Synthesis of Isoquinoline Derivatives by a Tandem Aza-Wittig/Electrocyclization Strategy and Preparation of the Unknown 1,9-Diazaphenalene Ring by a Consecutive Electrocyclic Ring Closure/Claisen Rearrangement/Intramolecular Amination Process

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Treatment of iminophosphorane **3**, derived from ethyl α-azido-2-(allyloxy)cinnamate, with aromatic isocyanates in toluene at 150 °C leads to the corresponding isoquinoline derivatives **5** by a tandem electrocyclic ring closure/Claisen rearrangement of the intermediate carbodiimide. Fremy's salt promoted oxidation of compounds **5** yields the 5,8-isoquinolinequinone allides **6**, which by heating undergo cyclization to 2*H*-pyrano[2,3-*f*]isoquinolines **7**. Iminophosphorane **14**, derived from ethyl α-azido-2-(allyloxy)-3-methoxycinnamate, reacts with aromatic isocyanates to give the corresponding carbodiimides, which by thermal treatment at 150 °C undergo a consecutive electrocyclic ring closure/Claisen rearrangement/intramolecular amination process to give 1,9-diazaphenalene derivatives **18** in moderate yields.

It has become increasingly apparent that α,β-unsaturated heterocumulenes are highly useful synthetic intermediates in preparative heterocyclic chemistry. Especially cycloaddition reactions of such unsaturated heterocumulenic systems provide an attractive entry to a variety of heterocycles.[1] However, relatively few examples of thermally induced 6π-electrocyclizations of conjugated heterocumulenes have been documented; only the thermal cyclization of styrylisocyanates,[2] β-carbamoylvinyl isocyanates,[3] β-substituted vinylketens,[4] styrylcarbodiimides,[5] and imidoyl ketenimines[6] have been mentioned.

Our recent work in this field has led us to develop the so-called tandem aza-Wittig/electrocyclization strategy for the synthesis of simple pyridines.[7] In essence our synthetic approach to unsaturated carbodiimides consists of treating iminophosphoranes bearing an unsaturated group with easily accessible heterocumulenes such as isocyanates in a Wittig-type reaction to give a 1,3,5-hextriene moiety containing cumulated double bonds at one end, which subsequently undergo electrocyclic ring closure to yield the cyclic valence tautomer pyridine ring.

As a further extention of the above methodology we would like now to report our results on the thermal ring-closure of β-arylvinyl carbodiimides. According to the proposed mechanism,[7] the title compounds should give rise to functionalized isoquinolines which either on Fremy's salt promoted oxidation should lead to isoquinolinequinones or on intramolecular amination should lead to 1,9-diazaphenalene derivatives.

The significant antitumor activity associated with many synthetic and naturally occurring isoquinolinequinones has spurred much interest in the search for new methodologies for the synthesis of this class of compounds.[8] In addition, isoquinolinequinones have recently been shown to be useful synthetic intermediates because the heterocyclic ring serves as a diene in regiospecific Diels–Alder reactions, and subsequently the quinone portion could be used as a dienophile.[9] On the other hand, current interest in the chemistry of fused 1,8-naphthyridine derivatives has continued to grow due to their physiological activities and the behavior of this ring system as a ligand.[10]

Table I. Isoquinoline Derivatives 5 and 5,8-Isoquinolinequinones 6

compd	Ar	yield, %	mp, °C
5a	C_6H_5	71	182–183
5b	4-$H_3CC_6H_4$	61	196–197
5c	4-$H_3COC_6H_4$	66	204–205
5d	4-FC_6H_4	62	193
6a	C_6H_5	75	140–143
6b	4-$H_3CC_6H_4$	79	125–127
6c	4-$H_3COC_6H_4$	94	135–137
6d	4-FC_6H_4	88	146–148

Results and Discussion

Preparation of Isoquinolinequinones. To this end, the key intermediate **3** was prepared from **1** following a well-known methodology: condensation with ethyl azidoacetate to give **2** in 50% yield, and further Staudinger reaction[11] with triphenylphosphine, led to the iminophosphorane **3** in 90% yield. Aza-Wittig type reaction of iminophosphorane **3** with several aromatic isocyanates in dry toluene at room temperature gave triphenylphosphine oxide and the corresponding carbodiimide **4**, which either could be isolated as viscous oils, by means of a short-column chromatography, or used without purification to the next step. When a solution of **4** in dry toluene was heated at 150 °C in a sealed glass tube, the crude reaction mixture gave, after chromatographic purification over silica

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(8) For a recent review, see: Tisler, M. *Adv. Heterocycl. Chem.* **1989**, *45*, 38.
(9) Potts, K. T.; Battacharjee, D.; Walsh, E. B. *J. Chem. Soc., Chem. Commun.* **1984**, 114. Dannenberg, J. J.; Franck, R. W. *J. Org. Chem.* **1985**, *50*, 2635. Potts, K. T.; Battacharjee, D.; Walsh, E. B. *J. Org. Chem.* **1986**, *51*, 2011. Potts, K. T.; Walsh, E. B.; Battacharjee, D. *J. Org. Chem.* **1987**, *52*, 2285.
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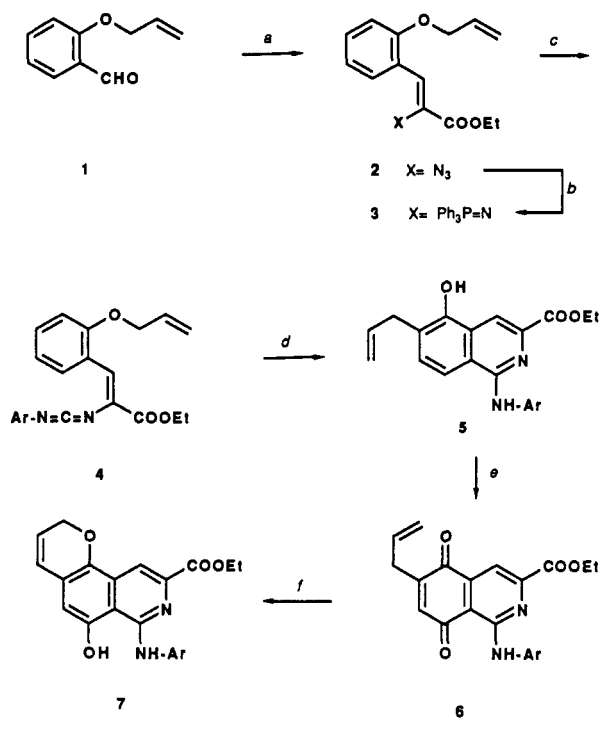
Scheme I[a]



[a] Reagents: (a) EtOOC-CH_2-N_3, NaOEt, EtOH, -20 °C; (b) Ph_3P, ether, room temperature; (c) ArNCO, toluene, room temperature; (d) sealed tube, toluene, 150–160 °C; (e) Fremy's salt, acetone–water–KH_2PO_4, room temperature; (f) benzene, reflux.

gel, the isoquinoline **5**, the yield of the isolated product being higher than 60%. The converstion **4** → **5** can be understood by an initial 6π-electrocyclization with the aryl group as a 2π-component followed by a 1,3-hydrogen shift and subsequent Claisen rearrangement to give **5**.

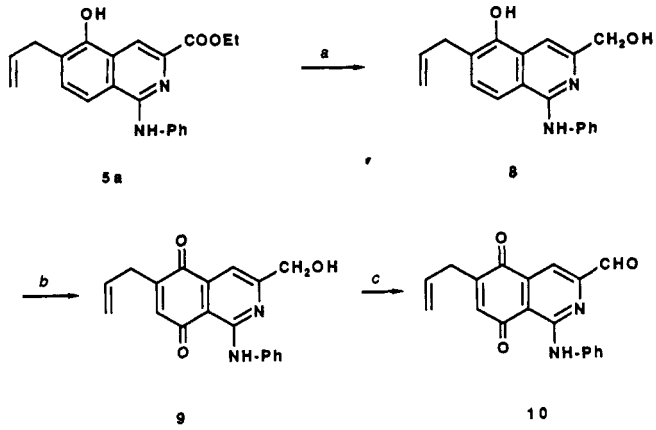
Limited success was met upon treatment of iminophosphorane **3** with carbon dioxide or carbon disulfide: this gave the corresponding isocyanate or isothiocyanate in moderate yields, which proved to be recalcitrant to cyclization by thermal treatment at 150 °C. They failed to form the corresponding isoquinoline derivatives.

Treatment of the above isoquinoline derivatives **5** with excess Fremy's salt in an acetone–water–KH_2PO_4 system led to rapid consumption of starting material and formation of the corresponding 5,8-isoquinolinequinones **6** in high isolated yields (75–94%) as blue-violet solids (Scheme I).

The 5,8-isoquinolinequinoneallides **6** are valuable precursors for the preparation of complex nitrogen heterocycles. Thus, when compounds **6** were heated in benzene solution for 24 h they were converted into the previously unknown 2*H*-pyrano[2,3-*f*]isoquinolines **7** in moderate yields. Presumably, the conversion **6** → **7** involves initial 1,5-hydrogen shift followed by electrocyclic ring closure in the intermediate quinol to give **7**. Although this type of conversion has been previously reported using basic reagents,[12] to the best of our knowledge this is the first example reported under completely neutral conditions.

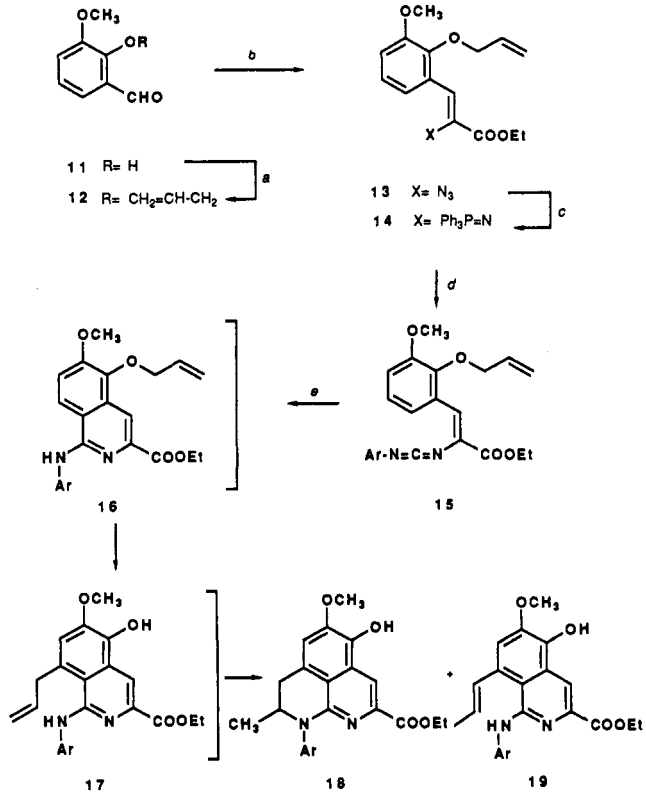
In passing, it is worth mentioning the use of formylquinoline as starting material[13] in the preparation of porphyrins linked to quinones. In this context, the above

Scheme II[a]



[a] Reagents: (a) i-Bu_2AlH, benzene, room temperature; (b) Fremy's salt, acetone–water–KH_2PO_4, room temperature; (c) MnO_2, room temperature.

Scheme III[a]



[a] Reagent: (a) $BrCH_2CH{=}CH_2$, K_2CO_3, acetone, reflux; (b) $EtOOCCH_2N_3$, NaEtO, EtOH, -20 °C; (c) Ph_3P, ether, room temperature; (d) ArNCO, toluene, room temperature; (e) sealed tube, toluene, 150–160 °C.

methodology allows the preparation of 3-formyl-5,8-isoquinolinequinone (**10**) in three step from isoquinoline derivative **5a**: (a) reduction of the ester group with diisobutylaluminum hydride gave **8** (57%); (b) selective oxidation with Fremy's salt led to 5,8-isoquinolinequinone **9** (75%); and (c) oxidation with activated manganese(IV) oxide gave the desired compound **10** (78%) (Scheme II).

Preparation of 1,9-Diazaphenalene Derivatives. To the best of our knowledge only one member of the diazaphenalene system (1,6-diazaphenalene) has been described.[14] We now report an efficient synthesis of some

(12) Merlini, L. *Adv. Heterocycl. Chem.* **1975**, *18*, 159.
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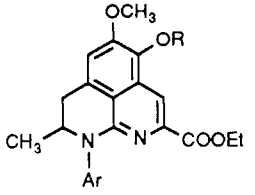
Table II. 1*H*-2,3-Dihydro-1,9-diazaphenalenes 18



compd	Ar	R	yield, %	mp, °C
18a	C_6H_5	H	55	182–184
18b	4-$H_3CC_6H_4$	H	52	190–191
18c	4-$H_3COC_6H_4$	H	50	177–178
18d	4-ClC_6H_4	H	52	205–206
18e	4-FC_6H_4	H	50	180–181
18f	4-$H_3COC_6H_4$	$C_6H_5CH_2$	51	176–177

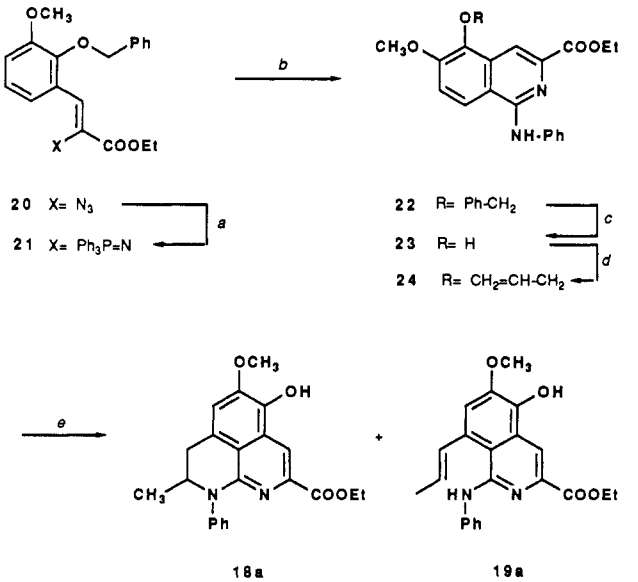
derivatives of the unknown 1,9-diazaphenalene (1*H*-benzo[*de*][1,8]naphthyridine) ring system based on the strategy shown in Scheme III. This approach, which involves as key step a consecutive electrocyclic ring closure/Claisen rearrangement/intramolecular amination process, has surprisingly been found to be useful in the construction of two fused pyridine rings.

The commercially available starting material, 2-hydroxy-3-methoxybenzaldehyde (**11**) was converted into the iminophosphorane **14** in 50% overall yield by standard chemistry: ortho-allylation with allyl bromide in acetone in the presence of potassium carbonate gave **12** in 70% yield; condensation with ethyl azidoacetate in the presence of sodium ethoxide at −15 °C led to **13** in 60% yield; and finally reaction with triphenylphosphine in ether at room temperature afforded **14** in 90%. Aza-Wittig type reaction between iminophosphorane **14** and aromatic isocyanates in dry toluene at room temperature led to the corresponding carbodiimides **15**. When carbodiimides **15** were heated at 150–160 °C for 12 h, after the usual reaction workup the 2,3-dihydro-1*H*-1,9-diazaphenalenes **18** (50–55%) together with the isoquinoline **19** (10–17%) were obtained, which were separated by column chromatography. Unfortunately, efforts to enhance the yield of **18** under a variety of reaction conditions were unsuccessful, and attempts to cyclize compounds **19** to compounds **18** (6-*endo-trig* allowed) at temperatures higher than 160 °C failed.

The structure of compounds **18** were readily determined from their analytical and spectral data, especially the ^1H NMR data in which the nonequivalence of the C-3 hydrogens resulted in two well-separated double doublets centered at δ 2.88 and 3.52, respectively, the C-2 methyl group was observed at δ 1.20 as a doublet, whereas the C-2 hydrogen was at δ 4.27 as a complex signal. In the ^{13}C NMR spectra the 2-methyl group carbon appeared at δ 18.30, whereas the carbon atoms C-2 and C-3 were observed at δ 35.74 and 54.70, respectively. Mass spectra show the expected molecular ion peaks in high intensity.

The conversion **15** → **18** can be rationalized in terms of an initial electrocyclic ring closure followed by 1,3-hydrogen shift to give the isoquinoline **16**, which under the reaction conditions undergoes a Claisen rearrangement leading to **17**. Finally, an intramolecular amination (6-*exo-trig*, allowed according to the Baldwin rules[15]) would lead to the 1,9-diazaphenalene **18**. Compounds **19** arise from initial formation of the isoquinoline derivatives **16** followed by Claisen rearrangement and a subsequent carbon–carbon double bond migration. Although allylic carbon–carbon double bonds remote from a primary or secondary amino group can be used in cyclizations mediated by transition-metal catalyst: palladium(0)-catalyzed preparation of indoles or quinolines from *o*-allylamines,[16] this work shows for the first time that this type of reaction can be also achieved under thermal conditions.

Scheme IV[a]



[a] Reagents: (a) Ph_3P, ether, room temperature; (b) PhNCO, toluene, 150 °C; (c) H_2, Pd/C, EtOH, room temperature; (d) $BrCH_2$-$CH{=}CH_2$, K_2CO_3, acetone, reflux; (e) toluene, 150 °C.

Variations were also considered in order to investigate the generality of this consecutive process, by inverting the sequence of reactions. Thus, iminophosphorane **21** reacted with aryl isocyanates at 150 °C to give the 1-(arylamino)isoquinoline **22** in 72% yield (tandem aza-Wittig/electrocyclic ring closure product). Deprotection of **22** to **23** was easily accomplished by catalytic hydrogenolysis in the presence of 10% palladium–charcoal in 74% yield. Ortho-allylation of **23** furnished **24** in 66% yield, which subjected to the above mentioned thermal conditions led to the isolation of the Claisen rearrangement/intramolecular amination product **18a** in 60% yield and the corresponding Claisen rearrangement product **19a** in low yield (10%) (Scheme IV). On the other hand, 5-allyl-2-hydroxy-3-methoxybenzaldehyde (**25**), available from **12** in modest yield (20%) by thermal Claisen rearrangement, was converted into the iminophosphorane **28** by the sequence: O-benzylation (90%), condensation with ethyl azidoacetate (73%), and finally Staudinger reaction with triphenylphosphine (89%). The reaction of compound **28** with several aromatic isocyanates in toluene in a glass sealed tube at 150 °C led to the electrocyclic ring closure/intramolecular amination products **18** in 30–35% yields as the only isolated products.

With these results it was not possible in the conversion **15** → **18** to determine whether the Claisen rearrangement preceded to the electrocyclic ring closure.

Concluding Remarks

In this paper we have developed a simple but effective general one-pot strategy for the synthesis of a variety of highly functionalized isoquinoline derivatives from readily available building blocks. Several trends have surfaced

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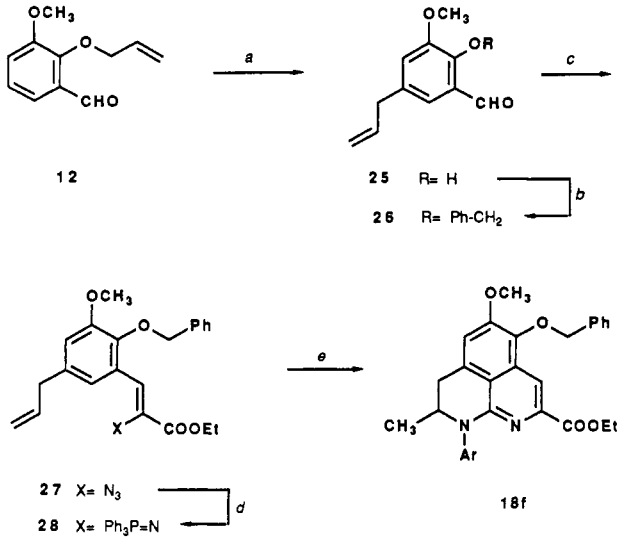
Scheme V[a]



[a] Reagents: (a) sealed tube, toluene, 215 °C; (b) $PhCH_2Br$, K_2CO_3, acetone, reflux; (c) $EtOOCCH_2N_3$, NaEtO, EtOH, −20 °C; (d) Ph_3P, ether, room temperature; (e) ArNCO, toluene, room temperature, then sealed tube, toluene, 160 °C.

from our studies. First, β-(2-(allyloxy)phenyl)vinylcarbodiimides undergo ready cyclization to 1-(arylamino)isoquinolines. Further Fremy's salt promoted oxidation can be used to prepare a variety of substituted 5,8-isoquinolinequinones. Secondly and foremost, in those cases where the carbodiimide has a substituent at position 3, initial Claisen rearrangement/electrocyclization is followed by an unusual intramolecular amination to give 1,9-diazaphenalene derivatives. We are continuing to explore the scope and generality of this strategy and we hope that it would find further useful applications to produce compounds of demonstrated utility or theoretical interest.

Experimental Section

General Methods. All melting points were determined on a Kofler hot-plate melting points apparatus and are uncorrected. IR spectra were obtained as Nujol emulsions on a Nicolet FT-5DX spectrophotometer. NMR spectra were recorded on a Bruker AC-200, and chemical shifts are expressed in parts per million (δ) relative to internal Me_4Si. Two-dimensional spectra and DEPT experiments were recorded using standard conditions. Electron-impact mass spectra were carried out on a Hewlett-Packard 5993C spectrometer at an ionization potential of 70 eV. Microanalyses were performed on a Perkin-Elmer 240C instrument.

Materials. 2-(Allyloxy)benzaldehyde[17] (1) and 2-(allyloxy)-3-methoxybenzaldehyde[18] (12) were prepared as described in the literature.

Preparation of Ethyl α-Azidocinnamates (2, 13, 20, and 27). A mixture of ethyl azidoacetate (10.32 g, 80 mmol) and the appropriate aldehyde (20 mmol) was added dropwise under nitrogen at −20 °C to a well-stirred solution containing sodium (0.76 g) in 50 mL of dry ethanol. The reaction mixture was stirred for 3 h, poured into aqueous 30% ammonium chloride (80 mL), and then extracted with diethyl ether (3 × 80 mL). The combined organic layers were washed with water (3 × 30 mL), dried over anhydrous sodium sulfate, and filtered. Concentration to dryness yielded a crude material which was recrystallized from the appropriate solvent.

Ethyl α-azido-2-(allyloxy)cinnamate (2): yield 58%; mp 89 °C (ethanol); IR (Nujol) 2118 (azide), 1699 (COOEt) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (t, 3 H, J = 7.0 Hz), 4.35 (q, 2 H, J = 7.0 Hz), 4.54–4.58 (m, 2 H), 5.25–5.50 (m, 2 H), 5.96–6.15 (m, 1 H), 6.83–6.87 (dd, 1 H, J = 7.5, 0.7 Hz), 6.94–7.02 (ddd, 1 H, J = 7.8, 7.7, 0.7 Hz), 7.23–7.31 (ddd, 1 H, J = 7.7, 7.5, 1.7 Hz), 7.47 (s, 1 H), 8.19 (dd, 1 H, J = 7.8, 1.65 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 62.1 (CH_2), 69.0 (CH_2), 111.0 (C_3), 117.1 (CH_2=), 119.5 (C_β), 120.6 (C_5), 122.5 (C_1), 125.3 (C_α), 130.6 (C_6), 130.7 (C_4), 133.0 (CH=), 156.6 (C_2), 163.7 (CO); mass spectrum (relative intensity) 273 (M^+, 2), 132 (100). Anal. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.37. Found: C, 61.42; H, 5.68; N, 15.17.

Ethyl α-azido-2-(allyloxy)-3-methoxycinnamate (13): yield 69%; mp 73 °C (ether/n-hexane, 1:1); IR (Nujol) 2125 (azide), 1710 (COOEt) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (t, 3 H, J = 7.0 Hz), 3.84 (s, 3 H, CH_3O), 4.34 (q, 2 H, J = 7.0 Hz), 4.47–4.51 (m, 2 H, OCH_2), 5.20–5.44 (m, 2 H), 5.98–6.18 (m, 1 H), 6.90 (dd, 1 H, J = 8.2, 1.5 Hz), 7.03–7.12 (m, 1 H), 7.40 (s, 1 H), 7.82 (dd, 1 H, J = 8.0, 1.4 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 55.8 (CH_3O), 62.1 (CH_2), 74.5 (CH_2), 113.6 (C_6), 117.7 (CH_2=), 119.6 (C_β), 122.1 (C_4), 123.7 (C_5), 126.0 (C_α), 127.6 (C_1), 133.8 (CH=), 146.9 (C_3), 152.6 (C_2), 163.6 (CO); mass spectrum (relative intensity) 303 (M^+, 5), 149 (100). Anal. Calcd for $C_{15}H_{17}N_3O_4$: C, 59.39; H, 5.65; N, 13.85. Found: C, 59.28; H, 5.73; N, 13.94.

Ethyl α-azido-2-(benzyloxy)-3-methoxycinnamate (20): yield 65%; mp 62 °C (ethanol); IR (Nujol) 2113 (azide), 1708 (COOEt) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (t, 3 H, J = 7.0 Hz), 3.86 (s, 3 H, CH_3O), 4.29 (q, 2 H, J = 7.0 Hz), 4.98 (s, 2 H, $PhCH_2O$), 6.92 (d, 1 H, J = 7.7 Hz), 7.08 (t, 1 H, J = 8.1 Hz), 7.30–7.45 (m, 6 H), 7.78 (d, 1 H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 55.8 (CH_3O), 62.1 (CH_2), 75.6 ($PhCH_2O$), 113.5 (C_6), 119.6 (C_β), 122.1 (C_4), 123.9 (C_5), 125.9 (C_α), 127.8 (C_1), 128.1 (C_p), 128.3 (C_m), 128.6 (C_o), 137.1 (C_i), 146.6 (C_2), 152.6 (C_3), 163.5 (CO); mass spectrum (relative intensity) 353 (M^+, 2), 91 (100). Anal. Calcd for $C_{19}H_{19}N_3O_4$: C, 64.58; H, 5.42; N, 11.89. Found: C, 64.51; H, 5.31; N, 11.97.

Ethyl α-azido-5-allyl-2-(benzyloxy)-3-methoxycinnamate (27): yield 73%; oil (chromatographed over silica gel, and n-hexane/ether, 7:3, as eluent); IR (Nujol) 2118 (azide), 1710 (COOEt) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7.0 Hz), 3.36 (d, 2 H, J = 6.6 Hz), 3.85 (s, 3 H, CH_3O), 4.28 (q, 2 H, J = 7 Hz), 4.94 (s, 2 H, $PhCH_2O$), 5.03–5.16 (m, 2 H), 5.88–6.05 (m, 1 H), 6.76 (d, 1 H, J = 1.8 Hz), 7.21–7.61 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 40.1 (CH_2), 55.8 (CH_3O), 61.9 (CH_2OOC), 75.7 ($PhCH_2O$), 113.9, 116.1, 119.7 (C_β), 121.8, 125.7 (C_α), 127.4 (C_1), 127.5, 128.0, 128.3, 128.6, 135.7, 137.1, 145.1 (C_2), 152.1 (C_3), 163.5 (CO); mass spectrum (relative intensity) 393 (M^+, 2), 91 (100), 77 (8). Anal. Calcd for $C_{22}H_{23}N_3O_4$: C, 67.16; H, 5.89; N, 10.68. Found: C, 67.39; H, 6.17; N, 10.35.

General Procedure for the Preparation of Ethyl α-[(Triphenylphosphoranylidene)amino]cinnamates (3, 14, 21, and 28). A solution of triphenylphosphine (2.62 g, 10 mmol) in 30 mL of dry ether was added dropwise under nitrogen at 0 °C to a solution of the appropriate ethy α-azidocinnamate **2**, **13**, **20**, or **27** (10 mmol) in 30 mL of the same solvent. The reaction mixture was stirred at room temperature for 12 h, and the solvent was removed off under reduced pressure at 25 °C. The residual material was purified by column chromatography or recrystallization from the adequate solvent.

Ethyl α-[(triphenylphosphoranylidene)amino]-2-(allyloxy)cinnamate (3): yield 89%; mp 139 °C (benzene/n-hexane, 1:1); IR (Nujol) 1692, 1198, 1108, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7.1 Hz), 3.85 (q, 2 H, J = 7.1 Hz), 4.55–4.59 (m, 2 H, OCH_2), 5.21–5.28 (ddd, 1 H, J = 7.8, 7.7, 0.7 Hz), 5.43–5.54 (ddd, 1 H, J = 7.8, 7.7, 0.7 Hz), 6.00–6.18 (m, 1 H), 6.83 (dd, 1 H, J = 7.7, 0.9 Hz), 6.88 (ddd, 1 H, J = 7.7, 7.6, 0.9 Hz), 7.04–7.13 (m, 1 H), 7.22 (d, 1 H, J_{H-P} = 7.2 Hz), 7.30–7.48 (m, 9 H), 7.68–7.78 (m, 6 H), 9.10 (dd, 1 H, J = 7.7, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 60.6 (CH_2), 69.1 (CH_2), 109.3 (d, $^3J_{P-C}$ = 19.3 Hz, C_β), 111.6, 116.4, 120.23, 126.5, 127.7 (d, $^4J_{P-C}$ = 1.3 Hz, C_1), 128.1 (d, $^3J_{P-C}$ = 12.0 Hz, C_m), 130.3, 130.8 (d, $^4J_{P-C}$ = 3.0 Hz, C_p), 132.4 (d, $^2J_{P-C}$ = 9.6 Hz, C_o), 133.2 (d, $^1J_{P-C}$ = 103.1 Hz, C_i), 133.8, 136.1 (d, $^2J_{P-C}$ = 6.7 Hz, C_α), 155.5 (C_2), 168.2 (d, $^3J_{P-C}$ = 6.9 Hz, CO); mass spectrum (relative intensity) 507 (M^+, 2), 278 (47), 277 (100). Anal. Calcd for $C_{32}H_{30}NO_3P$: C, 75.72; H, 5.95; N, 2.76. Found: C, 75.62; H, 6.19; N, 2.52.

Ethyl α-[(triphenylphosphoranylidene)amino]-2-(allyloxy)-3-methoxycinnamate (14): yield 90%; mp 98 °C (ether/n-hexane, 1:1); IR (Nujol) 1696, 1217, 1109, 1085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7.0 Hz), 3.80 (s, 3 H, CH_3O), 3.84 (q,

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2 H, J = 7.0 Hz), 4.50–4.53 (m, 2 H, OCH_2), 5.17–5.23 (ddd, 1 H, J = 7.8, 7.7, 0.8 Hz), 5.36–5.49 (ddd, 1 H, J = 7.8, 7.7, 0.7 Hz), 6.07–6.24 (m, 1 H), 6.72 (dd, 1 H, J = 8.1, 1.4 Hz), 6.96 (t, 1 H, J = 8.0 Hz), 7.22–7.43 (m, 9 H), 7.67–7.78 (m, 7 H), 8.74 (dd, 1 H, J = 8.0, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 55.9 (CH_3O), 60.7 (CH_2), 74.1 (OCH_2), 109.4 (d, $^3J_{P-C}$ = 19.6 Hz, C_β), 110.2, 116.9, 122.6, 123.1, 128.1 (d, $^3J_{P-C}$ = 12.2 Hz, C_m), 130.8 (d, $^4J_{P-C}$ = 3.0 Hz, C_p), 132.4 (d, $^2J_{P-C}$ = 10.0 Hz, C_o), 132.7 (d, $^4J_{P-C}$ = 1.4 Hz, C_1), 133.1 (d, $^1J_{P-C}$ = 103.0 Hz, C_i), 134.7, 136.9 (d, $^2J_{P-C}$ = 6.8 Hz, C_α), 145.5 (C_3), 152.5 (C_2), 168.1 (d, $^3J_{P-C}$ = 7.2 Hz, CO); mass spectrum (relative intensity) 537 (M^+, 3), 262 (46), 183 (100). Anal. Calcd for $C_{33}H_{32}NO_4P$: C, 73.73; H, 5.99; N, 2.60. Found: C, 73.58; H, 6.19; N, 2.48.

Ethyl α-[(triphenylphosphoranylidene)amino]-2-(benzyloxy)-3-methoxycinnamate (21): yield 95%; mp 149 °C (benzene/n-hexane, 1:1); IR (Nujol) 1688, 1181, 1108, 1088 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7.0 Hz), 3.83 (s, 3 H, CH_3O), 3.84 (q, 2 H, J = 7.0 Hz), 5.00 (s, 2 H, OCH_2), 6.76 (d, 1 H, J = 7.4 Hz), 6.99 (t, 1 H, J = 8.0 Hz), 7.23 (d, 1 H, J = 7.4 Hz), 7.28–7.39 (m, 12 H), 7.57–7.61 (m, 2 H), 7.67–7.77 (m, 6 H), 8.77 (d, 1 H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 55.9 (CH_3O), 60.7 (CH_2), 77.1 (CH_2), 109.3 (d, $^3J_{P-C}$ = 19.6 Hz, C_β), 110.3, 122.7, 123.2, 127.6, 128.1 (d, $^3J_{P-C}$ = 11.8 Hz, C_m), 128.2, 128.4, 130.8 (d, $^4J_{P-C}$ = 2.5 Hz, C_p), 132.4 (d, $^2J_{P-C}$ = 9.8 Hz, C_o), 132.7 (C_1), 133.1 (d, $^1J_{P-C}$ = 103.1 Hz, C_i), 137.0 (d, $^2J_{P-C}$ = 6.8 Hz, C_α), 138.1, 145.4 (C_3), 153.5 (C_2), 168.1 (d, $^3J_{P-C}$ = 7.4 Hz, CO); mass spectrum (relative intensity) 587 (M^+, 2), 262 (100), 183 (55). Anal. Calcd for $C_{37}H_{34}NO_4P$: C, 75.62; H, 5.83; N, 2.38. Found: C, 75.53; H, 6.03; N, 2.19.

Ethyl α-[(triphenylphosphoranylidene)amino]-5-allyl-2-(benzyloxy)-3-methoxycinnamate (28): yield 89%; oil (chromatographed over neutral alumina and n-hexane/ethyl acetate, 8:2, as eluent); IR (Nujol) 1695, 1114, 1108, 1086, 714 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (t, 3 H, J = 7.1 Hz), 3.26 (d, 2 H, J = 6.0 Hz), 3.82 (s, 3 H, CH_3O), 3.84 (q, 2 H, J = 7.1 Hz), 4.97 (s, 2 H, OCH_2), 4.94–5.03 (m, 2 H), 5.90–5.97 (m, 1 H), 6.60 (d, 1 H, J = 2.0 Hz), 7.16–7.78 (m, 22 H); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 40.3 ($ArCH_2$), 55.9 (CH_3O), 60.7 (CH_2), 75.1 (OCH_2), 109.4 (d, $^3J_{P-C}$ = 19.8 Hz, C_β), 110.7, 122.5, 127.6, 127.9, 128.2 (d, $^3J_{P-C}$ = 9.8 Hz, C_m), 128.5, 128.6, 130.8 (d, $^4J_{P-C}$ = 2.1 Hz, C_p), 132.3 (d, $^2J_{P-C}$ = 9.7 Hz, C_o), 133.1 (d, $^1J_{P-C}$ = 103.2 Hz, C_i), 133.4, 133.8, 134.9 (C_5), 136.8 (d, $^4J_{P-C}$ = 2.4 Hz, C_1), 137.1 (d, $^2J_{P-C}$ = 10.6 Hz, C_α), 138.1, 138.2, 143.8 (C_3), 152.3 (C_2), 168.1 (d, $^3J_{P-C}$ = 7.4 Hz, CO); mass spectrum (relative intensity) 627 (M^+, 8), 262 (43), 183 (54), 91 (100). Anal. Calcd for $C_{40}H_{38}NO_4P$: C, 76.54; H, 6.10; N, 2.23. Found: C, 76.29; H, 5.85; N, 2.43.

General Procedure for the Preparation of 6-Allyl-1-(arylamino)-3-(ethoxycarbonyl)-5-hydroxyisoquinolines (5). To a solution of iminophosphorane **3** (0.76 g, 1.5 mmol) in 20 mL of dry toluene was added the appropiate isocyanate (1.5 mmol). The reaction mixture was stirred at room temperature for 1 h, and then was heated in a sealed tube at 150 °C for 24 h. After cooling, the solvent was removed under reduced pressure and the crude product was chromatographed on a silica gel column, eluting with ethyl acetate/n-hexane (3:1) and then recrystallized from the adecuate solvent to afford **5** as crystalline solids.

5a: yield 71%; mp 182–183 °C, colorless prisms (chloroform/n-hexane); IR (Nujol) 3449, 3358, 1698 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.40 (t, 3 H, J = 7.0 Hz), 3.60 (d, 2 H, J = 6.3 Hz), 4.37 (d, 2 H, J = 7.0 Hz), 5.06–5.15 (m, 2 H), 5.59–6.15 (m, 1 H), 7.00 (m, 1 H), 7.34 (m, 2 H), 7.51 (d, 1 H, J = 8.6 Hz), 8.13 (d, 1 H, J = 8.6 Hz), 8.23 (d, 2 H, J = 8.0 Hz), 8.38 (s, 1 H), 9.19 (s, 1 H), 9.85 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 14.2 (CH_3), 33.6 ($ArCH_2$), 60.5 (OCH_2), 110.5, 114.2, 115.8, 119.6 (s), 119.7, 121.4, 126.1 (s), 128.2, 128.3 (s), 130.7, 136.4, 138.0 (s), 141.3 (s), 150.9 (s), 151.9 (s), 165.3 (CO); mass spectrum (relative intensity) 348 (M^+, 70), 77 (100). Anal. Calcd for $C_{21}H_{20}N_2O_3$: C, 72.40; H, 5.78; N, 8.04. Found: C, 72.21; H, 5.89; N, 7.87.

5b: yield 61%; mp 196–197 °C, colorless prisms (chloroform/n-hexane); IR (Nujol) 3443, 3364, 1698 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.40 (d, 3 H, J = 7.0 Hz), 2.29 (s, 3 H, $ArCH_3$), 3.59 (d, 2 H, J = 6.3 Hz), 4.35 (q, 2 H, J = 7.0 Hz), 5.05–5.14 (m, 2 H), 5.94–6.14 (m, 1 H), 7.13 (d, 2 H, J = 8.5 Hz), 7.49 (d, 1 H, J = 8.8 Hz), 8.09 (d, 2 H, J = 8.5 Hz), 8.11 (d, 1 H, J = 8.8 Hz), 8.31 (s, 1 H), 9.10 (s, 1 H), 9.69 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 14.2 (CH_3), 20.3 ($ArCH_3$), 33.7 ($ArCH_2$), 60.4 (OCH_2), 109.9, 114.4, 115.8, 119.5 (s), 119.8, 126.0 (s), 128.1 (s), 128.6, 130.2 (s), 130.5, 136.4, 138.1 (s), 138.7 (s), 150.5 (s), 151.9 (s), 165.6 (CO); mass spectrum (relative intensity) 362 (M^+, 84), 91 (100). Anal. Calcd for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73. Found: C, 73.08; H, 6.06; N, 7.61.

5c: yield 66%; mp 204–205 °C, colorless prisms (chloroform/n-hexane); IR (Nujol) 3449, 3375, 1692 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.40 (t, 3 H, J = 7.0 Hz), 3.59 (d, 2 H, J = 6.4 Hz), 3.78 (s, 3 H), 4.37 (q, 2 H, J = 7.0 Hz), 5.06–5.15 (m, 2 H), 5.96–6.12 (m, 1 H), 6.94 (d, 2 H, J = 9.0 Hz), 7.49 (d, 1 H, J = 8.5 Hz), 8.1 (d, 1 H, J = 8.5 Hz), 8.12 (d, 2 H, J = 9.0 Hz), 8.31 (s, 1 H), 9.09 (s, 1 H), 9.70 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 14.2 (CH_3), 33.8 ($ArCH_2$), 55.1 (CH_3O), 60.5 (OCH_2), 109.7, 113.4, 114.4, 115.8, 119.4 (s), 121.5, 126.0 (s), 128.1 (s), 130.5, 134.5 (s), 136.4, 138.3 (s), 150.5 (s), 152.1 (s), 154.3 (s), 165.7 (CO); mass spectrum (relative intensity) 378 (M^+, 100). Anal. Calcd for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.71; H, 6.06; N, 7.33.

5d: yield 62%; mp 193 °C, colorless prisms (chloroform/n-hexane); IR (Nujol) 3454, 3347, 1689 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.41 (t, 3 H, J = 7.1 Hz), 3.60 (d, 2 H, J = 6.3 Hz), 4.37 (q, 2 H, J = 7.1 Hz), 5.07–5.15 (m, 2 H), 5.95–6.16 (m, 1 H), 7.18 (t, 2 H, J = 8.8 Hz), 7.52 (d, 1 H, J = 8.6 Hz), 8.13 (d, 1 H, J = 8.6 Hz), 8.26 (dd, 2 H, J = 9.0, 5.0 Hz), 8.37 (s, 1 H), 9.26 (s, 1 H), 9.76 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 14.2 (CH_3), 33.8 ($ArCH_2$), 60.5 (OCH_2), 110.3, 114.4, 114.6 (d, $^2J_{C-F}$ = 19.7 Hz), 115.9, 119.4 (s), 121.4 (d, $^3J_{C-F}$ = 7.4 Hz), 126.1 (s), 128.1 (s), 130.7, 136.4, 137.7 (d, $^4J_{C-F}$ = 2.4 Hz), 138.0 (s), 150.5 (s), 151.8 (s), 157.1 (d, $^1J_{C-F}$ = 238.3 Hz), 156.0 (CO); mass spectrum (relative intensity) 366 (M^+, 93), 115 (95), 95 (100). Anal. Calcd for $C_{21}H_{19}FN_2O_3$: C, 68.84; H, 5.23; N, 7.64. Found: C, 68.72; H, 5.18; N, 7.79.

General Procedure for the Preparation of 6-Allyl-1-(arylamino)-3-(ethoxycarbonyl)-5,8-isoquinolinequinones (6). To a solution of KH_2PO_4 (0.53 g) in 70 mL of water was added Fremy's salt (0.80 g, 3 mmol), the mixture was stirred at room temperature for 5 min, and then a solution of the appropriate isoquinoline **5** (1 mmol) in 100 mL of acetone was added. The resultant mixture was stirred at room temperature for 5 h. To the deep violet solution was added 100 mL of water, and the resultant mixture was extracted with methylene chloride (3 × 50 mL). The combined organic layers were washed with water (3 × 25 mL), dried over anhydrous sodium sulfate, and filtered. The solution was concentrated to dryness, and the residual material was chromatographed on a silica gel column, eluting with ethyl acetate/n-hexane (3:7) to give **6** as blue-violet crystalline solids.

6a: yield 75%; mp 140–143 °C dec; IR (Nujol) 1723, 1717, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (t, 3 H, J = 7.0 Hz), 3.27 (dd, 2 H J = 6.8, 2.0 Hz), 4.44 (q, 2 H, J = 7.0 Hz), 5.18–5.28 (m, 2 H), 5.75–5.96 (m, 1 H), 6.71 (t, 1 H, J = 1.3 Hz), 7.08 (m, 1 H), 7.34 (m, 2 H), 7.88 (d, 2 H, J = 8.8 Hz), 7.94 (s, 1 H), 11.03 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 33.1 ($ArCH_2$), 62.2 (OCH_2), 109.3 (s), 110.7, 119.5, 120.7, 123.6, 129.0, 132.4, 136.3, 139.0 (s), 140.8 (s), 148,7 (s), 152.5 (s), 153.9 (s), 163.9 (s), 183.9 (s), 186.6 (s); mass spectrum (relative intensity) 362 (M^+, 10), 77 (92), 55 (100). Anal. Calcd for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73. Found: C, 69.79; H, 4.88; N, 7.51.

6b: yield 79%; mp 125–127 °C dec; IR (Nujol) 3358, 1720, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.46 (t, 3 H, J = 7.0 Hz), 2.33 (s, 3 H), 3.25 (dd, 2 H, J = 6.8, 1.3 Hz), 4.43 (q, 2 H, J = 7.0 Hz), 5.17–5.27 (m, 2 H), 5.74–5.95 (m, 1 H), 6.69 (t, 1 H, J = 1.5 Hz), 7.12 (d, 2 H, J = 8.5 Hz), 7.74 (d, 2 H, J = 8.5 Hz), 7.89 (s, 1 H), 10.96 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 20.9 ($ArCH_3$), 33.1 ($ArCH_2$), 62.1 (OCH_2), 109.1 (s), 110.4, 119.4, 120.7, 129.5, 132.4, 133.1 (s), 136.3, 136.4 (s), 140.8 (s), 148.5 (s), 152.5 (s), 153.9 (s), 163.9 (s), 184.0 (s), 186.5 (s); mass spectrum relative intensity) 376 (M^+, 20), 132 (100), 91 (96). Anal. Calcd for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.35; N, 7.44. Found: C, 69.93; H, 5.21; N, 7.57.

6c: yield 94%; mp 135–137 °C dec; IR (Nujol) 3341, 1731, 1719, 1646 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (t, 3 H, J = 7.0 Hz), 3.26 (dd, 2 H, J = 6.8, 1.2 Hz), 3.80 (s, 3 H), 4.42 (q, 2 H, J = 7.0 Hz), 5.17–5.29 (m, 2 H), 5.74–5.94 (m, 1 H), 6.68 (t, 1 H, J = 1.6 Hz), 6.85 (d, 2 H, J = 9.1 Hz), 7.75 (d, 2 H, J = 9.1 Hz), 7.85 (s, 1 H), 10.91 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 33.0 ($ArCH_2$), 55.5 (CH_3O), 62.1 (OCH_2), 108.8 (s), 110.2, 114.1, 119.4, 122.1, 132.2 (s), 132.4, 136.2 (s), 140.7 (s), 148.4 (s), 152.5 (s), 153.8 (s), 155.9 (s), 163.7 (s), 183.9 (s), 186.4 (s); mass spectrum (relative intensity) 392 (M^+, 10), 123 (100), 108 (91). Anal. Calcd for $C_{22}H_{20}N_2O_5$:

C, 67.34; H, 5.14; N, 7.14. Found: C, 67.28; H, 5.29; N, 7.29.

6d: yield 88%; mp 146–148 °C dec; IR (Nujol) 3358, 1729, 1715, 1648 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.46 (t, 3 H, J = 7.1 Hz), 3.28 (dd, 2 H, J = 6.8, 1.2 Hz), 4.43 (q, 2 H, J = 7.1 Hz), 5.19–5.29 (m, 2 H), 5.75–5.96 (m, 1 H), 6.72 (t, 1 H, J = 1.5 Hz), 7.02 (dd, 2 H, J = 8.7, 8.7 Hz), 7.82 (dd, 2 H, J = 9.1, 4.8 Hz), 7.93 (s, 1 H), 10.97 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 33.1 ($ArCH_2$), 62.3 (OCH_2), 109.2 (s), 110.8 (s), 115.6 (d, $^2J_{C-F}$ = 22.4 Hz), 119.6, 122.2 (d, $^3J_{C-F}$ = 7.7 Hz), 132.3, 135.1 (d, $^4J_{C-F}$ = 2.7 Hz), 136.2, 140.8 (s), 148.8 (s), 152.5 (s), 153.8 (s), 159.0 (d, $^1J_{C-F}$ = 243.2 Hz), 163.7 (s), 183.8 (s), 186.6 (s); mass spectrum (relative intensity) 380 (M^+, 27), 351 (100), 95 (89). Anal. Calcd for $C_{21}H_{17}FN_2O_4$: C, 66.31; H, 4.51; N, 7.36. Found: C, 66.24; H, 4.69; N, 7.56.

7-((4-Fluorophenyl)amino)-9-(ethoxycarbonyl)-6-hydroxy-2*H*-pyrano[2,3-*f*]isoquinoline (7). A solution of the 5,8-isoquinolinequinone **6d** (0.38 g, 1 mmol) in 50 mL of dry benzene was stirred at reflux temperature for 24 h. After cooling, the solvent was removed under reduced pressure and the crude product was chromatographied on a silica gel column, eluting with ethyl acetate/*n*-hexane (2:3) to give **7**: 0.17 g (45%); mp 218–219 °C, yellow prisms; IR (Nujol) 3364, 1704, 1249 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (t, 3 H, J = 7.1 Hz), 4.32 (q, 2 H, J = 7.1 Hz), 4.86 (dd, 2 H, J = 3.6, 1.8 Hz), 5.96 (dt, 1 H, J = 9.8, 3.6 Hz), 6.42 (dt, 1 H, J = 9.8, 1.8 Hz), 6.63 (s, 1 H), 7.11 (s, 2 H), 7.14 (s, 2 H), 7.38 (s, 1 H), 8.26 (br s, 1 H), 14.6 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 62.3 (CH_2O), 65.8 (OCH_2), 106.6, 110.9 (s), 114.6, 116.9 (d, $^2J_{C-F}$ = 22.5 Hz), 122.3, 123.9 (d, $^3J_{C-F}$ = 7.2 Hz), 124.4, 125.6, 126.4 (s), 135.4 (d, $^4J_{C-F}$ = 2.5 Hz), 139.7 (s), 141.3 (s), 151.9 (s), 156.3 (s), 159.8 (d, $^1J_{C-F}$ = 243.3 Hz), 162.4 (s); mass spectrum (relative intensity) 380 (M^+, 100), 306 (72). Anal. Calcd for $C_{21}H_{17}FN_2O_4$: C, 66.31; H, 4.50; N, 7.36. Found: C, 66.18, H, 4.72; N, 7.27.

6-Allyl-5-hydroxy-3-(hydroxymethyl)-1-(phenylamino)-isoquinoline (8). Diisobutylaluminum hydride (1.14 g, 8 mmol) was added dropwise to a solution of the isoquinoline **5a** (0.696 g, 2 mmol) in 50 mL of dry benzene. The reaction mixture was stirred at room temperature for 6 h. The reaction was quenched by addition of 1 mL of methanol and 1 mL of water, and the stirring was continued for additional 15 min. The resultant mixture was poured into 50 mL of water, and the organic layer was separated and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residual material was recrystallized from chloroform/*n*-hexane (1:1) to give **8**: 0.35 g (57%); mp 138 °C, colorless crystals; IR (Nujol) 3375, 3182, 1631 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.56 (d, 2 H, J = 6.4 Hz), 4.59 (d, 2 H, J = 5 Hz), 5.04–5.23 (m, 2 H), 5.33 (t, 1 H, J = 5.1 Hz), 5.93–6.14 (m, 1 H), 6.95 (m, 1 H), 7.26–7.34 (m, 3 H), 7.61 (s, 1 H), 7.94–8.01 (m, 3 H), 8.97 (s, 1 H), 9.23 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 33.9, 64.6, 102.3, 114.5, 115.6, 117.4 (s), 119.9, 121.1, 124.8 (s), 127.3, 128.2, 129.8 (s), 136.7, 141.6 (s), 149.0 (s), 151.7 (s), 152.1 (s); mass spectrum (relative intensity) 306 (M^+, 26), 305 (100), 304 (95). Anal. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 74.31; H, 6.19; N, 9.28.

6-Allyl-3-(hydroxymethyl)-1-(phenylamino)-5,8-isoquinolinequinone (9). This compound was prepared by the method above described for the preparation of 5,8-isoquinolinequinones **6**: yield 75%; mp 112–113 °C, violet prisms; IR (Nujol) 3500, 1661, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.24 (m, 2 H), 3.54 (t, 1 H, J = 3.5 Hz), 4.71 (d, 2 H, J = 3.5 Hz), 5.16–5.29 (m, 2 H), 5.74–5.95 (m, 1 H), 6.70 (t, 1 H, J = 1.5 Hz), 7.12 (m, 1 H), 7.18 (s, 1 H), 7.35 (m, 2 H), 7.57 (d, 2 H, J = 8.4 Hz), 11.08 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 33.0 ($ArCH_2$), 64.7 (CH_2OH), 106.2 (C_6), 106.7 (C_4), 119.3 (C_0), 122.1, 124.3 (C_p), 129.0 (C_m), 132.6 (CH=), 136.7 (C_7), 138.3 (C_i), 140.2 (C_{4a}),148.1 (C_{8a}), 154.1 (C_1), 166.6 (C_3), 184.6 (5-CO), 186.1 (8-CO). Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.08; H, 4.87; N, 8.63.

6-Allyl-3-formyl-1-(phenylamino)-5,8-isoquinolinequinone (10). Freshly prepared activated manganese(IV) oxide (3.47 g, 40 mmol) was added to a solution of **9** (0.32 g, 1 mmol) in 50 mL of chloroform. The mixture was stirred at room temperature for 1 h until the starting material disappeared (TLC). The reaction mixture was filtered, and the filtrate was concentrated to dryness. The crude product was chromatographed on a silica gel column, eluting with *n*-hexane/ethyl acetate (8:2) to give **10**: 0.25 g (78%); mp 145–147 °C dec, blue-violet prisms; IR (Nujol) 3358, 1715, 1646 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.32 (dd, 2 H, J = 7.0, 1.4 Hz), 5.20–5.29 (m, 2 H), 5.77–5.96 (m, 1 H), 6.82 (t, 1 H, J = 1.15 Hz), 7.15 (m, 1 H), 7.40 (m, 2 H), 7.80 (d, 2 H, J = 7.7 Hz), 7.87 (s, 1 H), 9.97 (s, 1 H), 11.15 (s, 1 H); ^{13}C NMR $CDCl_3$) δ 33.1, 107.5 (s), 110.0, 119.6, 121.6, 124.3, 129.1, 232.3, 136.5, 136.6 (s), 141.2 (s), 149.1 (s), 155.1 (s), 156.1 (s), 183.6 (s), 186.8 (s), 192.1; mass spectrum (relative intensity) 318 (M^+, 10)e, 83 (100). Anal. Calcd for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.79; H, 4.31; N, 8.62.

General Procedure for the Preparation of Ethyl 1-Aryl-6-hydroxy-2-methyl-5-methoxy-2,3-dihydro-1*H*-1,9-diazaphenalene-8-carboxylates (18). To a solution of iminophosphorane **13** (0.806 g, 1.5 mmol) in 35 mL of dry toluene was added the appropriate isocyanate (1.5 mmol). The reaction mixture was stirred at room temperature for 1 h and the formed carbodiimide **14** was heated in a sealed tube at 150 °C for 12 h. After cooling, the solvent was removed under reduced pressure, and the residual material was chromatographed on a silica gel column, eluting with ethyl acetate/*n*-hexane (1:1) to afford **18** and **19** as crystalline solids.

18a: yield 55%; mp 182–184 °C, pale yellow prisms; IR (Nujol) 3386, 1691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, 3 H, J = 6.5 Hz, 2-CH_3), 1.33 (t, 3 H, J = 7.0 Hz, CH_3 CH_2), 2.87 (dd, 1 H, J = 15.7, 3.2 Hz, 3-H_a), 3.52 (dd, 1 H, J = 15.7, 5.0 Hz, 3-H_b), 3.97 (s, 3 H, CH_3O), 4.29 (qdd, 1 H, J = 6.5, 5.0, 3.2 Hz, 2-H), 4.31 (q, 2 H, J = 7.0 Hz, CH_3 CH_2), 5.00 (br s, 1 H, OH), 6.99 (s, 1 H, 4-H), 7.15–7.25 (m, 1 H), 7.35–7.43 (m, 2 H), 7.49–7.53 (m, 2 H), 8.15 (s, 1 H, 7-H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3CH_2), 18.2 (2-CH_3), 35.7 (C_3), 54.5 (C_2), 56.5 (CH_3O), 60.9 (CH_3CH_2), 109.1 (C_7), 111.7 (C_4), 112.9 (s), 124.9 (s), 125.0, 126.2, 126.7 (s), 128.6, 138.6 (s), 140.1 (s), 144.2 (s), 145.1 (s), 152.9 (s), 166.5 (CO); mass spectrum (relative intensity) 378 (M^+, 51), 77 (100). Anal. Calcd for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40. Found: C, 70.04; H, 5.73; N, 7.35.

19a: yield 17%; mp 169 °C, white prisms; IR (Nujol) 3375, 1703, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (t, 3 H, J = 7.0 Hz), 1.71 (dd, 3 H, J = 6.9, 1.6 Hz), 3.92 (s, 3 H), 4.45 (q, 2 H, J = 7.0 Hz), 6.06 (br s, 1 H), 6.16–6.32 (m, 1 H), 6.68 (s, 1 H), 6.96–7.08 (m, 2 H), 7.34 (m, 2 H), 7.94 (dd, 2 H, J = 8.6, 0.9 Hz), 8.29 (s, 1 H), 8.78 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.3, 14.5, 56.4, 61.1, 110.0, 113.8 (s), 115.5, 118.8, 121.9, 125.2 (s), 128.0 (s), 128.8, 130.7, 131.6, 138.5 (s), 139.7 (s), 140.7 (s), 143.9 (s), 152.1 (s), 166.4 (s); mass spectrum (relative intensity) 378 (M^+, 100), 289 (67), 77 (45). Anal. Calcd for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.77; H, 5.62; N, 7.63.

18b: yield 52%; mp 190–191 °C, pale yellow prisms; IR (Nujol) 3332, 1698, 1649 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (d, 3 H, J = 6.5 Hz, 2-CH_3), 1.34 (t, 3 H, J = 7.0 Hz, CH_3CH_2), 2.35 (s, 3 H, $ArCH_3$), 2.86 (dd, 1 H, J = 15.8, 3.3 Hz, 3-H_a), 3.51 (dd, 1 H, J = 15.8, 5.0 Hz, 3-H_b), 3.96 (s, 3 H, CH_3O), 4.24 (qdd, 1 H, J = 6.5, 5.0, 3.3 Hz, 2-H), 4.30 (q, 2 H, J = 7.0 Hz, CH_2CH_2), 4.80 (br s, 1 H, OH), 6.97 (s, 1 H, 4-H), 7.19 (d, 2 H, J = 8.4 Hz, 2-H_0), 7.38 (d, 2 H, J = 8.4 Hz, 2-H_m), 8.12 (s, 1 H, 7-H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3CH_2) 18.4 (2-CH_3), 21.0 ($ArCH_3$), 35.7 (C_3), 54.7 (C_2), 56.6 (CH_3O), 60.9 (CH_3CH_2), 108.7 (C_7), 111.6 (C_4), 112.8 (s), 124.9 (s), 126.4 (C_0), 126.6 (s), 129.2 (C_m), 134.7 (s), 138.5 (s), 140.3 (s), 141.5 (s), 145.1 (s), 153.1 (s), 166.5 (CO); mass spectrum (relative intensity) 392 (M^+, 57), 91 (100). Anal. Calcd for $C_{23}H_{24}N_2O_4$: C, 70.39; H, 6.16; N, 7.14. Found: C, 70.18; H, 6.29; N, 6.97.

19b: yield 11%; mp 181 °C, white prisms; IR (Nujol) 3381, 1701, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (t, 3 H, J = 7.0 Hz), 1.69 (dd, 3 H, J = 6.9, 1.6 Hz), 2.30 (s, 3 H), 3.89 (s, 3 H), 4.43 (q, 2 H, J = 7.0 Hz), 6.17–6.39 (m, 2 H), 6.84 (s, 1 H), 6.70 (d, 1 H), J = 11.1 Hz), 7.12 (d, 2 H, J = 8.4 Hz), 7.81 (d, 2 H, J = 8.4 Hz), 8.28 (s, 1 H), 8.70 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.3, 14.5, 20.7, 56.3, 61.0, 109.7, 113.6 (s), 115.4, 118.8, 125.1 (s), 128.0 (s), 129.2, 130.7, 131.2 (s), 131.4, 138.1 (s), 138.5 (s), 139.6 (s), 143.9 (s), 152.2 (s), 166.5 (s); mass spectrum (relative intensity) 392 (M^+, 100), 91 (40). Anal. Calcd for $C_{23}H_{24}N_2O_4$: C, 70.39; H, 6.16; N, 7.14. Found: C, 70.48; H, 6.26; N, 7.29.

18c: yield 50%; mp 177–178 °C, pale yellow prisms; IR (Nujol) 3422, 1693 cm^{-1}, ^1H NMR ($CDCl_3$) δ 1.18 (d, 3 H, J = 6.5 Hz, 2-CH_3), 1.33 (t, 3 H, J = 7.0 Hz, CH_3 CH_2), 2.88 (dd, 1 H, J = 15.5, 3.6 Hz, 3-H_a), 3.51 (dd, 1 H, J = 15.5, 4.9 Hz, 3-H_b), 3.82 (s, 3 H, CH_3O), 3.96 (s, 3 H, CH_3O), 4.25 (qdd, 1 H, J = 6.5, 4.9, 3.6 Hz, 2-H), 4.29 (q, 2 H, J = 7.0 Hz, CH_3CH_2), 4.84 (br s, 1 H,

OH), 6.94 (d, 2 H, J = 9.0 Hz, 2 H_o), 6.96 (s, 1 H, 4-H), 7.39 (d, 2 H, J = 9.0 Hz, 2 H_m), 8.09 (s, 1 H, 7-H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3CH_2), 18.3 (2-CH_3), 35.9 (C_3), 55.0 (C_2), 55.5 (CH_3O), 56.5 (CH_3O), 60.9 (CH_3CH_2), 108.5 (C_7), 111.5 (C_4), 112.7 (s), 114.0, 125.1 (s), 126.5 (s), 128.3; 136.9 (s), 138.5 (s), 140.2 (s), 145.2 (s), 153.4 (C_p), 157.2 (s), 166.5 (CO); mass spectrum (relative intensity) 408 (M^+, 100), 407 (94). Anal. Calcd for $C_{23}H_{24}N_2O_5$: C, 67.63; H, 5.92; N, 6.86. Found: C, 67.54; H, 6.19; N, 6.73.

19c: yield 10%; mp 151–153 °C, white prisms; IR (Nujol) 3381, 1701, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (t, 3 H, J = 7.1 Hz), 1.71 (dd, 3 H, J = 6.9, 1.7 Hz), 3.80 (s, 3 H), 3.93 (s, 3 H), 4.42 (q, 2 H, J = 7.1 Hz), 6.19–6.31 (m, 2 H), 6.86 (s, 1 H), 6.90 (d, 2 H, J = 9.0 Hz), 7.06 (d, 1 H, J = 11.1 Hz), 7.85 (d, 2 H, J = 9.0 Hz), 8.25 (s, 1 H), 8.66 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 14.5, 55.5, 56.4, 61.1, 109.5, 113.7 (s), 114.1, 115.3, 120.4, 125.2 (s), 128.0 (s), 130.8, 131.5, 134.2 (s), 138.6 (s), 139.6 (s), 143.9 (s), 152.3 (s), 154.8 (s), 166.4 (s); mass spectrum (relative intensity) 408 (M^+, 100). Anal. Calcd for $C_{23}H_{24}N_2O_5$: C, 67.63; H, 5.92; N, 6.86. Found: C, 67.53; H, 6.21; N, 6.66.

18d: yield 52%; mp 205–206 °C, pale yellow prisms; IR (Nujol) 3369, 1687 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (d, 3 H, J = 6.5 Hz, 2-CH_3), 1.35 (t, 3 H, J = 7.0 Hz, CH_3CH_2), 2.88 (dd, 1 H, J = 15.7, 3.1 Hz, 3-H_a), 3.52 (dd, 1 H, J = 15.7, 5.2 Hz, 3-H_b), 3.99 (s, 3 H, CH_3O), 4.29 (qdd, 1 H, J = 6.5, 5.2, 3.1 Hz, 2-H), 4.32 (q, 2 H, J = 7.0 Hz, CH_3CH_2), 6.10 (br s, 1 H, OH), 7.00 (s, 1 H, 4-H), 7.33 (d, 2 H, J = 8.9 Hz, 2 H_o), 7.46 (d, 2 H, J = 8.9 Hz, 2 H_m),8.17 (s, 1 H, 7-H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3CH_2), 18.3 (2-CH_3), 35.7 (C_3), 54.6 (C_2), 56.5 (CH_3O), 61.1 (CH_3CH_2), 109.6 (C_7), 111.9 (C_4), 112.8 (s), 124.7 (s), 126.6 (s), 127.3, 128.5, 129.9 (s), 138.6 (s), 139.9 (s), 142.6 (s), 145.2 (s), 152.5 (s), 166.4 (CO); mass spectrum (relative intensity) 414 (M^+ + 2, 30) 412 (M^+, 89), 111 (100). Anal. Calcd for $C_{22}H_{21}ClN_2O_4$: C, 64.00; H, 5.13; N, 6.78. Found: C, 63.85; H, 5.29; N, 6.63.

19d: yield 11%; mp 193 °C, white prisms; IR (Nujol) 3375, 3335, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (t, 3 H, J = 7.1 Hz), 1.70 (dd, 3 H, J = 6.9, 1.5 Hz), 3.93 (s, 3 H), 4.43 (q, 2 H, J = 7.1 Hz), 6.20–6.39 (m, 2 H), 6.87 (s, 1 H), 7.03 (d, 1 H, J = 11.1 Hz), 7.24 (d, 2 H, J = 8.9 Hz), 7.87 (d, 2 H, J = 8.9 Hz), 8.29 (s, 1 H), 8.77 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.3, 14.5, 56.4, 61.1, 110.4, 113.6 (s), 115.6, 119.9, 125.1 (s), 126.3, 127.9 (s), 128.6, 130.6, 131.8, 138.2 (s), 139.3 (s), 139.7 (s), 144.0 (s), 151.7 (s), 166.2 (s); mass spectrum (relative intensity) 414 (M^+ + 2, 33), 412 (M^+, 98), 323 (100). Anal. Calcd for $C_{22}H_{21}ClN_2O_4$: C, 64.00; H, 5.13; N, 6.78. Found: C, 64.18; H, 5.16; 7.03.

18e: yield 50%; mp 179–180 °C, pale yellow prisms; IR (Nujol) 3426, 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, 3 H, J = 6.5 Hz, 2-CH_3), 1.33 (t, 3 H, J = 7.0 Hz, CH_3CH_2), 2.90 (dd, 1 H, J = 15.8, 3.5 Hz, 3-H_a), 3.52 (dd, 1 H, J = 15.8, 5.9 Hz, 3-H_b), 3.99 (s, 3 H, CH_3O), 4.25 (qdd, 1 H, J = 6.5, 5.9, 3.5 Hz, 2-H), 4.30 (q, 2 H, J = 7.0 Hz, CH_3CH_2), 5.03 (br s, 1 H, OH), 7.00 (s, 1 H, 4-H), 7.08 (t, 2 H, J = 9.1 Hz), 7.45 (dd, 2 H, J = 9.1, 5.0 Hz), 8.14 (s, 1 H, 7-H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3CH_2), 18.3 (2-CH_3), 35.8 (C_3), 54.9 (C_2), 56.6 (CH_3O), 61.0 (CH_3CH_2), 109.1 (C_7), 111.7 (C_4), 112.7 (s), 115.3 (d, $^2J_{C-F}$ = 22.3 Hz), 124.9 (s), 126.6 (s), 128.5 (d, $^3J_{C-F}$ = 8.3 Hz), 138.6 (s), 140.0 (d, $^4J_{C-F}$ = 3.2 Hz), 140.1 (s), 145.2 (s), 153.1 (s), 160.2 (d, $^1J_{C-F}$ = 244.3 Hz), 166.4 (CO); mass spectrum (relative intensity) 396 (M^+, 100), 95 (70). Anal. Calcd for $C_{22}H_{21}FN_2O_4$: C, 66.66; H, 5.34; N, 7.07. Found: C, 66.51; H, 5.52; N, 6.83.

19e: yield 11%; mp 173 °C, white prisms; IR (Nujol) 3381, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (t, 3 H, J = 7.0 Hz), 1.75 (dd, 3 H, J = 6.9, 1.7 Hz), 3.99 (s, 3 H), 4.44 (q, 2 H, J = 7.0 Hz), 6.12 (br s, 1 H), 6.20–6.36 (m, 1 H), 6.95–7.12 (m, 4 H), 7.89 (dd, 2 H, J = 9.2, 4.8 Hz), 8.29 (s, 1 H), 8.76 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 14.6, 56.6, 61.2, 110.1, 113.8 (s), 115.4 (d, $^2J_{C-F}$ = 23.0 Hz), 115.5, 120.4 (d, $^3J_{C-F}$ = 7.4 Hz), 125.4 (s), 128.1 (s), 130.8, 131.8, 136.9 (d, $^4J_{C-F}$ = 2.6 Hz), 138.6 (s), 139.8 (s), 144.0 (s), 152.2 (s), 158.2 (d, $^1J_{C-F}$ = 240.7 Hz),166.3 (s); mass spectrum (relative intensity) 396 (M^+, 77), 307 (100). Anal. Calcd for $C_{22}H_{21}FN_2O_4$: C, 66.66; H, 5.34; N, 7.07. Found: C, 66.74; H, 5.42; N, 7.18.

5-(Benzyloxy)-3-(ethoxycarbonyl)-6-methoxy-1-(phenylamino)isoquinoline (22). To a solution of iminophosphorane **21** (0.88 g, 1.5 mmol) in 20 mL of dry toluene was added phenyl isocyanate (0.18 g, 1.5 mmol). The reaction mixture was stirred at room temperature for 1 h and then was heated in a sealed tube at 150 °C for 24 h. Workup similar to the above described for the preparation of **5** led to **22**.

22: yield 72%; mp 145 °C, white prisms; IR (Nujol) 3381, 1716, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (t, 3 H, J = 7.1 Hz), 3.89 (s, 3 H), 4.40 (q, 2 H, J = 7.1 Hz), 5.13 (s, 2 H), 6.99 (t, 1 H, J = 7.3 Hz), 7.21 (t, 2 H, J = 9.1 Hz), 7.31–7.39 (m, 5 H), 7.46–7.51 (m, 2 H), 7.57 (d, 1 H, J = 9.1 Hz), 7.87 (d, 2 H, J = 8.0 Hz), 8.26 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.2, 56.2, 61.2, 75.5, 111.0, 115.3, 115.4 (s), 118.41, 119.3, 122.3, 128.1, 128.4, 128.8, 133.2 (s), 137.0 (s),139.7 (s), 140.56 (s), 142.3 (s), 151.6 (s), 152.0 (s), 162.3 (s); mass spectrum (relative intensity) 428 (M^+, 60), 337 (100). Anal. Calcd for $C_{26}H_{24}N_2O_4$: C, 72.88; H, 5.64; N, 6.54. Found: C, 73.19; H, 5.39; N, 6.44.

3-(Ethoxycarbonyl)-5-hydroxy-6-methoxy-1-(phenylamino)isoquinoline (23). To a solution of isoquinoline **22** (1.07 g, 2.5 mmol) in 100 mL of ethanol was added 10% Pd on charcoal (0.20 g), and the reaction mixture was stirred at room temperature under hydrogen for 2 h. Then the reaction mixture was filtered,and the filtrate was concentrated under reduced pressure until 20 mL. After cooling at 0 °C the precipitated solid was collected by filtration and recrystallized from ethanol to give **23**: 0.62 g, (74%); mp 173 °C, white prisms; IR (Nujol) 3381, 1695 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.42 (t, 3 H, J = 7.0 Hz), 4.01 (s, 3 H), 4.37 (q, 2 H, J = 7.0 Hz), 7.00 (t, 1 H, J = 7.9 Hz), 7.35 (t, 2 H, J = 7.9 Hz), 7.65 (d, 1 H, J = 9.0 Hz), 8.23 (s, 1 H), 8.17–8.27 (m, 3 H), 9.19 (s, 1 H), 9.76 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 14.2, 56.4, 60.5, 110.0, 114.7, 115.1, 115.2 (s), 119.8, 121.4, 127.7 (s), 128.1, 137.9 (s),140.9 (s), 141.3 (s), 146.2 (s), 151.6 (s), 165.6 (s); mass spectrum (relative intensity) 338 (M^+, 100). Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28. Foundb C, 67.32; H, 5.25; N, 8.39.

5-(Allyloxy)-3-(ethoxycarbonyl)-6-methoxy-1-(phenylamino)isoquinoline (24). To a solution of isoquinoline **23** (1.01 g, 3 mmol) in 60 mL of acetone were added potassium carbonate (0.41 g, 3 mmol) and allyl bromide (0.36 g, 3 mmol). The resultant mixture was stirred at reflux temperature for 20 h. After cooling, the solvent was removed under reduced pressure, and the residual material was treated with 25 mL of water and extracted with methylene chloride (3 × 20 mL). The combined organic layers were washed with water (3 × 10 mL), dried over anhydrous magnesium sulfate, and filtered. The solution was concentrated to dryness, and the crude product was recrystallized from ethanol to give **24**: 0.75 g (66%); mp 118 °C, white prisms; IR (Nujol) 3375, 1725, 1617 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (t, 3 H, J = 7.1 Hz), 3.86 (s, 3 H), 4.41 (q, 2 H, J = 7.1 Hz), 4.62 (d, 2 H, J = 5.9 Hz), 5.19–5.42 (m, 2 H), 6.02–6.22 (m, 1 H), 6.97 (t, 1 H, J = 7.4 Hz), 7.16 (d, 1 H, J = 9.1 Hz), 7.29 (t, 2 H, J = 7.6 Hz), 7.42 (s, 1 H), 7.69 (d, 1 H, J = 9.1 Hz), 7.90 (d, 2 H, J = 7.9 Hz), 8.29 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.17, 56.1, 61.2, 74.4, 110.8, 115.2, 115.3 (s), 118.0, 118.3, 119.3, 122.1, 128.6, 133.1 (s), 133.6, 139.6 (s), 140.5 (s), 142.0 (s), 151.5 (s), 151.8 (s), 166.4 (s); mass spectrum (relative intensity) 378 (M^+, 71), 337 (100). Anal. Calcd for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.7; H, 6.07; N, 7.71.

When a solution of compound **23** in dry toluene was heated at 150 °C for 12 h, compounds **18a** (60%) and **19a** (17%) were obtained.

5-Allyl-2-hydroxy-3-methoxybenzaldehyde (25). A solution of 2-(allyloxy)-3-methoxybenzaldehyde (**12**) (5.76 g, 30 mmol) in 30 mL of toluene in a sealed tube was heated at 215 °C for 5 h. After cooling, the solvent was removed under reduced pressure, and the residual oil was chromatographed on a silica gel column, eluting with n-hexane/ethyl acetate (4:1) to give 6-allyl-2-methoxyphenol (60%) and **25**: 1.15 g (20%); oil; IR (Nujol) 3352, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.35 (d, 2 H, J = 6.5 Hz), 3.90 (s, 3 H), 5.06–5.14 (m, 2 H), 5.84–6.05 (m, 1 H), 6.94 (s, 1 H), 6.97 (s, 1 H), 9.85 (s, 1 H), 10.97 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 39.2, 56.1, 116.3, 118.5, 120.3 (s), 123.5, 131.3, 136.5, 144.0 (s), 149.8 (s), 196.4; mass spectrum (relative intensity) 192 (M^+, 100). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.61; H, 5.99.

5-Allyl-2-(benzyloxy)-3-methoxybenzaldehyde (26). The reaction of **25** with benzyl bromide under the same conditions described for the preparation of **12** led to **26**: yield 90%; oil; IR (Nujol) 1689, 1146 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.32 (d, 2 H, J = 6.6 Hz), 3.85 (s, 3 H), 5.07–5.27 (m, 2 H), 5.10 (s, 2 H), 5.81–6.01 (m, 1 H), 6.96 (d, 1 H, J = 1.8 Hz), 7.19 (d, 1 H, J = 1.8 Hz), 7.23–7.35 (m, 5 H), 10.20 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 39.6, 55.8, 76.1, 116.3,

118.2, 118.3, 128.2, 128.3, 128.4, 129.7 (s), 136.1 (s), 136.3 (s), 136.4, 149.3 (s), 152.7 (s), 189.9; mass spectrum (relative intensity) 282 (M^+, 5), 91 (100). Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.42; H, 6.31.

Ethyl 1-(4-Methoxyphenyl)-6-(benzyloxy)-2-methyl-5-methoxy-2,3-dihydro-1*H*-1,9-diazaphenalene-8-carboxylate (18f). The reaction of iminophosphorane **28** with 4-methoxyphenyl isocyanate under the same conditions described for the preparation of **18** led to **18f**: yield 51%; mp 176–177 °C, white prisms; IR (Nujol) 1732, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (d, 3 H, J = 6.5 Hz, 2-CH_3), 1.32 (t, 3 H, J = 7.0 Hz, CH_3CH_2), 2.91 (dd, 1 H, J = 15.7, 3.7 Hz, 3-H_a), 3.51 (dd, 1 H, J = 15.7, 5.1 Hz, 3-H_b), 3.81 (s, 3 H, CH_3O), 3.97 (s, 3 H, CH_3O), 4.23 (qdd, 1 H, J = 6.5, 5.1, 3.7 Hz, 2-H), 4.28 (q, 2 H, J = 7.0 Hz, CH_3CH_2), 5.13 (s, 2 H, $PhCH_2O$), 6.94 (d, 2 H, J = 9.0 Hz, 2 H_0), 7.02 (s, 1 H, 4-H), 7.24–7.41 (m, 5 H), 7.52–7.57 (m, 2 H), 8.04 (s, 1 H, 7-H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3CH_2), 18.3 (2-CH_3), 35.9 (C_3), 54.8 (C_2), 55.4 (CH_3O), 56.3 (CH_3O), 60.8 (CH_3CH_2), 75.9 ($PhCH_2O$), 108.6 (C_7), 112.8 (s), 113.1, 113.8, 128.0, 128.2, 128.3, 128.4, 129.9 (s), 132.7 (s), 136.8 (s), 137.4 (s), 140.2 (s), 141.6 (s), 152.2 (s), 153.6 (s), 157.1 (s), 166.4 (CO); mass spectrum (relative intensity) 498 (M^+, 10), 407 (100). Anal. Calcd for $C_{30}H_{30}N_2O_5$: C, 77.27; H, 6.06; N, 5.62. Found: C, 77.38; H, 5.84; N, 5.79.

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Registry No. 1, 28752-82-1; 2, 92832-21-8; 3, 129732-98-5; 5a, 129708-13-0; 5b, 129708-14-1; 5c, 129708-15-2; 5d, 129708-16-3; 6a, 129733-03-5; 6b, 129708-17-4; 6c, 129708-18-5; 6d, 129708-19-6; 7, 129708-12-9; 8, 129732-99-6; 9, 129733-00-2; 10, 129708-05-0; 11, 148-53-8; 12, 23343-06-8; 13, 127983-47-5; 14, 127983-48-6; 18a, 127983-53-3; 18b, 127983-54-4; 18c, 127983-55-5; 18d, 127983-56-6; 18e, 127983-57-7; 18f, 129708-20-9; 19a, 129708-06-1; 19b, 129708-21-0; 19c, 129708-22-1; 19d, 129708-23-2; 19e, 129708-24-3; 20, 129708-07-2; 21, 129733-01-3; 22, 129708-08-3; 23, 129708-09-4; 24, 129708-10-7; 25, 22934-51-6; 26, 129708-04-9; 27, 129708-11-8; 28, 129733-02-4; $EtO_2CCH_2N_3$, 637-81-0; PhNCO, 103-71-9; p-MeC_6H_4NCO, 622-58-2; p-$MeOC_6H_4NCO$, 5416-93-3; H_2C=CH-CH_2Br, 106-95-6; $PhCH_2Br$, 100-39-0; p-FC_6H_4NCO, 1195-45-5; 2-(benzyloxy)-3-methoxybenzaldehyde, 2011-06-5; 5-allyl-2-(benzyloxy)-3-methoxybenzaldehyde, 129708-04-9; 6-allyl-2-methoxyphenyl, 579-60-2.

Novel Amino Acid Derivatives. Preparation and Properties of Aminoacylphosphonates and Amino Hydroxyimino Phosphonates

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Reaction of *N*-(benzyloxycarbonyl)prolyl chloride with $(MeO)_3P$ followed by treatment of the resulting acylphosphonate **5** with LiBr in MeCN gave lithium methyl Cbz-prolylphosphonate (**6a**). Didemethylation of **5** by treatment with Me_3SiBr led to sodium Cbz-prolylphosphonate (**6b**). Fmoc-alanyl chloride and Fmoc-phenylalanyl chloride were converted similarly to the corresponding dimethyl Fmoc-aminoacylphosphonates **7**, which were monodemethylated to methyl ester lithium salts **8**. Phthalimidoacyl **9** derived from β-Ala, γ-aminobutyric acid, and DL-Ala gave dimethyl phthalimidoacylphosphonates **10**, which were converted to oximes **11** by NH_2OH, to methyl phthalimidoacylphosphonate lithium salts **12** and methyl phthalimido α-hydroxyimino phosphonate lithium salts **13** by LiBr demethylation of compounds **10** and **11**, respectively. Diisopropyl phthalimidoacylphosphonates **14** derived from Gly, β-Ala, γ-aminobutyric acid, DL-Ala, and L-Phe were prepared by the Arbuzov reaction of their *N*-phthaloyl chlorides with $(2\text{-}PrO)_3P$, which in turn yielded oximes **16**. These were deblocked by hydrazine to yield diisopropyl amino-α-(hydroxyimino)alkylphosphonates **17**. Similarly oxime derivatives **18** of diethyl phthalimidoacylphosphonates **15** derived from amino acids Ala and Phe could be hydrazinolyzed to diethyl amino hydroxyimino phosphonates **19**.

Introduction

There is considerable economic and biological interest in phosphorus derivatives of amino acids since phosphonate and phosphinate analogues of amino acids (both natural and synthetic) have been proven to possess activities in a variety of fields. Among the phospha amino acids there are compounds active as pesticides,[1,2] insecticides,[1] herbicides,[3] bactericides,[4] enzyme inhibitors,[3] and receptor antagonists.[5] These observations stimulated extensive synthetic activity, which yielded phospha analogues of all natural amino acids.[6] In addition to phospha amino acids, there is considerable interest in other types

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