an appropriate aldehyde. Furthermore, it might be possible to find conditions in which anil formation and cyclization could be performed in one step. We undertook a more detailed study of this cyclization to determine its general synthetic utility and to better understand the mechanism(s) responsible for quinoline formation.

Results and Discussion

A variety of anils, shown in Table I, were prepared by treating a tetrahydrofuran solution of the aniline with 1 equiv of the aldehyde in the presence of a mixture of anhydrous sodium sulfate and magnesium sulfate at room temperature.[9] Removal of solvent afforded high yields of the crude anils. The neat crude anils were usually stable in the cold. However, several anils readily hydrolyzed and/or decomposed in solution or upon attempts to purify them by column chromatography. In these cases, the crude anils were used directly in the cyclization reaction without further purification. Anils **8a**, **8b**, and **8f** were isolated as stable crystalline solids. Attempts to prepare primary aliphatic anils from a primary aldehyde were not successful. The resulting anils rapidly isomerized to enamines, especially when heated, thus precluding cyclization to dihydroquinolines. Anils **8f** and **8g** were prepared from methyl o-aminocinnamate, which was in turn prepared by reduction of methyl o-nitrocinnamate according to known procedures.[10]

The cyclizations were performed by heating a dilute solution of the anil in nondegassed 1,2,4-trichlorobenzene under a blanket of nitrogen or, preferably, open to the air. The results are summarized in Table II. Quinolines **9** were produced in good yields along with varying amounts of amine byproducts **10**. No byproducts such as **6** were observed. The desired quinolines were purified easily by flash chromatography. Anils **8f** and **8g** required higher temperature to effect efficient cyclization to the more hindered 2,3-disubstituted quinolines.

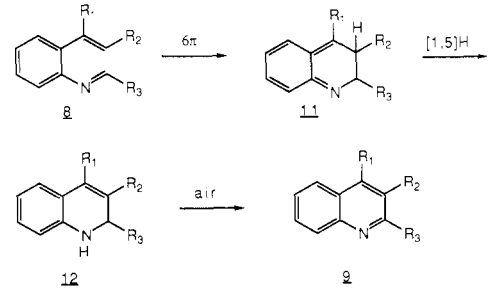
Table II



	R_1	R_2	R_3	temp, °C	time, h	yield,[d] % **9**	**10**
a	CH_3	H	p-$PC_6H_4NO_2$	155	7	82	3
b	CH_3	H	o-$PC_6H_4NO_2$	155	5	68	0[a]
c	CH_3	H	p-PC_6H_4OMe	155	14	74	10
						46	30[c]
d	CH_3	H	o-PC_6H_4OMe	155	14	66	17
e	CH_3	H	t-Bu	155	42	38	6
				180	10	56	15[b]
f	H	CO_2CH_3	p-$PC_6H_4NO_2$	200	12	86	0[a]
g	H	CO_2CH_3	p-PC_6H_4OMe	200	38	70	0[a]

[a] None detected. [b] The aniline was treated with 100% excess of pivaldehyde in situ. [c] Reaction was degassed and performed under nitrogen. [d] All yields are for isolated pure materials.

Scheme V



These quinolines can also be prepared directly in one pot from their precursor aldehyde and aniline substrates without isolation of the intermediate anils (for example, see **8e**). However, attempts to prepare quinolines in this way from primary aliphatic aldehydes were unsuccessful. For example, treatment of o-isopropenylaniline with pentanal in 1,2,4-trichlorobenzene at 155 °C gave only the product resulting from condensation of the aniline with the aldol product of pentanal.[11]

A proposed mechanism for the cyclization is shown in Scheme V. The cyclization is thought to occur via a thermal 6π electrocyclic rearrangement[12] of anil 8, followed by a rapid [1,5]-H shift, with rearomatization, to afford dihydroquinoline **12**. The dihydroquinoline is then oxidized to the product quinoline **9**, probably by air. We feel confident that the cyclization is not being catalyzed by traces of acid, because the reaction also proceeds in the presence of 0.5 equiv of 1,8-bis(dimethylamino)-naphthalene, a strong, nonnucleophilic base. In several cases where the cyclizations were performed with degassed solvent under an inert atmosphere, dihydroquinolines **12c**, **12d**, and **12f** could be isolated and characterized. Dihydroquinolines **12c** and **12d** were unstable and slowly

(7) McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2200. See also: Pictet, A.; Ankersmit. H. J. *Chem. Ber.* **1889**, *22*, 3339. Scheuer, H.; Zsindely, J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 478. Easton, N. R.; Cassady, D. R. *J. Org. Chem.* **1962**, *27*, 4713.

(8) For some methods of preparation of 2-aminostyrenes, see: Gassman, P. G.; Drewes, H. R. *J. Am. Chem. Soc.* **1978**, *100*, 7600. Horino, H.; Inoue, N. *Tetrahedron Lett.* **1979**, 2403. Butcher, M.; Mathews, R. J.; Middleton, S. *Aust. J. Chem.* **1973**, *26*, 2067. Plevyak, J. E.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2454. Padwa, A.; Nahm, S. *J. Org. Chem.* **1981**, *46*, 1402. Haefliger, W.; Knecht, H. *Tetrahedron Lett.* **1984**, *25*, 285. Gassman, P. G.; Schenk, W. N. *J. Org. Chem.* **1977**, *42*, 3240.

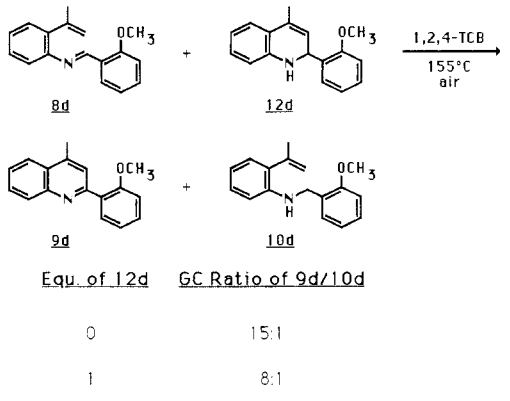
(9) We thank Prof. L. Overman for providing us with details of this method. Attempts at imine formation with other conditions such as toluene at reflux with azeotropic removal of water resulted in lower yields.

(10) Skinner, W. A.; Schelstraete, M. G. M.; Baker, B. R. *J. Org. Chem.* **1961**, *26*, 1554.

(11) Chromatographic separation afforded 51% of 2-isopropenylaniline, 15% of 2-butyl-2-octenal as a mixture of E and Z isomers, and about 22% of a mixture of 2-(1-butyl-1-heptenyl)-4-methylquinoline and its corresponding dihydroquinoline.

(12) Neiman, Z. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1746. For related examples, see ref 6 and: Overman, L. E.; Tsuboi, S. *J. Am. Chem. Soc.* **1977**, *99*, 2813. Scheiss, P.; Monnier, C.; Ringele, P.; Sendi, E. *Helv. Chim. Acta* **1974**, *57*, 1676. Eloy, F.; Deryckere, A. *J. Heterocycl. Chem.* **1970**, *7*, 1191.

Scheme VI



oxidized to the corresponding quinolines upon standing in deuteriochloroform.

Amine byproducts **10** (Table II) are believed to arise from reduction of starting anils **8**. More reduced amine **10c** was isolated when the cyclization was performed under a degassed, inert atmosphere, compared to a control performed in a flask open to air (see **c**, Table II). It seems that anils **8** can compete with air under the reaction conditions to effect the oxidation of dihydroquinolines to quinolines.

The redox chemistry of dihydroquinoline **12d** with anil **8d** was examined briefly. When equimolar amounts of **8d** and **12d** were subjected to the cyclization conditions, nearly twice as much amine **10d** was produced, compared to controls run in the absence of dihydroquinoline **12d** (see Scheme VI). This suggests that under aerobic conditions anils **8** appear to be capable of oxidizing dihydroquinolines to quinolines. This pathway may account for the frequent presence of small amounts of reduced amine byproducts **10** produced under aerobic cyclization conditions.

Conclusion

The electrocyclic rearrangement of anils **8** offers a convenient, high-yield entry to a variety of substituted quinolines. These reactions often can be performed in a single step from the starting 2-aminostyrene derivative and an appropriate aldehyde. The intermediate dihydroquinolines are oxidized by air to the desired quinolines, and the reaction is performed best in a flask open to air. Although the reaction is limited to aldehydes that do not self-condense readily, we are working toward the development of nonacidic cyclization conditions that will permit the introduction of primary substituents into the 2-position of the product quinoline.

Experimental Section

Unless stated elsewhere, experiments were performed under a slight static pressure of nitrogen. Quinolines **9a–g** are best prepared in a flask open to air. TCB refers to 1,2,4-trichlorobenzene, which was dried by passing through a column of 150-mesh neutral activated alumina (Aldrich) and stored over 4A molecular sieves. Tetrahydrofuran was freshly distilled from sodium under a nitrogen atmosphere, using benzophenone as an indicator. Flash chromatography[13] was performed with J. T. Baker silica. Elution with hexane separated TCB from the product. The product was then eluted with 4% ethyl acetate/hexane. Preparative thin-layer chromatography was performed with Merck Kieselgel 60 F_{254} plates, 0.25 mm, eluting with 20% ethyl acetate/hexane. Nuclear magnetic resonance spectra were obtained on a Bruker AM 400, a Bruker WM 360, or a Varian EM-360L for 400-, 360-, and 60-MHz spectra, respectively, using tetramethylsilane as a reference. Infrared spectra were measured on a Perkin-Elmer Model 1320 infrared spectrophotometer. Gas chromatography was performed on a Hewlett-Packard Model 5790A GC using a HP Ultra Performance cross-linked methylsilicone column, 25 m × 0.20 mm i.d. × 0.33 μm film thickness. Mass spectra were recorded in the EI mode on a Hewlett-Packard Model 5790 GC equipped with a 5790A mass detector using a Durabond DB-1 column, 30 m × 0.25 mm i.d. × 0.25 μm film thickness programed for 180–300 °C at 15 °C/min. High-resolution mass spectra were measured on a VG70-SE in the EI mode at 70 eV with a resolution of at least 10 000. Melting points were measured on a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analyses were performed on a Perkin-Elmer 240C CHN analyzer.

Preparation of *N*-[(4-Nitrophenyl)methylene]-2-(2-propenyl)benzenamine (8a). A solution of 2-isopropenylaniline (2.0 g, 150 mmol) in tetrahydrofuran (60 mL) was treated with *p*-nitrobenzaldehyde (2.27 g, 150 mmol) in the presence of anhydrous sodium sulfate (5.0 g) and magnesium sulfate (5.0 g) at room temperature for 12 h. The salts were removed by filtration and washed with tetrahydrofuran twice (20 mL each). Upon concentration and drying in vacuo, the filtrate gave yellow crystals, which were recrystallized from 95% ethanol to afford anil **8a**, 3.64 g, 91% yield.

8a: mp 63–63.5 °C; ^{1}H NMR ($CDCl_3$), 400 MHz) δ 8.46 (1 H, s), 8.32–8.29 (2 H, AB type, J = 8.9, 2.1, 1.7), 8.06–8.02 (2 H, J = 8.9, 2.0, 1.9), 7.33–7.30 (2 H, m), 7.29–7.21 (1 H, m), 6.98–6.96 (1 H, dd, J = 7.9, 1.2), 5.19–5.18 (1 H, t, J = 1.65), 4.98–4.97 (1 H, d, J = 1.0), 2.14 (3 H, s); IR (Nujol, cm^{-1}) 1620, 1600, 1510, 1460, 1375, 1350, 895, 860, 765; MS (CH_4) m/e 307 ($M^+ + C_3H_5^+$), 295 ($M^+ + C_2H_5^+$), 267 ($M^+ + H^+$, 100), 251 ($M^+ - 15$), 237 ($M^+ + H - NO$). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.36; H, 5.22; N, 10.79.

Preparation of 4-Methyl-2-(4-nitrophenyl)quinoline (9a). A solution of **8a** (300 mg, 1.13 mmol) in dried TCB (15 mL) was heated at 155 °C (oil bath) for 7 h. The mixture was subjected directly to flash chromatography to give quinoline **9a** (243 mg, 82% yield) and 4-nitro-*N*-[2-(2-propenyl)phenyl]benzenemethanamine (**10a**, 9 mg, 3% yield).

9a: mp 125–126 °C; ^{13}C NMR ($CDCl_3$, 360 MHz) δ 154.0 (Cq), 148.2 (Cq), 147.9 (Cq), 145.6 (Cq), 145.4 (Cq), 130.4 (CH), 129.8 (CH), 128.1 (2 CH), 127.5 (Cq), 126.9 (Cq), 123.8 (2 CH), 123.6 (CH), 119,3 (CH), 18.9 (CH_3); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37–8.32 (4 H, m), 8.21 (1 H, m), 8.04–8.02 (1 H, d, J = 7.8), 7.78–7.75 (2 H, m), 7.63–7.59 (1 H, m), 2.80 (3 H, s); MS m/e 264.2 (M^+, 100), 234.2 ($M^+ - 30$, 60.5), 218.2 ($M^+ - 46$, 78.9); IR (Nujol, cm^{-1}) 1610, 1600, 1550, 1510, 1465, 1375, 1340, 860, 850, 765, 720. Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.82; H, 4.56; N, 10.82.

10a: mp 85–86 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13–8.10 (2 H, dd, J = 7.1, 1.8), 7.47–7.44 (2 H, d, J = 8.8), 7.06–7.00 (2 H, m), 6.72–6.66 (1 H, td, J = 7.4, 0.9), 6.43–6.40 (1 H, dd, J = 8.4, 0.9), 5.34–5.33 (1 H, t, J = 2.2), 5.10–5.09 (1 H, d, J = 0.9), 4.75 (1 H, b), 4.44 (2 H, s), 2.09 (3 H, s); ^{13}C NMR ($CDCl_3$, 360 MHz) δ 147.6 (Cq), 146.8 (Cq), 143.2 (Cq), 129.4 (Cq), 127.9 (CH), 127.8 (CH), 127.4 (2 CH), 123.6 (2 CH), 117.2 (CH), 115.8 (Cq), 110.4 (CH), 47.3 (CH_2), 24.0 (CH_3); IR (film, cm^{-1}) 3420, 3060, 1660, 1600, 1580, 1500, 1330, 1100, 895, 845, 750; MS m/e 268.2 (M^+, 4.4), 253 ($M^+ - 15$, 1.1), 207 (1.8), 132 (100), 117 (23.9), 106 (5.7). Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.68; H, 6.10; N, 10.23.

Preparation of 9a in the Presence of 1,8-Bis(dimethylamino)naphthalene. To a solution of **8a** (200 mg, 0.75 mmol) in TCB (10 mL) was added 1,8-bis(dimethylamino)naphthalene (85 mg, 0.38 mmol). The mixture was heated at 155 °C (oil bath) for 7 h. Workup as above gave **9a** (119 mg, 60% yield). This material coeluted on GC and had an NMR spectrum identical with that of **9a** prepared without 1.8-bis(dimethylamino)-naphthalene treatment.

Preparation of *N*-[(2-Nitrophenyl)methylene]-2-(2-propenyl)benzenamine (8b). In the same manner as **8a**, **8b** was prepared from 2-nitrobenzaldehyde (1.136 g, 7.52 mmol), 2-isopropenylaniline (1 g, 7.52 mmol), sodium sulfate (2.5 g), magnesium sulfate (2.5 g), and tetrahydrofuran (30 mL) in a yield of 90% (mp 56–57 °C). (Note: The material should be kept in the refrigerator in the dark.)

(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

8b: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 8.80 (1 H, s), 8.35–7.90 (2 H, m), 7.85–7.53 (2 H, m), 7.35–6.92 (4 H, m), 5.15 and 4.90 (2 H), 2.14 (3 H, s); IR (Nujol, cm^{-1}) 1620, 1600, 1570, 1500, 1460, 1370, 1330, 890, 790, 760, 740, 720; MS (CI, CH_4) m/e 307 ($M^+ + C_3H_5$, 5.69), 2.95 ($M^+ + C_2H_5$, 9.96), 267 ($M^+ + H$, 100), 250 (21.36), 219 (9.94), 144 (3.85).

Preparation of 4-Methyl-2-(2-nitrophenyl)quinoline (9b). A solution of **8b** (200 mg, 0.75 mmol) in TCB (10 mL) was heated at 155 °C for 5 h. The usual workup gave 166 mg of crude product, which was purified by preparative TLC to provide 135 mg of **9b**, 68.2%, mp 103–104 °C.

9b: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.13–8.11 (1 H, d, J = 8.3), 8.05–8.02 (1 H, d, J = 8.2), 8.00–7.97 (1 H, d, J = 8.2), 7.76–7.68 (3 H, m), 7.63–7.55 (2 H, m), 7.38 (1 H, s), 2.77 (3 H, s); ^{13}C NMR ($CDCl_3$, 360 MHz) δ 155.2 (Cq), 149.2 (Cq), 147.3 (Cq), 145.7 (Cq), 135.5 (Cq), 132.6 (CH), 131.6 (CH), 129.9 (CH), 129.4 (CH), 127.3 (CH), 126.9 (CH), 124.5 (CH), 123.7 (CH), 121.2 (CH), 18.9 (CH_3); MS m/e 264 (M^+, 88.7), 249 ($M^+ - 15$, 5.5), 234 ($M^+ - 30$, 57.2), 221 ($M^+ - 43$, 100), 217 (52.2), 204 (26.9), 190 (18.19), 165 (10.0), 131 (26.9), 108 (32.9), 95 (28.9), 77 (24.0), 63 (19.4); IR (Nujol cm^{-1}) 1600, 1540, 1460, 1370, 860, 850, 720. Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.99; H, 4.74; N, 10.64.

Preparation of *N*-[(4-Methoxyphenyl)methylene]-2-(2-propenyl)benzenamine (8c). In the same manner as **8a**, **8c** was prepared from 2-isopropenylaniline (2.0 g, 15 mmol), *p*-anisaldehyde (2.65 g, 15 mmol), magnesium sulfate (5 g), sodium sulfate (5 g), and tetrahydrofuran (80 mL). The progress of the reaction was monitored by IR spectroscopy, and the reaction was complete usually within 48 h. After filtration and concentration to dryness, a nearly quantitative yield of crude anil was obtained. The material was used in the cyclization reaction without further purification.

8c: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.28 (1 H, s), 7.85–7.82 (2 H, AB, J = 8.6), 7.30–7.25 (2 H, m), 7.17–7.13 (1 H, t, J = 7.4), 6.99–6.97 (2 H, AB, J = 8.6), 6.94–6.92 (1 H, d, J = 7.7), 5.16–5.15 (1 H, d, J = 1.2), 5.03 (1 H, s), 3.86 (3 H, s), 2.14–2.13 (3 H, d, J = 0.7); IR (film, cm^{-1}) 3040, 1680, 1610, 1600, 1570, 1500, 890, 750; MS (CI, CH_4) m/e 292 ($M^+ + C_3H_5$, 3.54), 280 ($M^+ + C_2H_5$, 21.42), 266 ($M^+ + CH_3$, 0.33), 252 (100), 236 (3.06), 144 (18.43), 121 (3.12).

Preparation of 2-(4-Methoxyphenyl)-4-methylquinoline (9c). In the same manner as **9a**, **8c** (400 mg, 1.59 mmol) was heated in TCB (20 mL) at 155 °C for 14 h. The resulting quinoline **9c** and 4-methoxy-*N*-[2-(2-propenyl)phenyl]benzenemethanamine **10c** were separated by flash chromatography to give **9c** (292 mg, 73.5% yield) and **10c** (42 mg, 10.4% yield).

9c: mp 68–69 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.17–8.12 (3 H, m), 7.99–7.96 (1 H, d, J = 6.9), 7.73–7.68 (2 H, m), 7.55–7.49 (1 H, td, J = 8.1, 1.1), 7.06–7.03 (2 H, m), 3.88 (3 H, s), 2.75 (3 H, s); ^{13}C NMR ($CDCl_3$, 360 MHz) δ 160.7 (Cq), 156.5 (Cq), 148.1 (Cq), 144.5 (Cq), 132.3 (Cq), 130.0 (CH), 129.2 (CH), 128.8 (2 CH), 126.9 (Cq), 125.6 (CH), 123.5 (CH), 119.2 (CH), 114.1 (2 CH), 55.3 (CH_3), 18.9 (CH_3); IR (Nujol, cm^{-1}) 3040, 1600, 1580, 1550, 1500, 1460, 950, 830, 760, 745; MS m/e 249 (M^+, 100), 234 ($M^+ - 15$, 37.0), 219 ($M^+ - 15 - 15$, 45), 218 ($M^+ - 15 - 16$, 3.3), 206 ($M^+ - 43$, 18.8), 204 ($M^+ - 45$, 15.1), 191 ($M^+ - 58$, 21.4). HRMS Calcd for $C_{17}H_{15}NO$: 249.1154. Found: 249.1163.

10c: mp 47.5–48.5 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.28–7.25 (2 H, d, J = 8.4), 7.14–7.08 (1 H, td, J = 8.1, 1.8), 7.04–7.01 (1 H, dd, J = 7.3, 1.5), 6.89–6.85 (2 H, m), 6.72–6.66 (1 H, td, J = 8.4, 1.1), 6.64–6.61 (1 H, d, J = 8.0), 5.27–5.26 (1 H, dd, J = 2.2, 1.5), 5.05–5.04 (1 H, t, J = 1.1), 4.51 (1 H, b), 4.26 (2 H, s), 3.81 (3 H, s), 2.06–2.05 (3 H, s); ^{13}C NMR ($CDCl_3$, 360 MHz) δ 144.1, 143.4, 131.4, 129.2, 128.4, 128.0, 127.7, 116.6, 115.6, 113.9, 110.5, 55.0, 47.6, 23.9; IR (film, cm^{-1}) 3410 (b), 3080, 1620, 1600, 1580, 1510, 1500, 900, 825, 750; MS m/e 253 (M^+, 32), 238 ($M^+ - 15$, 1.0), 132 (100), 121 ($^+H_2CC_6H_4OCH_3$, 78.3), 91.1 ($^+CH_2C_6H_5$, 36.1). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 81.00; H, 7.85; N, 5.53.

Preparation of *N*-[(2-Methoxyphenyl)methylene]-2-(2-propenyl)benzenamine (8d). In the same manner as **8a**, **8d** was obtained from 2-isopropenylaniline (2.0 g, 15 mmol), *o*-anisaldehyde (2.05 g, 15 mmol), magnesium sulfate (5 g), sodium sulfate (95 g), and tetrahydrofuran (80 mL). The progress of the reaction was monitored by IR spectroscopy, and the reaction was complete usually within 48 h. After filtration and concentration to dryness, a nearly quantitative yield of crude anil was obtained. The material was used in the cyclization reaction without further purification.

8d: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.86 (1 H, s), 8.20–8.18 (1 H, d, J = 7.2), 7.44–7.42 (1 H, m), 7.30–7.26 (2 H, m), 7.18–7.14 (1 H, m), 7.07–7.00 (2 H, m), 6.96–6.93 (1 H, m), 5.17–5.16 (1 H, m), 5.02–5.01 (1 H, m), 3.88 (3 H, s), 2.15–2.14 (3 H, t, J = 1.1); IR (film, cm^{-1}) 1685, 1620, 1600, 1565, 1485, 1465, 1250, 890, 860, 750; MS (CH_4) m/e 292 ($M^+ + C_3H_5^+$, 1.82), 280 ($M^+ + C_2H_5^+$, 1.20), 252 ($M^+ + H^+$), 236.1 ($M^+ - 15$, 3.56), 144 ($NCC_6H_4C_3H_5^+$, 12.2), 121 ($^+H_2CC_2H_4OCH_3$, 3.07).

Preparation of 1,2-Dihydro-2-(2-methoxyphenyl)-4-methylquinoline (12d). A degassed solution of **8d** (400 mg, 1.59 mmol) in TCB (20 mL) was heated at 155 °C under a nitrogen atmosphere for 8 h. After workup, the dihydroquinoline **12d** was purified by flash chromatography and its spectral properties were measured immediately. When exposed to air, dihydroquinoline **12d** slowly oxidized to **9d** over 3–6 days.

12d: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 7.50–6.27 (8 H, m), 5.68–5.46 (2 H, dd), 4.23 (1 H, s, NH), 3.83 (3 H, s), 2.05 (3 H, s); IR (film, cm^{-1}) 3400 (b), 1640, 1600, 1550, 1480, 1465, 1435, 1100, 1020, 750; MS m/e 251 (M^+, 100), 236 ($M^+ - 15$, 30.4), 220 ($M^+ - OCH_3$, 34.0), 204 ($M^+ - 47$, 10.8), 144 ($M^+ - C_6H_5OCH_3$, 89.0), 108 ($C_6H_5OCH_3$, 11.9), 91 ($C_6H_5CH_2^+$, 20.6).

Preparation of 2-(2-Methoxyphenyl)-4-methylquinoline (9d). In the same manner as **9a**, **8d** (400 mg, 1.59 mmol) was dissolved in TCB (20 mL) and heated at 155 °C for 14 h. After the usual workup, quinoline **9d** (264 mg, 66.3%) and 2-methoxy-*N*-[2-(2-propenyl)phenyl]benzenemethanamine (**10d**, 67 mg, 16.6%) were obtained.

9d: mp 83–84 °C; ^{13}C NMR ($CDCl_3$, 360 MHz) δ 157.0 (Cq), 156.7 (Cq), 148.0 (Cq), 142.9 (Cq), 131.3 (CH), 130.0 (CH), 129.8 (Cq), 128.7 (CH), 127.0 (Cq), 125.7 (CH), 123.8 (CH), 123.4 (CH), 121.0 (CH), 111.3 (CH), 55.5 (CH_3), 18.6 (CH_3); ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.19–8.16 (1 H, dd, J = 8.4), 8.02–7.98 (1 H, dd, J = 8.4, 1.1), 7.80–7.77 (1 H, dd, J = 7.3, 1.8), 7.73–7.67 (2 H, m), 7.58–7.52 (1 H, td, J = 7.5, 1.4), 7.44–7.40 (1 H, td, J = 7.7, 1.8), 7.15–7.09 (1 H, td, J = 7.5, 1.1), 7.05–7.01 (1 H, dd, J = 8.4, 0.8), 3.86 (3 H, s), 2.74 (3 H, d, J = 0.7); IR (Nujol, cm^{-1}) 1600, 1580, 1490, 1460, 1380, 1250, 750; MS m/e 249 (M^+, 98.0), 248 ($M^+ - 1$, 100), 234 ($M^+ - 15$, 33.4), 220 ($M^+ - 29$, 40.2), 218 ($M^+ - OCH_3$, 37.0), 204 ($M^+ - OCH_3 - 15$, 66.5). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.87; H, 6.16; N, 5.65.

10d: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.21–7.18 (2 H, m), 7.08–6.98 (1 H, m), 6.94–6.91 (1 H, dd, J = 7.6, 1.8), 6.88–6.77 (2 H, m), 6.61–6.55 (2 H, m), 5.21–5.19 (1 H, td, J = 3.7, 1.5), 4.97–4.96 (1 H, dd, J = 2.2, 0.7), 4.57 (1 H, b), 4.26 (2 H, s), 3.75 (3 H, s), 1.98–1.97 (3 H, dd, J = 1.4, 0.7); ^{13}C NMR ($CDCl_3$, 360 MHz) δ 157.3 (Cq), 144.3 (Cq), 143.6 (Cq), 129.5 (Cq), 128.6 (CH), 128.1 (CH), 128.0 (CH), 127.7 (CH), 127.3 (Cq), 120.4 (CH), 116.5 (CH), 115.5 (CH_2), 110.9 (CH), 110.1 (CH), 55.1 (CH_3), 43.6 (CH_2), 24.1 (CH_3); IR (film, cm^{-1}) 3420, 3040, 1640, 1600, 1580, 1250, 900, 750; MS m/e 253.2 (M^+, 3.2), 238 ($M^+ - 15$, 10), 132 (100), 144 ($NCC_6H_4C_3H_5$, 1.6), 121 ($H_2CC_6H_4OCH_3$), 91 ($C_6H_5CH_2$, 36.1). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.54; H, 7.36; N, 5.56.

Preparation of 2-(1,1-Dimethylethyl)-4-methylquinoline (9e). 2-Isopropenylaniline (400 mg, 3 mmol) and pivaldehyde (516 mg, 6 mmol) were stirred for 2.5 h at room temperature. TCB (20 mL) was added to the resulting homogeneous mixture, and the solution was heated for 10 h at 180 °C (oil bath). The usual workup gave 335 mg of quinoline **9e** (56.1% yield) and 89 mg of *N*-(2,2-dimethylethyl)-2-(2-propenyl)benzeneamine (**10e**, 14.6% yield).

9e: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.17–8.13 (1 H, d, J = 8.3), 7.96–7.93 (1 H, d, J = 8.3), 7.72–7.66 (1 H, t, J = 8.1), 7.54–7.48 (1 H, t, J = 7.2), 7.39 (1 H, s), 2.70 (3 H, s), 1.51 (9 H, s); IR (film, cm^{-1}) 3070, 1600, 1560, 1510, 930, 760; MS m/e 199 (M^+, 30.7), 198 ($M^+ - 1$, 26.6), 184 ($M^+ - 15$, 100), 168 (7.3), 157 (44.1), 143 (22.0), 115 (19.6). HRMS Calcd for $C_{14}H_{17}N$: 199.1361. Found: 199.1356.

10e: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30–7.24 (1 H, m), 7.17–7.12 (1 H, td, J = 8.4, 1.4), 7.04–7.03 (1 H, d, J = 1.4), 6.79 (1 H, b), 6.75–6.72 (1 H, d, J = 7.3), 5.34 (s, 1 H), 5.05 (1 H, s), 2.91 (2 H, s), 2.08 (3 H, s), 0.99 (9 H, s); IR (film, cm^{-1}) 3420, 3080, 1750, 1625, 1600, 1575, 1505, 900, 730; MS m/e 203 (M^+, 13.7), 188 (M^+

- 15, 2.2), 146 (100), 131 (29.3), 130 (25.2), 118 (14.2).

Preparation of Methyl 3-(2-Nitrophenyl)-2-propenoate. To a suspension of *o*-nitrocinnamic acid (38.6 g, 0.2 mol) in methanol (240 mL) was added boron trifluoride–methanol complex (22 mL). The solution was stirred and heated at reflux for 24 h. The clear solution was cooled to room temperature and concentrated to half of its original volume. As the solution cooled, light green, flat crystals formed: 36.8 g; 88.9% yield; mp 72–73 °C (lit[14] mp 72–73 °C); ^{1}H NMR ($CDCl_3$, 60 MHz) δ 8.26–8.00 (1 H, d, J = 15)), 8.12–7.44 (4 H, m), 6.50–6.23 (1 H, d, J = 15), 3.87 (3 H, s).

Preparation of Methyl 3-(2-Aminophenyl)-2-propenoate. To a solution of methyl 3-(2-nitrophenyl)-2-propenoate (2.90 g, 0.014 mol) in methanol (60 mL) were added water (7 mL) and ammonium chloride (1.3 g, 0.024 mol). To this stirred solution was added zinc chloride (9.0 g, 0.14 mol) over a period of 15 min. The mixture was heated at reflux for 2 h. The hot solution was filtered through Florisil and diluted with water (100 mL). After the solution cooled, yellow needles were collected: 1.23 g; 72% yield; mp 64–65 °C (lit.[9] mp 62–63 °C); ^{1}H NMR ($CDCl_3$, 60 MHz) δ 7.95–7.70 (1 H, d, J = 16), 7.42–6.60 (4 H, m), 6.45–6.21 (1 H, d, J = 16), 3.80 (3 H, s); IR (Nujol, cm^{-1}) 3420, 360, 1700, 1625, 1600, 1580, 1200, 1180, 980, 770, 705; MS m/e 177 (M^+, 49.5), 160 (M^+ - 17, 13.5), 146 (M^+ - CH_3OH, 100), 128 (57.4), 118 (75.6), 117 (68.4), 91 (24.4).

Preparation of Methyl 3-[2-(((4-Nitrophenyl)-methylene)amino)phenyl]-2-propenoate (8f). A solution of methyl 3-(2-aminophenyl)-2-propenoate (885 mg, 5 mmol) in tetrahydrofuran (30 mL) was treated with *p*-nitrobenzaldehyde (755 mg, 5 mmol) in the presence of anhydrous sodium sulfate (2.5 g) and magnesium sulfate (2.5 g) at room temperature for 30 h. The filtrate was concentrated and dried in vacuo. The residue was recrystallized from 95% ethanol/Water to give **8f** as yellow needles, 1.26 g, 81.3% yield.

8f: mp 138–138.5 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.50 (1 H, s), 8.37–8.34 (2 H, dd, J = 10.7, 1.8), 8.22–8.18 (1 H, d, J = 16.2), 8.13–8.11 (2 H, dd, J = 10.7, 1.8), 7.68–7.66 (1 H, dd, J = 7.8, 1.2), 7.46–7.42 (1 H, td, J = 7.7, 1.2), 7.33–7.29 (1 H, td, J = 7.8, 7.1), 7.06–7.04 (1 H, dd, J = 7.1, 0.7), 6.49–6.45 (1 H, d, J = 16.2), 3.79 (3 H, s); IR (Nujol, cm^{-1}) 1710, 1620, 1600, 1520, 910, 735; MS m/e 310 (M^+, 20.8), 295 (M^+ - 15, 21), 279 (M^+ - 31, 3.0), 251 (M^+ - 59, 100), 205 (44.2), 188 (6.2), 176 (3.9), 128 (13.7), 102 (8.7). Anal. Calcd for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.88; H, 4.49; N, 9.27.

Preparation of Methyl 2-(4-Nitrophenyl)-3-quinolinecarboxylate (9f). A solution of **8f** (420 mg, 1.35 mmol) in 20 mL of TCB was heated at 200 °C (oil bath) for 12 h. After workup by flash chromatography, **9f** was collected (359 mg, 86% yield). An analytical sample was obtained by recrystallization from ethyl acetate/hexane to give light yellow needles.

9f: mp 147.5–148 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.81 (1 H, s), 8.36–8.32 (2 H, dd, J = 8.8, 2.0), 8.21–8.18 (1 H, d, J = 8.8), 8.00–7.97 (1 H, d, J = 8.0), 7.92–7.81 (1 H, m), 7.80–7.77 (2 H, dd, J = 8.8, 2.0), 7.76–7.65 (m), 3.80 (3 H, s); MS m/e 308 (M^+, 29), 293 (M^+ - 15, 100), 277 (M^+ - 31, 7.8), 247 (M^+ - 61, 48.3), 231 (12.5), 219 (6.9), 176 (5.3), 203 (13.0); IR (Nujol, cm^{-1}) 1715, 1620, 1600, 1510, 1350, 1280, 1250, 860, 800, 760; ^{13}C NMR (360 MHz) ($CDCl_3$) δ 166.8 (Cq), 155.8 (Cq), 148.2 (Cq), 147.6 (Cq), 146.9 (Cq), 139.9 (CH), 132.1 (CH), 129.6 (CH), 129.4 (CH), 128.3 (CH), 127.9 (CH), 125.9 (Cq), 123.8 (Cq), 123.0 (CH), 52.4 (CH_3). Anal. Calcd for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.92; N, 9.09. Found: C, 66.23; H, 3.93; N, 9.19.

Isolation and Identification of Methyl 1,2-Dihydro-2-(4-nitrophenyl)-3-quinolinecarboxylate (12f). A degassed solution of **8f** (420 mg, 1.35 mmol) in 20 mL of TCB was heated at 160 °C for 125 h under nitrogen. Quinoline **9f** and dihydroquinoline **12f** were detected in a ratio of approximately 40:60 by GC analysis. Flash chromatography afforded 140 mg of **12f** contaminated with a small amount of **9f**. Repeated recrystallizations from ethyl acetate/hexane gave pure brown crystals of **12f**.

12f: mp 144.5–145.5 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.11–8.09 (2 H, AB type, J = 8.6), 7.60 (1 H, s), 7.55–7.53 (2 H, AB type, J = 8.6), 7.13–7.11 (2 H, m), 6.73–6.69 (1 H, d, J = 7.4), 6.52–6.50 (1 H, d, J = 7.8), 5.73 (1 H, s), 3.72 (3 H, s); ^{13}C NMR ($CDCl_3$, 360 MHz) δ 165.8 (Cq), 150.9 (Cq), 147.5 (Cq), 143.7 (Cq), 122.5 (Cq), 117.6 (Cq), 135.7 (CH), 132.5 (CH), 125.9 (CH), 127.1 (CH), 124.0 (CH), 118.3 (CH), 113.1 (CH), 54.7 (CH), 51.8 (CH_3); IR (film, cm^{-1}) 3400, 1700, 1630, 1600, 1580, 1520, 1490, 1350, 1240, 1210, 1160, 860; MS m/e 310 (M^+, 11.0), 295 (M^+ - 15, 7.4), 251 (M^+ - 59, 3.8), 221 (1.5), 204 (7.5), 188 (M^+ - $O_2NC_6H_5$, 100), 128 (14.7). Anal. Calcd for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.94; H, 4.64; N, 9.03.

Preparation of Methyl 3-[2-(((4-Methoxyphenyl)-methylene)amino)phenyl]-2-propenoate (8g). **8g** was prepared in the same manner as **8d** from methyl 3-(2-aminophenyl)-2-propenoate (885 mg, 5 mmol) *p*-anisaldehyde (681 mg, 5 mmol), anhydrous sodium sulfate (2.5 g), and magnesium sulfate (2.5 g) by stirring for 2 days in tetrahydrofuran (35 mL). **8g** was used for the next electrocyclization step without further purification.

8g: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 8.32 (1 H, s), 8.05–6.90 (7 H, m), 6.58 and 6.30 (1 H, d, J = 15), 3.88 (3 H, s), 3.77 (3 H, s); IR (film, cm^{-1}) 3080, 1700, 1620, 1600, 1590, 1570, 1510, 1250, 870, 830, 760, 730; MS m/e 295 (M^+, 24.0), 280 (M^+ - 15, 0.9), 264 (M^+ - 31, 5.2), 236 (M^+ - 59, 100), 221 (12.3), 204 (12.5), 193 (28.5), 167 (6.8), 128 (11.7), 77 (10.8).

Preparation of Methyl 2-(4-Methoxyphenyl)-3-quinolinecarboxylate (9g). In the same manner as **9f**, a solution of crude **8g** (430 mg, 1.56 mmol) in 20 mL of TCB was heated for 38 h at 200 °C. Workup via flash chromatography gave **9g** (299 mg, 70% yield over two steps (1 to **8g** to **9g**)).

9g: mp 98–98.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (1 H, s), 8.27–8.25 (1 H, d, = J = 8.4), 7.92–7.90 (1 H, d, J = 7.8), 7.84–7.80 (1 H, td, J = 7.0, 1.3), 7.72–7.60 (2 H, m), 7.04–7.00 (m, 2 H), 3.88 (3 H, s), 3.79 (3 H, s); ^{13}C NMR ($CDCl_3$, 360 MHz) δ 168.5 (Cq), 160.2 (Cq), 157.2 (Cq), 148.2 (Cq), 139.0 (CH), 132.7 (Cq), 131.5 (CH), 130.0 (2 CH), 129.2 (CH), 128.1 (CH), 126.9 (CH), 125.5 (Cq), 124.9 (Cq), 113.7 (2 cH), 113.5 (Cq), 55.2 (CH_3), 52.4 (CH_3); IR (film, cm^{-1}) 3060, 3000, 1715, 1600, 1590, 1510, 1485, 1250, 840, 790, 760; MS m/e 293 (M^+, 36.6), 278 (M^+ - 15, 100), 262 (M^+ - 31, 13.0), 247 (M^+ - 46, 2.9), 235 (M^+ - 58, 7.9), 219 (9.1), 191 (13.3). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.67; H, 5.12, N, 4.73.

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(14) Kadaba, P. K. *Synthesis* **1971**, 316.