# Preparation and Thermal Ring-closure of β-Aryl Vinyl Carbodi-imides: Synthesis of Isoquinoline Derivatives

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Reaction of the iminophosphoranes (**7**)–(**9**), derived from α-azidocinnamates and triphenylphosphine, with aromatic isocyanates gives either 1-arylaminoisoquinoline-3-carboxylates (**10**)–(**12**) or the corresponding carbodi-imides (**14**)–(**18**) which by thermal treatment at 230 °C are converted into 1-(*N*-aryl-*N*-imidazolylamino)isoquinoline-3-carboxylates (**19**)–(**20**). The iminophosphoranes (**7**) and (**8**) also react with aroyl chlorides to give the oxazolone derivatives (**23**)–(**26**).

The isoquinoline skeleton, when selectively functionalized, is a building block for the preparation of numerous alkaloids and substances with pronounced biological activities. However, isoquinolines carrying substituents in position 3 are often difficult to prepare by the general cyclization reactions used for preparing this type of compounds.

In the Pictet–Spengler reaction these compounds are obtained only in a few cases and an oxidation step is required.[1] In the Bischler–Napieralski reaction, substituents at the α-position of the *N*-acyl β-arylethylamines usually undergo reaction[2] or are dealkylated.[3] The problem associated with the Pictet–Gams modification is the migration of groups from the α-position of the α-substituted β-arylethylamines to the carbenium ion at the β-position.[4] Thus, groups which should appear at the 3-position of the isoquinoline ring are found at 4-position. For this reason, the expected isoquinoline derivatives substituted in position 3 are not obtained in many cases or their yields are very low. Attempts to cyclize the α-substituted *N*-styrylamides of carboxylic acids[5] gave 3-substituted isoquinoline derivatives in good yield. However, since the preparation of styrylamides[6] is rather difficult, this method is inconvenient for the synthesis of such compounds.

Recently, it has been reported that thermal decomposition of azidocinnamates containing an *ortho*-methyl or methylene group gives 3-substituted isoquinolines[7] and that the treatment of 4-aryl-3-methylbut-3-en-2-one oximes leads to 1,3-dimethylisoquinolines.[8]

In the course of our studies directed toward the synthesis of fused heterocycles, we had occasion to explore heterocyclization reactions of carbodi-imides.[9] We now report a fundamentally new approach to the synthesis of 1,3-disubstituted isoquinolines by thermally induced 6π electrocyclization of conjugated carbodi-imides. Our approach is centred on the aza-Wittig type reaction of iminophosphoranes with isocyanates to give a 2-azahexatriene entity containing a carbodi-imide function at one end which undergoes cyclization to give the isoquinoline ring.

This pyrido annelation methodology uses the same starting materials, α-azidocinnamates, as previously reported,[7] which is based on the thermal decomposition of *ortho*-alkylated α-azidocinnamates.

## Results and Discussion

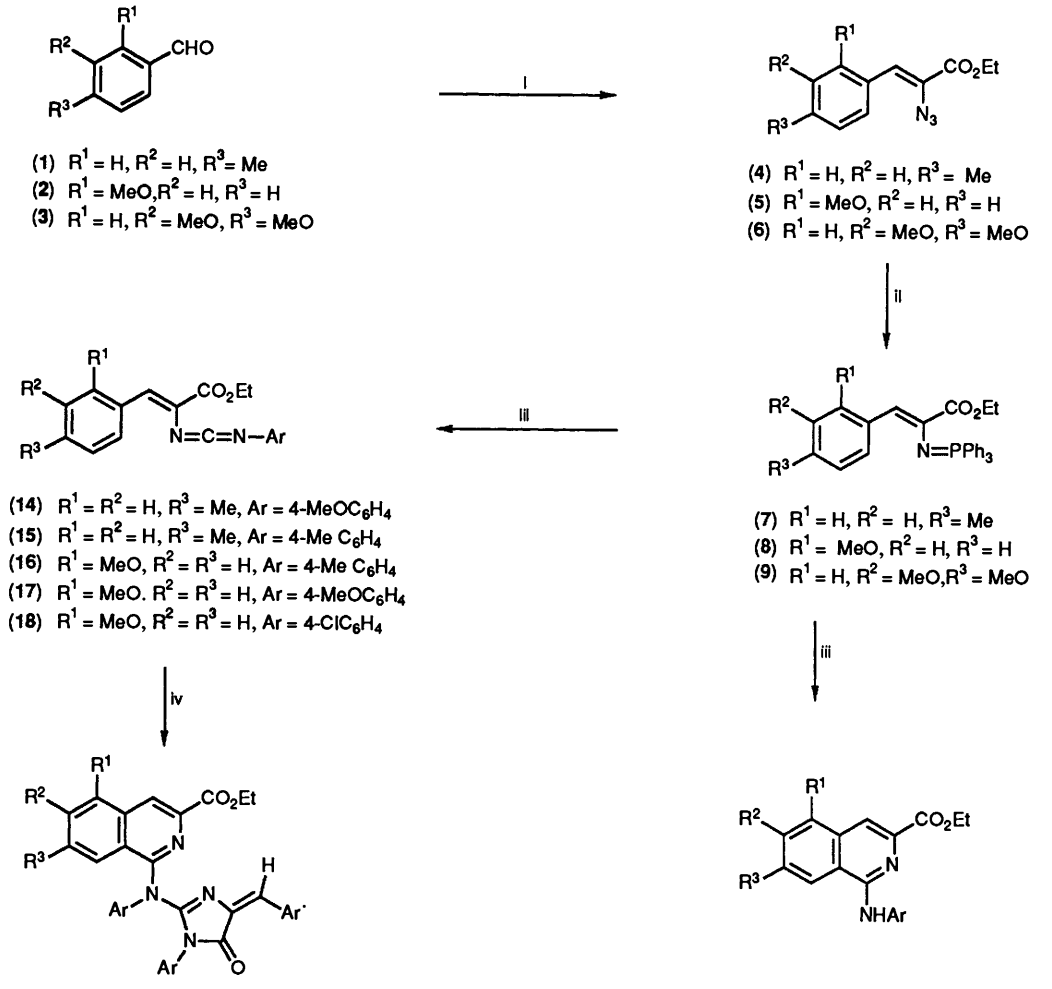
The aldehydes (**1**)–(**3**) were condensed with ethyl azidoacetate in the presence of sodium ethoxide at 0 °C to give the corresponding ethyl α-azidocinnamates (**4**)–(**6**) as crystalline solids in 55–60%. The preparation of the iminophosphoranes (**7**)–(**9**) was accomplished easily by Staudinger's reaction of (**4**)–(**6**) with triphenylphosphine in dry dichloromethane at room temperature. The IR spectra of the iminophosphoranes (**7**)–(**9**) show a carbonyl absorption at 1 693–1 687 $cm^{-1}$ and the $^1H$ NMR spectra display among other signals a doublet at δ 6.72–6.80 ($^4J_{PH}$ 7), corresponding to the β-proton. Mass spectra show the expected molecular ion peaks in low intensity, the base peak appearing at *m/z* 183 $[Ph_2P]^+$.

An aza-Wittig reaction of the iminophosphoranes (**7**) and (**8**) with aromatic isocyanates in dry refluxing toluene for 24 h gave the corresponding carbodi-imides (**14**)–(**18**) which were isolated in 65–72% yields as viscous oils, by means of short-column chromatography. However, an aza-Wittig reaction of the iminophosphorane (**9**) with aromatic isocyanates under the same reaction conditions directly gave the corresponding isoquinolines (**10**)–(**12**) in 60–62% yields. We believe that the conversion (**9**)→(**10**)–(**12**) involves an initial aza-Wittig reaction between the iminophosphorane and the isocyanate to give a carbodi-imide as a highly reactive intermediate which undergoes regioslective cyclization either by electrocyclic ring-closure followed by 1,3-proton shift or by electrophilic attack of the sp-hybridized central carbon atom of the carbodi-imide moiety on the aromatic ring to give the corresponding isoquinoline derivative. This assumption is supported by the fact that the carbodi-imide (**18**) was converted into the isoquinoline (**13**) by thermal treatment at 230 °C for 4 h (Scheme 1).

The IR spectra of the isoquinolines (**10**–(**13**) show absorption bands due to NH stretching at 3 541–3 426 $cm^{-1}$, and to the carbonyl group at 1 715–1 689 $cm^{-1}$. The $^1H$ NMR spectra show two singlets at δ 7.09–7.23 and δ 7.85–8.45 ppm due to 4-H and the NH respectively; in addition compounds (**10**)–(**12**) show a singlet at δ 7.19–7.26 attributable to 5-H and 8-H. Mass spectra show the expected molecular ion as the base peaks and the fragmentation pattern is in accordance with the proposed structure.

On the other hand, when the carbodi-imides (**14**)–(**17**) were heated at 230 °C *in vacuo* for 4 h, compounds (**19**)–(**22**) were isolated in 61–72% yields as crystalline solids. Presumably, the conversion (**14**)–(**17**) into (**19**)–(**22**) involves initial formation of an ethyl 1-arylaminoisoquinoline-3-carboxylate which reacts with a second molecule of the starting carbodi-imide to give a 1-guanidinoisoquinoline; this then cyclizes to form the imidazolone ring.

Finally, the iminophosphoranes (**7**)–(**9**) reacted with acid




**Scheme 1.** i, $EtO_2CCH_2N_3$, NaOEt, EtOH, 0 °C; ii, $Ph_3P$, $CH_2Cl_2$, r.t.; iii, ArNCO, toluene, heat; iv, 230 °C, 4 h.

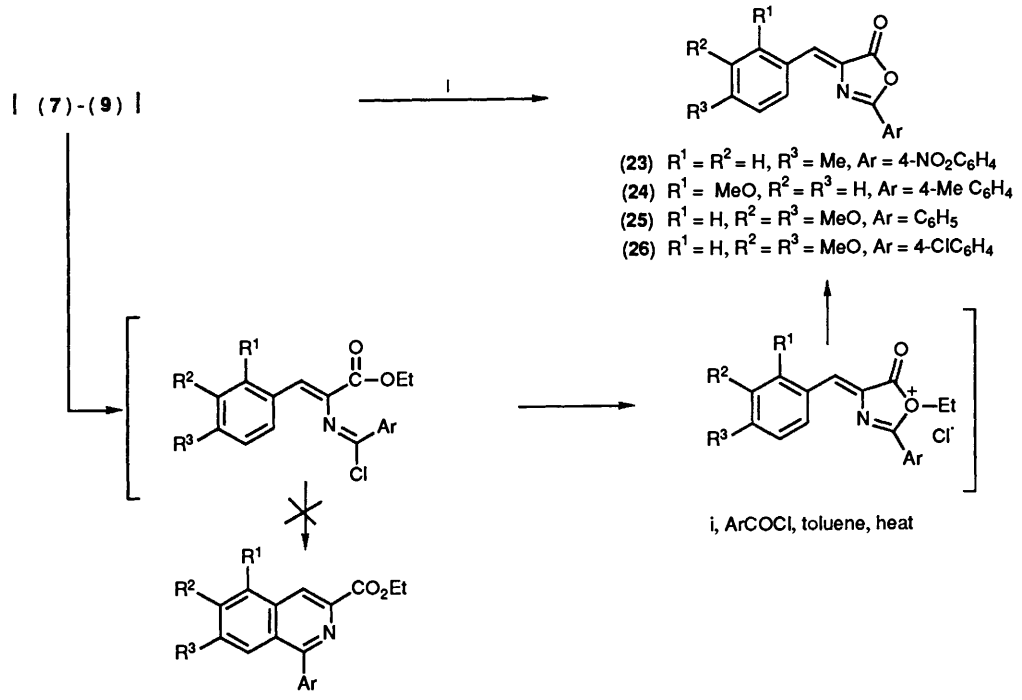
chlorides in dry refluxing toluene for 8 h to give the corresponding 2-aryl-4-arylideneoxazol-5(4*H*)-ones (**23**)–(**26**) in 78–82% yields instead of the expected ethyl 1-arylisoquinoline-3-carboxylate (Scheme 2). This conversion can be understood by initial aza-Wittig type reaction between the iminophosphorane and acyl chloride to give an imidoyl chloride[10] as intermediate which is easily cyclized and then dealkylated to give the oxazolone ring.

The identity of compounds (**19**)–(**22**) has been accomplished by 2D-NMR, HCCOR, and DEPT experiments. The $^1H$ NMR spectra of compounds (**19**)–(**22**) show the following features: (*a*) two singlets at δ 6.92–7.60 and 8.00–8.56 corresponding to the 4-H and vinylic protons respectively; (*b*) two doublets at δ 7.64–7.44 ($^3J$ 8.3 Hz), and at 7.54–7.67 ($^4J$ 1.3 Hz) due to the 5-H and 8-H respectively as well as a double doublet at δ 7.41–7.49 ($^3J$ 8.3, $^4J$ 1.3 Hz) corresponding to 6-H. In the $^{13}C$ NMR the quaternary carbons appear at: 151.2–152.8 (C-1), 137.6–138.2 (C-3), 131.7–132.6 (C-4a), 116.3–125.9 (C-8a), 159.0–159.4 (C-2′), 135.5–136.2 (C-4′), 168.8–170.6 (C-5′) as well as the exocyclic carbonyl group at δ 163.0–165.3. The mass spectra show the expected molecular ion peaks in low intensity, and the fragmentation pattern is in agreement with the proposed structures. The $^1H$ NMR spectra of compounds (**23**)–(**26**) show among others a singlet at δ 7.16–7.44 due to the vinylic proton which is in agreement with a *Z* configuration.[11]

The present study demonstrates that the thermal cyclization of β-aryl vinyl carbodi-imides affords a new route to highly functionalized isoquinolines. Structures (**10**)–(**13**) and (**19**)–(**22**) indicate the scope of these transformations: availability of a variety of aldehydes and isocyanates open new possibilities for the efficient preparation of substituted isoquinoline. The majority of the prepared isoquinoline derivatives represent variations in structural diversity not easily accessible by other routes.

## Experimental

M.p.s were recorded on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Nicolet-FT 5DX spectrometer. $^1H$ and $^{13}C$ NMR were recorded on a Bruker AC 200 with $Me_4Si$ as internal standard. Two-dimensional spectra were recorded using standard conditions.[12] Electron-impact mass spectra were carried out on a Hewlett-Packard 5993 C spectrometer at an ionization potential of 70 eV. Elemental analyses were performed with a Perkin-Elmer 240 C instrument.




**Scheme 2.**

**Table 1.** Isoquinoline derivatives (**10**)–(**13**) and (**19**)–(**22**).

| (Compound) Formula | Crystal form | Yield (%) | M.p. (°C)[a] | Found (%) [Required (%)] C | H | N |
|---|---|---|---|---|---|---|
| (**10**) $C_{21}H_{22}N_2O_4$ | Yellow needles | 60 | 135–135 | 68.9 (68.84 | 6.1 6.05 | 7.7 7.64) |
| (**11**) $C_{20}H_{19}ClN_2O_4$ | Yellow needles | 62 | 170–172 | 62.2 (62.10 | 4.8 4.95 | 7.2 7.24) |
| (**12**) $C_{20}H_{19}FN_2O_4$ | Yellow needles | 60 | 163–165 | 64.8 (64.86 | 5.1 5.17 | 7.6 7.56) |
| (**13**) $C_{19}H_{17}ClN_2O_3$ | Yellow needles | 70 | 207–209 | 63.9 (63.96 | 4.9 4.80 | 7.8 7.85) |
| (**19**) $C_{38}H_{34}N_4O_5$ | Yellow plates | 72 | 289–291 | 72.6 (72.83 | 5.5 5.47 | 9.1 8.94) |
| (**20**) $C_{38}H_{34}N_4O_3$ | Yellow plates | 65 | 200–202 | 76.8 (76.75 | 5.6 5.76 | 9.6 9.42) |
| (**21**) $C_{38}H_{34}N_4O_5$ | Yellow plates | 61 | 269–271 | 72.6 (72.83 | 5.3 5.47 | 8.8 8.94) |
| (**22**) $C_{38}H_{34}N_4O_7$ | Yellow plates | 63 | 220–222 | 69.4 (69.29 | 5.1 5.20 | 8.6 8.51) |

[a] From EtOH.

*General Procedure for the Preparation of Ethyl α-Azidocinnamates* (**4**)–(**6**).—To a well stirred solution containing sodium (0.76 g, 33 mmol) in dry ethanol (10 ml), a solution of ethyl azidoacetate (4.3 g, 33 mmol) in dry ethanol (3 ml) and the appropriate aldehyde (**1**)–(**3**) (15 mmol) were added dropwise at −5 °C under nitrogen. The reaction mixture was allowed to warm to room temperature and was then stirred for 17 h. After this it was poured into aqueous 30% ammonium chloride (30 ml) and was extracted with diethyl ether (3 × 30 ml). The combined extracts were washed with water (3 × 10 ml), dried ($Na_2SO_4$) and evaporated under reduced pressure at 30 °C. The residual material was recrystallized from dichloromethane–hexane (1:1, v/v).

As a typical product of this reaction *ethyl α-azido-4-methylcinnamate* (**4**) was obtained in 60% yield as white needles, m.p. 52–54 °C (Found: C, 62.4; H, 5.7; N, 18.3. Calc. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.66; N, 18.17%); $\nu_{max}$(Nujol) 2 118vs ($N_3$), 1 715s (C=O), 1 619, 1 608, 1 466, 1 376, 1 325, 1 296, 1 262, 1 245, 1 183, 1 075, 1 019, 888, 815, 758, and 724 $cm^{-1}$; $\delta_H(CDCl_3)$ 7.70 (2 H, d, *J* 8 Hz), 7.17 (2 H, d, *J* 8 Hz), 6.88 (1 H, s), 4.33 (2 H, q, *J* 7 Hz), 2.35 (3 H, s), and 1.38 (3 H, t, *J* 7 Hz); $\delta_C(CDCl_3)$ 163.57, 139.69, 130.51, 130.41, 129.14, 125.48, 124.60, 62.06, 21.39, and 14.13; *m/z*(%) 231 ($M^+$, 9), 203 (18), 189 (5), 158 (7), 131 (85), 130 (59), 119 (92), 116 (9), and 91 (100).

Compounds (**8**) and (**9**) were prepared similarly. Their yields, m.p.s, elemental analyses, IR, MS, and $^1H$ and $^{13}C$ NMR data have been deposited as a Supplementary Publication.*

* Supplementary data available: [No. 56781 (6pp)]. Deposited at the British Library Document Supply Centre. See Instructions for Authors, Section 4.0 in the January issue.

**Table 2.** $^1H$ and $^{13}C$ Chemical shifts (ppm from $Me_4Si$ and coupling constants Hz) of compounds (**10**)–(**13**) and (**19**)–(**22**) in $CDCl_3$.

| Compound | $^1H$ NMR (200 MHz) | $^{13}C$ NMR (50 MHz) |
|---|---|---|
| (**10**) | 7.85 (1 H, s), 7.43 (2 H, d, *J* 8.2), 7.25 (2 H, s), 7.10 (1 H, s), 7.07 (2 H, d, *J* 8.2), 4.44 (2 H, q, *J* 7), 4.03 (3 H, s), 3.96 (3 H, s), 2.35 (3 H, s), 1.45 (3 H, t, *J* 7). | 166.20, 152.60, 151.17, 150.49, 140.56, 137.70, 135.41, 133.49, 131.32, 123.55, 116.41, 115.74, 107.23, 101.74, 64.84, 56.15, 56.04, 20.75, 14.18. |
| (**11**) | 7.95 (1 H, s), 7.63 (2 H, d, *J* 8.7), 7.20 (2 H, d, *J* 8.7), 7.19 (2 H, s), 7.09 (1 H, s), 4.44 (2 H, q, *J* 7), 4.00 (3 H, s), 3.93 (3 H, s), 1.45 (3 H, t, *J* 7). | 166.15, 152.71, 151.25, 150.35, 139.74, 138.22, 133.37, 128.62, 126.76, 120.54, 116.72, 115.73, 107.37, 101.89, 61.26, 56.13, 56.02, 14.28. |
| (**12**) | 7.99 (1 H, s), 7.66 (2 H, dd, $J_{AB}$ 8.6 $^4J_{H,F}$ 4.6), 7.26 (2 H, s), 7.16 (1 H, s), 7.02 (2 H, st $J_{AB}$ 8.6 $^3J_{H,F}$ 8.6), 4.44 (2 H, q, *J* 7), 4.03 (3 H, s) 3.96 (3 H, s), 1.45 (3 H, t, *J* 7). | 166.30,163.38 ($^1J_{C,F}$ 239.2), 152.43, 150.96, 150.57, 137.62 ($^4J_{C,F}$ 2.6), 137.11, 133.18, 121.07, ($^3J_{C,F}$ 7.55), 116.33, 115.47, 115.06 ($^2J_{C,F}$ 22), 107.20, 101.92, 61.30, 55.94, 55.90, 14.17. |
| (**13**) | 8.45 (1 H, s), 8.01–7.89 (3 H, m), 7.65 (2 H, d *J* 8.7), 7.42 (2 H, d, *J* 8.7), 7.23 (1 H, s), 4.44 (2 H, q, *J* 7), 4.12 (3 H, s), 1.46 (3 H, t, *J* 7). | 161.46, 156.96, 151.74, 137.20, 134.46, 132.21, 130.63, 127.07, 126.82, 124.40, 120.22, 116.16, 116.09, 113.20, 64.84, 56.76, 14.18. |
| (**19**) | 8.16 (1 H, s), 7.90 (2 H, d, *J* 8.1), 7.64 (1 H, d, $^3J$ 8.3), 7.54 (1 H, d, $^4J$ 1.3), 7.41 (1 H, dd, $^3J$ 8.3, $^4J$ 1.3), 7.20 (2 H, d, *J* 9), 7.11 (2 H, d, *J* 8.1), 7.01 (1 H, s), 6.84 (2 H, d, *J* 9), 6.79 (2 H, d, *J* 8.9), 6.24 (2 H, d, *J* 8.9), 4.44 (2 H q, *J* 7.1), 3.80 (3 H, s), 3.47 (3 H, s), 2.40 (3 H, s), 2.33 (3 H, s), 1.44 (3 H, t, *J* 7.1). | 170.62, 165.30, 159.20, 158.54, 157.70, 151.86, 140.05, 139.77, 139.33, 137.62, 136.09, 136.03, 132.86, 132.33, 131.67, 129.25, 128.78, 128.04, 126.94, 126.18, 125.86, 124.36, 123.27, 122.65, 114.29, 113.39, 61.62, 55.50, 55.29, 22.34, 21.56, 14.43. |
| (**20**) | 8.00 (1 H, s), 7.82 (2 H, d, *J* 8.1), 7.44 (1 H, d, $^3J$ 8.3), 7.67 (1 H, d, $^4J$ 1.4), 7.49 (1 H, dd, $^3J$ 8.3, $^4J$ 1.4), 7.34 (2 H, d, *J* 8), 7.24 (2 H, d, *J* 8), 7.20 (2 H, d, *J* 8), 7.16 (2 H, d, *J* 8), 7.09 (2 H, d, *J* 8.1), 6.92 (1 H, s), 4.46 (2 H, q, *J* 7), 2.52 (3 H, s), 2.43 (3 H, s), 2.38 (3 H, s), 2.32 (3 H, s), 1.46 (3 H, t, *J* 7). | 168.82, 163.04, 159.38, 151.23, 139.80, 139.74, 139.40, 138.16, 136.10, 135.90, 132.20, 131.70, 131.61, 130.44, 130.29, 129.31, 128.79, 128.43, 128.22, 127.10, 126.70, 126.40, 125.85, 125.01, 123.32, 121.10, 61.16, 22.06, 21.34, 21.12, 20.73, 14.28. |
| (**21**) | 8.56 (1 H, s), 7.60 (1 H, s), 7.32 (2 H, d, *J* 8.1), 7.26 (2 H, d, *J* 8.1), 7.20 (2 H, d, *J* 8.1), 7.15 (2 H, d, *J* 8.1), 6.90–6.84 (3 H, m), 6.75 (2 H, d, *J* 8), 6.55 (2 H, d, *J* 8), 4.44 (2 H, q, *J* 7), 3.96 (3 H, s), 3.67 (3 H, s), 2.33 (3 H, s), 1.94 (3 H, s), 1.45 (3 H, t, *J* 7). | 170.24, 165.32, 159.02, 158.87, 155.74, 152.84, 140.62, 140.02, 137.93, 135.51, 132.59, 130.75, 130.41, 130.36, 128.72, 127.38, 127.30, 126.87, 126.50, 125.21, 124.17, 124.08, 120.74, 119.89, 117.92, 116.49, 114.60, 110.36, 61.57, 55.82, 55.59, 21.01, 20.61, 14.44. |
| (**22**) | 8.56 (1 H, s), 7.58 (1 H, s), 7.32–7.15 (4 H, m), 6.89–6.78 (9 H, m), 6.26 (2 H, d, *J* 8.9), 4.44 (2 H, q, *J* 7.1), 3.95 (3 H, s), 3.85 (3 H, s), 3.78 (3 H, s), 3.49 (3 H, s), 1.44 (3 H, t, *J* 7.1). | 170.42, 165.32, 159.28, 158.69, 158.54, 157.70, 155.84, 152.15, 140.01, 139.90, 137.93, 136.24, 132.56, 130.39, 128.79, 126.96, 126.54, 126.20, 124.22, 124.19, 120.77, 120.10, 117.97, 116.33, 114.33, 113.66, 113.56, 111.16, 61.59, 55.85, 55.62, 55.51, 55.30, 14.47. |

*General Procedure for the Preparation of Ethyl α-Triphenylphosphoranylidenaminocinnamates* (**7**)–(**9**).—To a well stirred solution of triphenylphosphine (1.20 g, 5.17 mmol) in dry dichloromethane (15 ml), a solution of the appropriate azide (**4**)–(**6**) (5.17 mmol) in the same solvent (10 ml) was added dropwise at 0 °C under nitrogen. The reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure at 35 °C and the residual material was recrystallized from benzene–hexane (1:1, v/v). As a typical product of this reaction, *ethyl α-triphenylphosphoranylidene-amino-4-methylcinnamate* (**7**) was obtained in 69% as white plates, m.p. 179–181 °C (Found: C, 77.3; H, 6.1; N, 3.0. Calc. for $C_{30}H_{28}NO_2P$: C, 77.40; H, 6.06; N, 3.01%); $\nu_{max}$(Nujol) 1 693s (C=O), 1 585, 1 460, 1 414, 1 376, 1 313, 1 228, 1 201, 1 109, 1 039, 860, 817, 754, 740, 723, and 711 $cm^{-1}$; $\delta_H(CDCl_3)$ 8.05 (2 H, d, *J* 8 Hz), 7.77–7.67 (6 H, m), 7.48–7.35 (9 H, m), 7.06 (2 H, d, *J* 8 Hz), 6.72 (1 H, d, $^4J_{P,C}$ 7 Hz), 3.83 (2 H, q, *J* 7 Hz), 2.31 (3 H, s), and 0.97 (3 H, t, *J* 7 Hz); $\delta_C(CDCl_3)$ 168.07 (C=O, $^3J_{P,C}$ 6.5 Hz), 138.13, 136.91, 135.10 ($C_o$, $J_{P,C}$ 9.9 Hz), 134.85 (=*C*-$CO_2Et$, $^3J_{P,C}$ 3 Hz), 133.52 ($C_p$ $J_{P,C}$ 2.96 Hz), 132.17 ($C_i$, $J_{P,C}$ 117.26 Hz), 132.01, 130.98, 130.71 ($C_m$, $J_{P,C}$ 12.23 Hz), 116.62 (=CH, $^3J_{P,C}$ 19.5 Hz), 60.57, 21.28, and 14.01; *m/z*(%) 465 ($M^+$, 4), 262 (22), 202 (13), 201 (98), 185(10), 183 (100), 130 (21), 108 (57), 91 (21), and 77 (14).

The yields, m.p.s, elemental analyses, IR, MS, and $^1H$ and $^{13}C$ NMR for compounds (**8**) and (**9**) have been deposited in the Supplementary Publication.

*General Procedure for the Preparation of Ethyl 1-Aryl-aminoisoquinoline-3-carboxylates* (**10**)–(**13**).—To a stirred solution of the corresponding iminophosphorane (**9**) (0.51 g, 1 mmol) in dry toluene (20 ml), a solution of the appropriate aryl isocyanate (1 mmol) in the same solvent (10 ml) was added dropwise at room temperature under nitrogen. The resulting mixture was heated under reflux temperature for 52 h. After cooling the solvent was removed under reduced pressure at 50 °C and the residual material was chromatographed over silica gel with ethyl acetate–hexane (10:1) as eluant. Removal of the solvent afforded the corresponding isoquinoline which was recrystallized from ethanol. Yields, m.p.s, and elemental analyses of the products (**10**)–(**13**) are given in Table 1, and $^1H$ and $^{13}C$ NMR data in Table 2. Thus prepared was ethyl 6,7-dimethoxy-1-(4-tolylamino)isoquinoline-3-carboxylate (**10**); $\nu_{max}$(Nujol) 3 541m (NH), 1 698s (C=O), 1 619, 1 604, 1 553, 1 510, 1 466, 1 456, 1 439, 1 406, 1 329, 1 251, 1 167, 1 030, 1 006, 900, 817, and 785 $cm^{-1}$; *m/z*(%) 366 ($M^+$, 100), 294 (12), 293 (20), 260 (3), 249 (6), 235 (10), 187 (13), 177 (5), 176 (10), 163 (8), 162 (14), 138 (10), 107 (14), 105 (8), and 91 (40). The IR and MS spectra data for compounds (**11**)–(**13**) have been deposited in the Supplementary Publication.

*General Procedure for the Preparation of N-Aryl-N'-(β-arylvinyl)carbodi-imides* (**14**)–(**18**).—A solution of the appropriate aryl isocyanate (2 mmol) in dry toluene (10 ml) was added dropwise to a stirred solution of the iminophosphorane (**7**) or (**8**) (2 mmol) in the same solvent (20 ml) at room temperature under nitrogen. The reaction mixture was heated at reflux temperature for 24 h. After cooling, the solvent was removed

under reduced pressure at 50 °C. The carbodi-imide was separated as an unstable oil by column chromatography over silica gel using ethyl acetate–hexane (3:7) as eluant. Thus, N-(4-*methoxy*)*phenyl*-, N'-[α-*ethoxycarbonyl*-β-(4-*tolyl*)*vinyl*]-*carbodi-imide* (**14**) was obtained in 72% yield as viscous oil (Found: C, 71.2; H, 6.3; N, 8.5. $C_{20}H_{20}N_2O_3$ requires C, 71.41; H, 5.99; N, 8.32%); $\nu_{max}$(Nujol) 2 135vs (NCN), 1 710s (C=O), 1 630, 1 608, 1 579, 1 511, 1 466, 1 319, 1 291, 1 245, 1 183, 1 064, 1 036, 832, and 815 $cm^{-1}$; $\delta_H(CDCl_3)$ 7.84 (2 H, d, *J* 8 Hz), 7.24 (1 H, s), 7.15 (2 H, d, *J* 8 Hz), 7.11 (2 H, d, *J* 8 Hz), 6.80 (2 H, d, *J* 8 Hz), 4.35 (2 H, q, *J* 7 Hz), 3.75 (3 H, s), 2.35 (3 H, s), and 1.35 (3 H, t, *J* 7 Hz); $\delta_C(CDCl_3)$ 164.65, 157.15, 139.70, 135.01, 131.67, 130.97, 130.53, 129.11, 128.00, 125.22, 124.91, 114.57, 62.15, 55.36, 21.40, and 14.18; *m*/*z*(%) 336 ($M^+$, 100), 264 (10), 262 (33), 229 (5), 203 (6), 133 (12), 131 (46), 130 (74), 116 (7), and 91 (15). Their yields, elemental analyses, IR, $^1H$ NMR and MS data for compounds (**15**)–(**18**) have been deposited in the Supplementary Publication.

*General Procedure for the Preparation of Ethyl* 1-[N-*Aryl*-N-*imidazol*-2-*ylamino*]*isoquinolin*-3-*carboxylates* (**19**)–(**22**).—The appropriate *N*-aryl-*N'*-(β-arylvinyl)carbodi-imide (3 mmol) was heated at 230 °C *in vacuo* (55 mmHg) for 4 h. After cooling, the resultant solid was slurried with cold ethanol (25 ml), filtered, and recrystallized from ethanol. Thus prepared was ethyl 1-{*N*-(4-methoxyphenyl)-*N*-[4-(4-methylbenzylidene-5-oxo-1-(4-methoxyphenyl)imidazol-2-yl]-amino}-7-methylisoquinoline-3-carboxylate (**19**), $\nu_{max}$(Nujol) 1 721s (C=O), 1 647, 1 551, 1 506, 1 460, 1 404, 1 376, 1 359, 1 296, 1 251, 1 166, 1 109, 1 030, 837, 820, and 750 $cm^{-1}$; *m*/*z*(%) 626 ($M^+$, 14), 335 (5), 291 (30), 263 (6), 262 (19), 254 (5), 149 (23), 147 (10), 143 (10), 142 (41), 133 (19), 131 (39), 130 (100), 122 (46), 116 (21), 115 (31), 107 (12), 104 (19), 103 (66), and 91 (35).

The IR and MS spectra data for compounds (**20**)–(**22**) have been deposited in the Supplementary Publication.

*General Procedure for the Preparation of* (Z)-4-*Benzylidene*-2-*aryloxazol*-5(4H)-*ones* (**23**)–(**26**).—To a solution of the appropriate iminophosphorane (**7**)–(**9**) (3 mmol) in dry toluene (25 ml) the acyl chloride (3 mmol) was added at 0 °C under nitrogen. After addition, the resulting solution was heated at reflux temperature for 8 h. After cooling, the solvent was removed under reduced pressure (25 mmHg) and the residue was slurried with ether (25 ml) and the solid was separated by filtration and recrystallized from acetonitrile–ether (5:1, v/v). Thus, (Z)-4-(4-*methylbenzylidene*)-2-(4-*nitrophenyl*)*oxazol*-5(4H)-*one* (**23**) was obtained in 78% yield as yellow plates, m.p. 255–257 °C (Found: C, 66.1; H, 4.2; N, 8.8. Calc. for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.92; N, 9.09%); $\nu_{max}$(Nujol) 1 789s (C=O), 1 766, 1 659, 1 596, 1 523, 1 460, 1 376, 1 353, 1 313, 1 291, 1 160, 1 104, 979, 894, 854, 820, and 701 $cm^{-1}$; $\delta_H(CDCl_3)$ 8.43 (2 H, d, *J* 9 Hz), 8.34 (2 H, d, *J* 9 Hz), 8.22 (2 H, d, *J* 8 Hz), 7.44 (1 H, s), 7.35 (2 H, d, *J* 8 Hz), and 2.07 (3 H, s); *m*/*z*(%) 308 ($M^+$, 17), 150 (100), 130 (10), 122 (5), and 91 (10). The yields, elemental analyses, and IR, MS, and $^1H$ NMR data for compounds (**24**)–(**26**) have been deposited in the Supplementary Publication.

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