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A Straightforward Preparation of Benz[*f*]indoles by an Intramolecular Diels-Alder Cycloaddition of Unsaturated Ketenimines.

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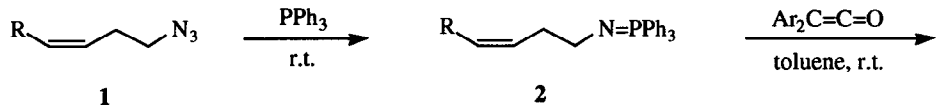
Abstract: An intramolecular Diels-Alder cycloaddition of de ketenimines **3**, available by aza Wittig reaction between iminophosphoranes **2**, derived from azido olefins **1**, and diaryl ketenes followed by an oxidative aromatization of the cycloadduct provided benz[*f*]indoles **5**. Attempts to apply this process either with ethylphenylketene, 5-aryl-4-pentenylazides or with the related carbodiimides failed.

Although the linear benz[*f*]indole ring system constitutes the ABC framework of the potent antibiotics kinamycins, and some derivatives occur naturally[1], there are only a few reports dealing with the synthesis of such ring system. Three main synthetic routes for linear benz[*f*]indole derivatives may be proposed with respect to the final ring-construction step: (i) pyrrole ring-construction on a naphthalene derivative (mode A), *e. g.* palladium-catalyzed reaction of ethyl 3-bromo-2-naphthylcarbamate with trimethylsilylacetylene and subsequent cyclization with bases[2] and amine- or azide-mediated cyclization of 2,3-disubstitued-1,4-naphthoquinones[3]; (ii) central phenyl ring-formation between a phenyl and a pyrrole residue (mode B), *e. g.* Diels-Alder cycloaddition of pyrano[3,4-*b*]pyrrol-5-ones with benzyne[4], and Friedel-Crafts acylation of pyrrole derivatives with phthalic anhydride and further phenyl ring-formation by the action of acids[5]; (iii) building-up the peripheral phenyl ring on an indole nucleus (mode C), *e.g.* regioselective Diels-Alder cycloaddition between an indole-4,7-dione derivative and 1-methoxy-1,3-cyclohexadiene[6]. However, synthesis of linear benz[*f*]indole derivatives involving the simultaneous formation of the pyrrole and central phenyl ring has, to our knowledge, not been reported.

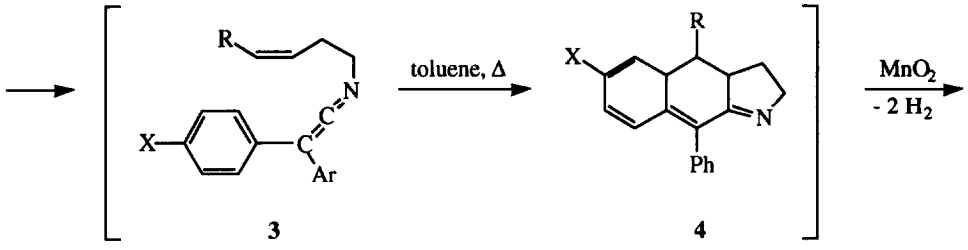
The vinyl ketenimine variant of the intramolecular Diels-Alder (IMDA) cycloaddition in which the vinyl ketenimine serves as the diene component of the reaction has been applied to a convergent route of pyridocarbazole alkaloids[7]. In this context, we have reported[8] that functionalized ketenimines, derived from the aza Wittig-type reaction between aryl iminophosphoranes bearing unsaturated functionalities and ketenes, undergo IMDA cycloaddition whereby the aryl ketenimine moiety has functioned as the diene component using one cumulative carbon-carbon double bond and one carbon-carbon bond of the aromatic ring.

Herein, we wish to report a new indole synthesis based on the intramolecular Diels-Alder cycloaddition of aryl ketenimines and styrene-like dienophiles that are linked with a flexible alkyl chain containing two carbon atoms. The synthesis, which has been found to be useful in the simultaneous formation of the pyrrole and central phenyl ring in the synthesis of linear benz[*f*]indoles, is characterized by the efficient one-flask construction of this ring system via the aryl ketenimine intramolecular cycloaddition strategy.

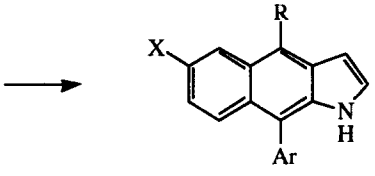


1 2

1a; R= C_2H_5
1b; R= CH_2=CH
1c; R= C_6H_5
1d; R= (E)-C_6H_5-CH=CH
1e; R= 4-$H_3COC_6H_4$
1f; R= 4-ClC_6H_4
1g; R= 4-$O_2NC_6H_4$
1h; R= 4-pyridyl
1i; R= 3-thienyl



3 4



5

5a; R= C_2H_5, Ar= C_6H_5, X= H
5b; R= CH_2=CH, Ar= C_6H_5, X= H
5c; R= C_6H_5, Ar= C_6H_5, X= H
5d; R= C_6H_5, Ar= 4-$H_3CC_6H_4$, X= CH_3
5e; R= (E)-C_6H_5-CH=CH, Ar= C_6H_5, X= H
5f; R= 4-$H_3COC_6H_4$, Ar= C_6H_5, X= H
5g; R= 4-$H_3COC_6H_4$, Ar= 4-$H_3CC_6H_4$, X= CH_3
5h; R= 4-ClC_6H_4, Ar= C_6H_5, X= H
5i; R= 4-ClC_6H_4, Ar= 4-$H_3CC_6H_4$, X= CH_3
5j; R= 4-$O_2NC_6H_4$, Ar= C_6H_5, X= H
5k; R= 4-pyridyl, Ar= C_6H_5, X= H
5l; R= 4-pyridyl, Ar= 4-$H_3CC_6H_4$, X= CH_3
5m; R= 3-thienyl, Ar= C_6H_5, X= H

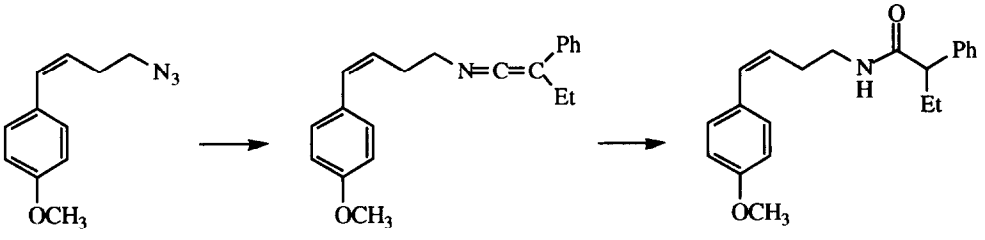
Scheme 1

The requisite azides **1** were prepared in 51-84% overall yields by the four-step sequence[9]: (a) reaction of triphenylphosphine with excess of 1,3-dibromopropane, (b) subsequent reaction with excess of sodium azide, (c) conversion of the resulting phosphonium salt to the corresponding ylid by the action of potassium bis(trimethylsilyl)amide and (d) Wittig coupling with the appropriate aldehyde. ^{1}H NMR spectra of **1** revealed the Z stereochemistry of the newly formed carbon-carbon double bond manifested itself in $^3J_{HaHb}$ values ranging from 10.6 to 11.7 Hz. Staudinger reaction of azido olefins **1** with triphenylphosphine in diethyl ether at room temperature for 2 h leads to the corresponding iminophosphoranes **2** in almost quantitative yields, which were

used without further purification for the next step. The ^{31}P NMR spectra of **2** only showed one signal at δ= 11.6 ppm, and in the ^{13}C NMR spectra the C-1 and C-2 carbon atoms appeared as two doublets at δ= 34.9 ppm ($^{2}J_{PC}$= 17.12 Hz) and δ= 45.8 ppm ($^{3}J_{PC}$= 5.04 Hz) respectively. Aza Wittig-type reaction of iminophosphoranes **2** with diphenylketene in toluene at room temperature for a short period of time leads to the corresponding ketenimines **3** (X= H, Ar= C_6H_5), which by treatment with activated manganese dioxide in toluene at reflux temperature for 2 h provided the benz[*f*]indoles **5** in 27-59% overall yields. Aza Wittig-type reaction with bis(p-tolyl)ketene and further heating resulted in the formation of the tricyclic compounds **5** in yields (25-27%) somewhat lower. However, considering the number of steps involved in this one-flask reaction the yields could be considered as good. Unfortunately, efforts to improve the yield of the tricyclic compound **5** under a variety of reaction conditions were unsuccessful, *e. g.* heating in toluene the intermediate ketenimine **3** led to a complex mixture in which the tricyclic compound **5** could be detected as a minor component while in boiling nitrobenzene the benz[*f*]indoles **5** were obtained albeit in low yields (25-30%) (Scheme 1).

The conversion **2** → **5** includes an initial formation of a ketenimine **3** (as evidenced by IR ν= 2016 cm^{-1}) as highly reactive intermediate which undergoes a [4+2] cycloaddition whereby the arylketenimine portion has functioned as a diene and the carbon-carbon double bond of the styryl portion has taken the role of the dienophile. A final oxidative aromatization of the cycloadduct **4** followed by a [1,3]-proton shift furnishes the benz[*f*]indoles **5**.

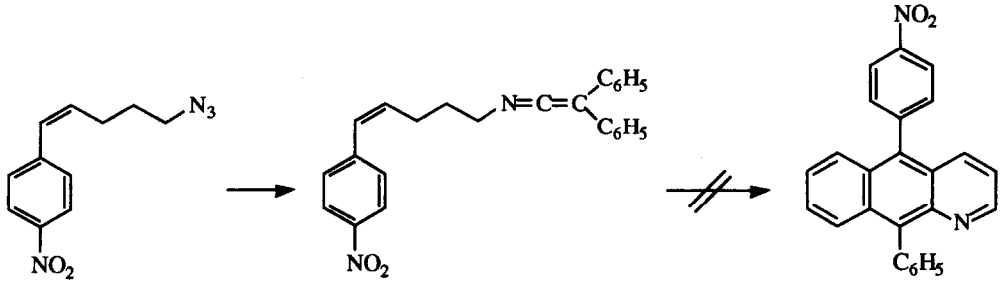
In order to investigate the scope of this process, variations were considered. At first it was of interest to see what would happen with alkyl,aryl ketenimines. To this end, the azido olefin **1e** was converted into ketenimine **6**, which was recovered as its amide derivative **7** after prolonged heating in toluene at reflux temperature and further isolation by column chromatography (Scheme 2).



1e **6** **7**

Scheme 2

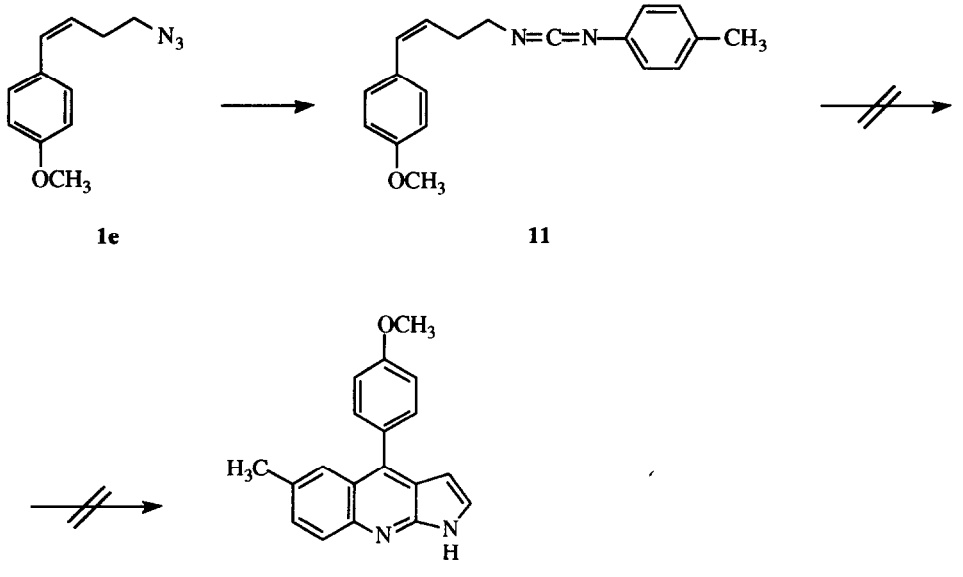
Varying the length of the flexible alkyl chain in the starting azido olefin **1** was effectless in producing benzoquinolines **10**. Azido olefin **8**, prepared as compounds **1** starting from 1,4-dibromobutane, reacted with diphenylketene at room temperature to give the ketenimine **9**, which was recovered unchanged after prolonged heating in toluene at reflux temperature, while heating in a sealed tube at 150 °C led to an intractable tar (Scheme 3).



8 **9** **10**

Scheme 3

In order to prove whether this process was operative with another heterocumulenes, we studied the thermal behaviour of the related carbodiimide **11**. This compound was easily prepared from **1e** by sequential treatment with triphenylphosphine and 4-tolylisothiocyanate at room temperature. When a toluene solution of **11** was heated at reflux temperature for 48 h, the starting carbodiimide was recovered unchanged, and when was heated in a sealed tube at 160 °C a complex mixture was obtained in which neither carbodiimide **11** nor pyrroloquinoline **12** could be detected (Scheme 4).



1e **11**

12

Scheme 4

In conclusion, the consecutive Staudinger reaction / aza Wittig reaction / intramolecular Diels-Alder cycloaddition of ketenimines process is apparently a useful method for obtaining various benz[*f*]indoles in one-flask procedure. Due to the easy access of the azido olefins, and due to the simplicity of the experimental procedure, we think that the synthetic approach discussed here in many cases compares favorably with other existing methods.

Experimental.

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as Nujol emulsions or films on a Nicolet 5DX spectrophotometer. NMR spectra were recorded on a Brucker AC-200 (200 MHz) or a Varian Unity 300 (300 MHz). Mass spectra were recorded on a Hewlett-Packard 5993C spectrometer. Microanalyses were performed on a Perkin-Elmer 240C instrument.

Azido Olefins 1. The previously unreported azido olefins **1e-1i** and **8** have been prepared according to the method described in the literature[9].

1e (R= 4-$H_3COC_6H_4$): (86%), colourless oil; (Found: C, 65.14; H, 6.52; N, 20.58. $C_{11}H_{13}N_3O$ requires: C, 65.01; H, 6.45; N, 20.67); i.r. (film) 2101 (N_3) cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 2.61 (dc, 2H, J= 1.83, 7.09 Hz, H-2), 3.35 (t, 2H, J= 7.09 Hz, H-1), 3.80 (s, 3H, OCH_3), 5.53 (dt, 1H, J= 7.09, 11.54 Hz, H-3), 6.49 (d, 1H, J= 11.54 Hz, H-4), 6.87 (d, 2H, J= 8.79 Hz, aryl), 7.21 (d, 2H, J= 8.79 Hz, aryl); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 28.33, 51.21, 55.27, 113.74, 126.04, 129.61 (q), 129.91, 131.15, 158.58 (q); m/z (%) 203 (M^+, 12), 175 (20), 115 (100).

1f (R= 4-ClC_6H_4): (93%), colourless oil; (Found: C, 57.80; H, 4.74; N, 20.30. $C_{10}H_{10}N_3Cl$ requires: C, 57.84; H, 4.85; N, 20.23); i.r. (film) 2098 (N_3) cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 2.57 (dc, 2H, J= 1.70, 6.70 Hz, H-2), 3.62 (t, 2H, J= 6.70 Hz, H-1), 5.66 (dt, 1H, J= 6.70, 11.54 Hz, H-3), 6.51 (d, 1H, J= 11.54 Hz, H-4), 7.18 (d, 2H, J= 8.43 Hz, aryl), 7.31 (d, 2H, J= 8.43 Hz, aryl); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 28.29, 51.04, 128.44, 128.50, 129.97, 130.58, 132.79 (q), 135.38 (q); m/z (%) 209 (M^++2, 6), 207 (M^+, 21), 179 (13), 115 (100).

1g (R= 4-$O_2NC_6H_4$): (77%), colourless oil; (Found: C, 55.15; H, 4.70; N, 25.60. $C_{10}H_{10}N_4O_2$ requires: C, 55.04; H, 4.62; N, 25.67); i.r. (film) 2100 (N_3) cm^{-1}; ^1H n.m.r. (200 MHz, $CDCl_3$) δ 2.61 (dc, 2H, J= 1.40, 6.90 Hz, H-2), 3.44 (t, 2H, J= 6.90 Hz, H-1), 5.86 (dt, 1H, J= 6.90, 11.71 Hz, H-3), 6.63 (d, 1H, J= 11.71 Hz, H-4), 7.46 (d, 2H, J= 8.70 Hz, aryl), 8.21 (d, 2H, J= 8.70 Hz, aryl); ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 28.47, 50.66, 123.67, 129.39, 129.94, 131.59, 143.64 (q), and one quaternary carbon not observed; m/z (%) 218 (M^+, 5), 190 (8), 116 (100).

1h (R= 4-pyridyl): (99%), colourless oil; (Found: C, 62.14; H, 5.75; N, 32.30. $C_9H_{10}N_4$ requires: C, 62.05; H, 5.79; N, 32.16); i.r. (film) 2101 (N_3) cm^{-1}; ^1H n.m.r. (200 MHz, $CDCl_3$) δ 2.62 (dc, 2H, J= 1.55, 7.00 Hz, H-2), 3.41 (t, 2H, J= 7.00 Hz, H-1), 5.84 (dt, 1H, J= 7.00, 11.71 Hz, H-3), 6.51 (d, 1H, J= 11.71 Hz, H-4), 7.17 (d, 2H, J= 5.90 Hz, pyridyl), 8.58 (d, 2H, J= 5.90 Hz, pyridyl); ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 28.36, 50.78, 123.28, 129.39, 131.69, 144.38 (q), 149.86; m/z (%) 174 (M^+, 9), 146 (15), 115 (100).

1i (R= 3-thienyl): (97%), colourless oil; (Found: C, 53.60; H, 5.14; N, 23.49. $C_8H_9N_3S$ requires: C, 53.61; H, 5.06; N, 23.44); i.r. (film) 2101 (N_3) cm^{-1}; ^1H n.m.r. (200 MHz, $CDCl_3$) δ 2.61 (dc, 2H, J= 1.73, 6.97 Hz, H-2), 3.37 (t, 2H, J= 6.97 Hz, H-1), 5.55 (dt, 1H, J= 6.97, 11.50 Hz, H-3), 6.48 (d, 1H, J= 11.50 Hz, H-4), 7.09 (dd, 1H, J= 1.16, 4.93 Hz, thienyl), 7.18 (dd, 1H, J= 1.16, 2.94 Hz, thienyl), 7.30 (dd, 1H, J= 2.94, 4.93 Hz, thienyl); ^{13}C n.m.r. (50

MHz, $CDCl_3$) δ 28.71, 50.96, 123.20, 125.32, 125.74, 126.67, 128.30, 138.06 (q); m/z (%) 179 (M^+, 11), 151 (7), 115 (100).

8 : (94%), colourless oil; (Found: C, 58.79; H, 5.31; N, 24.05. $C_{11}H_{12}N_4O_2$ requires: C, 58.69; H, 5.21; N, 24.12); i.r. (film) 2095 (N_3) cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 1.77 (q, 2H, J= 6.82 Hz, H-2), 2.43 (dc, 2H, J= 1.84, 6.82 Hz, H-3), 3.34 (t, 2H, J= 6.82 Hz, H-1), 5.84 (dt, 1H, J= 6.82, 11.81 Hz, H-4), 6.53 (d, 1H, J= 11.81 Hz, H-5), 7.43 (d, 2H, J= 7.08 Hz, aryl), 8.22 (d, 2H, J= 7.08 Hz, aryl); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 25.90, 28.85, 50.83, 123.62, 128.33, 129.40, 134.85, 144.00 (q), 146.50 (q); m/z (%) 232 (M^+, 14), 204 (10), 115 (100).

General Procedure for the Preparation of Benz[*f*]indoles 5. To a solution of triphenylphosphine (0.72 g, 2 mmol) in dry diethyl ether (10 ml) was added dropwise a solution of the appropriate azide **1** (2 mmol) in the same solvent and the reaction mixture was stirred at room temperature until N_2 evolution was ceased (about 2 h). The solvent was removed under reduced pressure at room temperature and to the crude iminophosphorane **2** were added dry toluene (60 ml) and the appropriate diaryl ketene (2 mmol). The resultant solution was stirred at room temperature for 5 min and then activated manganese dioxide (1.74 g, 20 mmol) was added. The resultant mixture was stirred at reflux temperature for 2 h. After cooling, the solvent was removed and the filtrate was concentrated to dryness. The crude product was chromatographed on silica gel column, eluting with diethyl ether / n-hexane (1:4) and recrystallized from the appropriate solvent to afford **5**.

5a (R= C_2H_5, Ar= C_6H_5, X=H): (22%), m.p. 136-138 °C (green prisms from n-hexane); (Found: C, 88.59; H, 6.40; N, 5.10. $C_{20}H_{17}N$ requires: C, 88.52; H, 6.31; N, 5.16); i.r. (Nujol) 3358, 3205, 1410, 1359, 1132, 752, 718, 701 cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 1.47 (t, 3H, J= 7.50 Hz, CH_3), 3.47 (c, 2H, J= 7.50 Hz, CH_2), 6.78 (dd, 1H, J= 1.32, 2.09 Hz, H-3), 7.24-8.24 (m, 10H, aryl), 7.91 (bs, 1H, NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 15.44, 22.96, 100.88, 117.71 (q), 122.33, 123.46, 123.96, 125.56, 126.06 (q), 127.62, 127.72, 127.87 (q), 128.74 (q), 129.12, 130.91 (q), 130.94, 134.71 (q), 137.35 (q); m/z (%) 271 (M^+, 72), 257 (22), 256 (100), 254 (17), 241 (13), 127 (13), 120 (12), 113 (7).

5b (R= CH_2=CH, Ar= C_6H_5, X=H): (28%), m.p. 120-123 °C (green prisms from n-hexane); (Found: C, 89.26; H, 5.72; N, 5.27. $C_{20}H_{15}N$ requires: C, 89.19; H, 5.61; N, 5.20); i.r. (Nujol) 3432, 3211, 1400, 1350, 1130, 910, 763, 746, 735, 715, 702 cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 5.72 (dd, 1H, J= 1.32, 11.55 Hz, CH=C$\underline{H}_A$$H_B$), 5.84 (dd, 1H, J= 1.32, 17.70 Hz, CH=C$H_A$$\underline{H}_B$), 6.82 (dd, 1H, J=1.31, 3.00 Hz, H-3), 7.15-7.73 (m, 11H, aryl + C$\underline{H}$=CH_2), 7.81 (bs, 1H, NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 102.15, 119.42 (q), 119.90, 122.75, 123.78, 124.62, 125.25, 126.07 (q), 126.43 (q), 127.10 (q), 127.80, 128.50, 129.16, 130.81, 133.79, 134.95 (q), 136.99 (q), 138.46 (q); m/z (%) 269 (M^+, 100), 268 (79), 267 (19), 266 (11), 192 (30), 149 (33), 134 (11), 133 (11), 120 (13), 77 (25).

5c (R= C_6H_5, Ar= C_6H_5, X=H): (49%), m.p. 256-258 °C (brown prisms from chloroform/n-hexane); (Found: C, 90.31; H, 5.41; N, 4.30. $C_{24}H_{17}N$ requires: C, 90.25; H, 5.36; N, 4.39); i.r. (Nujol) 3387, 3371, 1601, 1516, 1442, 1409, 1390, 1335, 1264, 1139, 1120, 1083, 1072, 1027, 942, 763, 757, 735, 720, 698 cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 6.43 (dd, 1H, J=2.10, 3.15 Hz, H-3), 7.15-7.98 (m, 16H, aryl + NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 101.97, 119.04 (q), 122.51, 123.66, 124.88, 126.07, 126.70 (q), 127.08, 127.70, 128.25, 128.28, 128.31 (q), 128.39 (q), 129.09, 130.06 (q), 130.74, 130.92, 134.46 (q), 136.97 (q), 139.24 (q); m/z (%) 320 (M^++1, 25), 319 (M^+, 100), 318 (19), 317 (12), 289 (5), 242 (7), 241 (15), 213 (5), 160 (6), 158 (12), 151 (8), 143 (8), 120 (8), 77

(6).

5d (R= C_6H_5, Ar= 4-$H_3CC_6H_4$, X=CH_3): (21%), m.p. 210-212 °C (white needles from dichloromethane/n-hexane); (Found: C, 89.81; H, 6.17; N, 4.15. $C_{26}H_{21}N$ requires: C, 89.88; H, 6.09; N, 4.03); i.r. (Nujol) 3256, 2917, 1522, 1441, 1400, 1358, 1138, 793, 741, 702, 668 cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 2.34 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 6.36 (dd, 1H, J=2.10, 3.15 Hz, H-3), 7.06-7.74 (m, 13H, aryl) 7.88 (s, 1H, NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 21.40, 21.83, 101.99, 119.55 (q), 124.47, 124.96, 126.20, 126.98, 126.99 (q), 128.01, 128.31, 128.42 (q), 129.05 (q), 129.83, 130.62, 131.02, 131.84 (q), 134.07 (q), 134.15 (q), 137.38 (q), 139.54 (q) and one quaternary carbon not observed; m/z (%) 348 (M^++1, 28), 347 (M^+, 100), 331 (10), 164 (10), 158 (23), 151 (14), 150 (10), 149 (27), 143 (11), 127 (12), 91 (14).

5e (R= (E)-C_6H_5-CH=CH, Ar= C_6H_5, X=H): (30%), m.p. 123-125 °C (yellow prisms from chloroform/n-hexane); (Found: C, 90.30; H, 5.70; N, 4.02. $C_{26}H_{19}N$ requires: C, 90.40; H, 5.54; N, 4.05); i.r. (Nujol) 3364, 1602, 1494, 1313, 1036, 1013, 752, 702, 667, 639 cm^{-1}; ^1H n.m.r. (200 MHz, $CDCl_3$) δ 6.99 (dd, 1H, J=2.20, 3.42 Hz, H-3), 7.01-8.39 (m, 17H, aryl), 7.99 (bs, 1H, NH); ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 102.42, 119.69 (q), 122.89, 123.91, 124.73, 125.41, 125.52 (q), 125.71, 126.60, 127.00 (q), 127.27 (q), 127.69, 127.88, 128.53 (q), 128.60, 128.86, 129.21, 130.86, 134.27, 135.09 (q), 137.04 (q), 138.23 (q); m/z (%) 346 (M^++1, 30), 345 (M^+, 100), 317 (20), 304 (10), 268 (20), 255 (13), 242 (23), 90 (30), 77 (14).

5f (R= 4-$H_3COC_6H_4$, Ar= C_6H_5, X=H): (40%), m.p. 219-220 °C (yellow prisms from chloroform/n-hexane); (Found: C, 85.90; H, 5.60; N, 4.14. $C_{25}H_{19}NO$ requires: C, 85.93; H, 5.48; N, 4.01); i.r. (Nujol) 3415, 1608, 1517, 1511, 1506, 1453, 1441, 1406, 1384, 1292, 1241, 1184, 1174, 1139, 1120, 1112, 1029, 827, 810, 767, 755, 720, 702, 673 cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 3.90 (s, 3H, OCH_3), 6.47 (dd, 1H, J=1.80, 3.50 Hz, H-3), 7.10-8.00 (m, 14H, aryl), 7.94 (bs, 1H, NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 55.42, 102.15, 113.85, 118.89 (q), 122.49, 123.72, 124.96, 126.23, 127.01 (q), 127.76, 128.21, 128.54 (q), 128.64 (q), 129.18, 129.90 (q), 130.85, 131.55 (q), 132.06, 134.57 (q), 137.13 (q), 158.81 (q); m/z (%) 351 (M^++2, 100), 350 (M^++1, 21), 349 (M^+, 17), 241 (21), 228 (25), 202 (28), 201 (11), 176 (44), 167 (17), 158 (22), 152 (36), 145 (52), 139 (46), 131 (21), 125 (25), 121 (13), 108 (40), 77 (38).

5g (R= 4-$H_3COC_6H_4$, Ar= 4-$H_3CC_6H_4$, X=CH_3): (23%), m.p. 231-233 °C (white needles from n-hexane); (Found: C, 85.84; H, 6.29; N, 3.80. $C_{27}H_{23}NO$ requires: C, 85.91; H, 6.14; N, 3.71); i.r. (Nujol) 3341, 3217, 1514, 1456, 1244, 1177, 1036, 812, 791, 715 cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 2.27 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.93 (s, 3H, OCH_3), 6.44 (dd, 1H, J=1.50, 1.80 Hz, H-3), 7.06-7.80 (m, 12H, aryl), 7.94 (bs, 1H, NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 21.44, 21.89, 55.41, 102.05, 113.98, 118.86 (q), 124.58, 124.99, 126.19, 127.04 (q), 127.22 (q), 127.95, 128.73 (q), 128.79 (q), 129.85, 130.66, 131.76 (q), 131.79 (q), 132.07, 134.13 (q), 134.17 (q), 137.37 (q), 158.68 (q); m/z (%) 377 (M^+, 72), 189 (65), 174 (32), 165 (27), 158 (97), 152 (96), 151 (100), 146 (46), 138 (43), 131 (28), 91 (89).

5h (R= 4-ClC_6H_4, Ar= C_6H_5, X=H): (24%), m.p. 184-186 °C (brown prisms from chloroform/n-hexane); (Found: C, 81.35; H, 4.70; N, 3.85. $C_{24}H_{16}NCl$ requires: C, 81.46; H, 4.56; N, 3.96); i.r. (Nujol) 3392, 1495, 1407, 1393, 1367, 1354, 1338, 1138, 1090, 1016, 814, 763, 715, 700, 667 cm^{-1}; ^1H n.m.r. (300 MHz, $CDCl_3$) δ 6.44 (dd, 1H, J=1.90, 3.30 Hz, H-3), 7.24-7.93 (m, 14H, aryl), 8.00 (bs, 1H, NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 101.82, 119.56

(q), 122.88, 123.85, 125.12, 125.77, 126.73 (q), 127.92, 128.36 (q), 128.61, 128.68, 129.24, 130.80, 132.36, 133.14 (q), 134.54 (q), 136.91 (q), 137.80 (q) and two quaternary carbons not observed; m/z (%) 355 (M^++2, 36), 353 (M^+, 100), 317 (20), 241 (14), 159 (25), 157 (56), 151 (19), 144 (19), 143 (28), 129 (13), 97 (17), 85 (16), 83 (21), 71 (20), 69 (31).

5i (R= 4-ClC$_6$H$_4$, Ar= 4-H$_3$CC$_6$H$_4$, X=CH$_3$): (22%), m.p. 154-155 °C (white needles from chloroform/n-hexane); (Found: C, 81.90; H, 5.14; N, 3.52. $C_{26}H_{20}NCl$ requires: C, 81.77; H, 5.28; N, 3.67); i.r. (Nujol) 3488, 1522, 1491, 1435, 1402, 1360, 1136, 1086, 1016, 810, 793, 752, 716, 638 cm^{-1}; ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ 2.41 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 6.39 (dd, 1H, J=1.95, 3.27 Hz, H-3), 7.13-7.80 (m, 12H, aryl), 7.96 (bs, 1H, NH); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 21.43, 21.87, 101.67, 119.55 (q), 124.04, 125.12, 126.22, 126.95 (q), 126.98 (q), 127.10 (q), 125.56 (q), 128.34 , 128.54, 129.78, 130.50, 132.04 (q), 132.23, 132.97 (q), 133.99 (q), 134.15 (q), 137.54 (q), 138.07 (q); m/z (%) 383 (M^++2, 32), 381 (M^+, 100), 191 (10), 183 (14), 166 (13), 165 (27), 164 (29), 158 (56), 151 (16), 150 (16), 144 (12).

5j (R= 4-O$_2$NC$_6$H$_4$, Ar= C$_6$H$_5$, X=H): (42%), m.p. 246-247 °C (brown prisms from chloroform/n-hexane); (Found: C, 79.01; H, 4.41; N, 7.62. $C_{24}H_{16}N_2O_2$ requires: C, 79.11; H, 4.43; N, 7.69); i.r. (Nujol) 3460, 3409, 1597, 1512, 1410, 1347, 1138, 764, 747, 702 cm^{-1}; ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 6.39 (dd, 1H, J=2.10, 3.40 Hz, H-3), 7.27-8.41 (m, 14H, aryl), 7.99 (bs, 1H, NH); ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 101.36, 120.66 (q), 123.50, 123.81, 124.08, 125.17, 125.42, 126.43 (q), 127.20 (q), 128.16, 128.34 (q), 128.39, 128.47 (q), 129.35, 130.74, 132.04, 134.54 (q), 136.60 (q), 146.80 (q), 147.13 (q); m/z (%) 365 (M^++1, 32), 364 (M^+, 100), 318 (32), 317 (21), 315 (18), 241 (20), 158 (19), 151 (10), 144 (11).

5k (R= 4-pyridyl, Ar= C$_6$H$_5$, X=H): (30%), m.p. 287-289 °C (brown prisms from dimethylsulfoxide); (Found: C, 86.30; H, 5.14; N, 8.60. $C_{23}H_{16}N_2$ requires: C, 86.22; H, 5.03; N, 8.74); i.r. (Nujol) 3400, 3077, 1599, 1542, 1522, 1505, 1440, 1415, 1145, 1069, 1006, 850, 815, 766, 756, 744, 719, 701, 686 cm^{-1}; ^{1}H n.m.r. (200 MHz, DMSO-d$_6$) δ 6.34 (bs, 1H, H-3), 7.25-7.80 (m, 12H, aryl + pyridyl), 8.80 (d, 2H, J= 6.20 Hz, pyridyl), 10.80 (bs, 1H, NH); ^{13}C n.m.r. (50 MHz, DMSO-d$_6$) δ 99.41, 120.06 (q), 122.70, 123.23, 124.43, 124.74, 124.97 (q), 125.38 (q), 125.69, 127.44 (q), 127.56, 128.36 (q), 128.85, 130.54, 131.37, 134.12 (q), 136.29 (q), 146.86 (q), 149.82; m/z (%) 321 (M^++1, 25), 320 (M^+, 100), 319 (31), 243 (23), 241 (18), 160 (12), 146 (10), 132 (19), 119 (10).

5l (R= 4-pyridyl, Ar= 4-H$_3$CC$_6$H$_4$, X=CH$_3$): (27%), m.p. 310-311 °C (white needles from dichloromethane); (Found: C, 86.13; H, 5.85; N, 8.14. $C_{25}H_{20}N_2$ requires: C, 86.18; H, 5.79; N, 8.04); i.r. (Nujol) 3386, 3115, 1601, 1456, 1416, 1148, 814, 806, 648 cm^{-1}; ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 2.46 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 6.45 (dd, 1H, J=2.00, 3.16 Hz, H-3), 7.17-7.66 (m, 10H, aryl + pyridyl), 8.18 (bs, 1H, NH), 8.82 (d, 2H, J= 6.40 Hz, pyridyl); ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 21.33, 21.77, 101.18, 120.36 (q), 123.50, 125.20, 125.52 (q), 126.17, 126.36, 126.86 (q), 128.08 (q), 128.80, 129.83, 130.45, 132.61 (q), 133.61 (q), 134.08 (q), 137.61 (q), 147.98 (q), 149.83 and one quaternary carbon not observed; m/z (%) 348 (M^+, 100), 174 (12), 166 (33), 159 (15), 151 (11), 145 (21), 91 (13).

5m (R= 3-thienyl, Ar= C$_6$H$_5$, X=H): (55%), m.p. 199-200 °C (brown prisms from chloroform/n-hexane); (Found: C, 81.21; H, 4.72; N, 4.39. $C_{22}H_{15}NS$ requires: C, 81.20; H, 4.65; N, 4.30); i.r. (Nujol) 3381, 1404, 1336, 1262, 1132, 1115, 1081, 1030, 792, 775, 758, 718, 702, 679, 667 cm^{-1}; ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 6.53 (dd, 1H,

J=1.96, 3.10 Hz, H-3), 7.16-8.10 (m, 14H, aryl + NH); ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 102.22, 119.31 (q), 122.74, 123.81, 124.40, 124.91 (q), 125.02 (q), 125.03, 125.09, 126.07, 127.23 (q), 127.82, 128.39, 128.52 (q), 129.19, 130.46, 130.81, 134.59 (q), 137.02 (q), 139.31 (q); m/z (%) 326 (M^++1, 24), 325 (M^+, 100), 278 (8), 241 (11), 162 (13), 84 (10), 77 (9).

Preparation of Carbodiimide 11. To a solution of triphenylphosphine (0.72 g, 2 mmol) in dry diethyl ether (10 ml) was added dropwise a solution of azide **1e** (0.41 g, 2 mmol) in the same solvent and the reaction mixture was stirred at room temperature until N_2 evolution was ceased (about 2 h). This solution of iminophosphorane was added dropwise over a solution of p-tolylisothiocianate (0.30 g, 2 mmol) in dry diethyl ether (10 ml) at 0 °C under nitrogen atmosphere. The resultant mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the crude was extracted with dry n-hexane to afford the carbodiimide **11** (85 %), yellow oil; (Found: C, 78.12; H, 6.80; N, 9.70. $C_{19}H_{20}N_2O$ requires: C, 78.05; H, 6.89; N, 9.58); i.r. (film) 2135, 1609, 1512, 1250, 1175, 1034, 839, 819, 696 cm^{-1}; ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 2.26 (s, 3H, CH_3), 2.65 (c, 2H, J=6.80 Hz, H-2), 3.44 (t, 3H, J=6.80 Hz, H-1), 3.73 (s, 3H, OCH_3), 5.55 (dt, 1H, J=6.80, 11.40 Hz, H-3), 6.46 (d, 1H, J= 11.40 Hz, H-4), 6.80-7.29 (m, 8H, aryl); ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 20.70, 30.43, 46.66, 54.96, 113.49, 123.24, 126.42, 129.47 (q), 129.69, 129.76, 131.02, 131.95 (q), 134.04 (q), 137.37 (q), 158.35 (q); m/z (%) 292 (M^+, 8), 261 (15), 201 (21), 175 (31), 115 (100), 107 (22), 105 (18), 91 (61).

Reaction of Iminophosphorane Derived from Azido Olefin 1e with Ethylphenylketene. To a solution of triphenylphosphine (0.72 g, 2mmol) in dry diethyl ether (10 ml) was added dropwise a solution of the azido olefin **1e** (0.41 g, 2 mmol) in the same solvent and the reaction mixture was stirred at room temperature until N_2 evolution was ceased (about 2 h). The solvent was removed under reduced pressure at room temperature and to the crude iminophosphorane **2** was added dry toluene (60 ml) and ethylphenylketene (0.29 g, 2 mmol). The solution was stirred at room temperature for 20 min and the resultant ketenimine **6** (as evidenced by IR)was treated with activated manganese dioxide (1.74 g, 20 mmol) and treated at reflux temperature for 5 h. After cooling, the solvent was removed and the filtrate concentrated to dryness. The crude product was chromatographed on silica gel column, eluting with diethylether/n-hexane and recrystallized from n-hexane to give the amide **7** (62 %); m.p. 266-267 °C (white prisms); (Found: C, 78.10; H, 7.89; N, 4.25. $C_{21}H_{25}NO_2$ requires: C, 77.99; H, 7.79; N, 4.33); i.r. (Nujol) 3300, 1647, 1608, 1546, 1512, 1455, 1251, 1177, 1036, 837, 752 cm^{-1}; ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ 0.83 (t, 3H, J= 6.56 Hz, CH_2-$C\underline{H}_3$), 1.74 (m, 1H, $C\underline{H}_AH_B$-CH_3), 2.14 (m, 1H, $CH_A\underline{H}_B$-CH_3), 2.44 (c, 2H, J= 7.06 Hz, CH=CH-$C\underline{H}_2$), 3.15 (t, 1H, J= 7.40 Hz, $C\underline{H}C_6H_5$), 3.29 (m, 2H, $C\underline{H}_2$-NHCO), 3.78 (s, 3H, OCH_3), 5.40 (dt, 1H, J= 7.06, 11.54 Hz, CH=C$\underline{H}$-CH_2), 5.60 (bs, 1H, NH), 6.39 (d, 1H, J= 11.54, C$\underline{H}$=CH-CH_2), 6.82 (d, 2H, J= 8.90 Hz, aryl), 7.13 (d, 2H, J= 8.90 Hz, aryl), 7.20-7.26 (m, 5H, aryl); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 12.37, 26.39, 28.62, 39.35, 55.24, 55.25, 113.67, 112.11, 127.13, 128.02, 128.72, 129.70 (q), 129.91, 130.75, 140.01 (q), 158.43 (q), 173.59 (q); m/z (%) 323 (M^+, 6), 292 (13), 177 (31), 162 (22), 147 (18), 115 (100).

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REFERENCES

1. Omura, S.; Nakagawa, A.; Yamada, H.; Hata, T.; Furusaki, A.; Watanabe, T. *Chem. Pharm. Bull.* **1973**, *21*, 931; Bowden, B. F.; Ritchie, E.; Taylor, W. C. *Aust. J. Chem.* **1972**, *25*, 2659.
2. Sakamoto, T.; Kondo, Y.; Yamanaka, H. *Heterocycles* **1986**, *24*, 1845.
3. Shakhnovich, A. I. *J. Heterocyclic Chem.* **1991**, *28*, 33; Maruyama, K.; Osuka, A.; Nakagawa, K.; Nabeshima, T.; Tabuchi, K. *Synthesis* **1989**, 628; Germeraad, P.; Moore, H. W. *J. Org. Chem.* **1974**, *39*, 774.
4. Jackson, P. M.; Moody, C. J. *J. Chem. Soc. Perkin Trans. 1* **1990**, 2156; Jackson, P. M.; Moody, C. J. *Tetrahedron* **1992**, *48*, 7447.
5. Murakami, Y.; Watanabe, T. *J. Chem. Soc. Perkin Trans. 1* **1988**, 3005.
6. Weeratunga, G.; Prasad, G. K. B.; Dilley, J.; Taylor, N. J.; Dmitrienko, G. *Tetrahedron Lett.* **1990**, 5713.
7. Differding, E.; Ghosez, L. *Tetrahedron Lett.* **1985**, 1647.
8. Molina, P.; Alajarín, M.; Vidal, A.; Fenan-Dupont, J.; Declerq, J. P. *J. Org. Chem.* **1991**, *56*, 4008; Molina, P.; Alajarín, M.; Vidal, A.; Sánchez-Andrada, P. *J. Org. Chem.* **1992**, *57*, 929; Molina, P.; Alajarín, M.; Vidal, A. *J. Org. Chem.* **1992**, *57*, 6703.
9. Corey, E. J.; Desai, M. C. *Tetrahedron Lett.* **1985**, 5747; Chhen, A.; Vaultier, M.; Carrié, R. *Tetrahedron Lett.* **1989**, 4953.

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