Pergamon

Tetrahedron, Vol. 52, No. 27, pp. 9237-9248, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00473-5

Diels-Alder Cycloaddition of Vinylpyrazoles. Synergy between Microwave Irradiation and Solvent-Free Conditions

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Abstract: When subjected to microwave irradiation and solvent-free conditions vinylpyrazoles undergo Diels-Alder cycloadditions within 6-30 min to give acceptable yields of easily purified products. This methodology overcomes the most important disadvantages of the classical conditions and it permits the reaction to be extended to low reactive dienophiles, such as ethyl phenylpropiolate, not described by classical heating. The regiochemistry of the later reaction has been inferred by NOE experiments and molecular orbital calculations.

Diels-Alder cycloaddition is the most useful and widely extended method for the construction of six-membered rings.[1] Vinyl substituted 5-membered heterocycles have been used as dienes in Diels-Alder reactions to build compounds of medicinal interest.[2] Although vinylpyrroles and vinylindoles react in mild conditions with several dienophiles, vinylpyrazoles do not react in similar conditions, and the use of highly reactive dienophiles, such are diethyl azodicarboxylate (DEAZD) and 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD), produces a [2 + 2] cycloaddition with the exocyclic double bond.[3]

Diels-Alder cycloadditions of vinylpyrazoles requires the use of a highly reactive dienophile in extreme conditions: high pressures and temperatures (8-10 atm and 120-140 °C) for long reaction times (several days) to obtain, in most cases, moderate yields.[4] With respect to acetylenic esters, dimethyl acetylenedicarboxylate (DMAD) reacts with the vinylpyrazole **1** or **2** in a sealed vessel to afford the corresponding products in 18 and 53%, respectively; methyl propiolate (MP) reacts with **1** or **2** to give less than 8% overall yield; finally, cycloaddition of ethyl phenylpropiolate with vinylpyrazoles have not been described by classical heating.[2] Furthermore, in these conditions extensive polymerization occurs.

Microwave irradiation in solvent-free conditions has well demostrated its utility as energy source to dramatically improve yields and/or reactions conditions in Diels-Alder cycloadditions.[5]

Recently, we have shown that microwave irradiation induces unstable or unreactive compounds, such are cyclic ketene acetals[5c,5e] or pyridinium N-dicyanomethylylide,[6] to undergo Diels-Alder and/or 1,3-dipolar cycloadditions in a few minutes with excellent yields, avoiding the drastic classical conditions and the polymerization or decomposition of the reagents.

In this work, we have studied the cycloaddition of 4- and 5-vinylpyrazoles with DMAD and methyl (or ethyl) propiolate to check the improvements that microwave irradiation in solvent-free conditions produces. Likewise, we have extended the reaction to ethyl phenylpropiolate, a low reactive dienophile not described by classical heating.

RESULTS AND DISCUSSION

Cycloadditions with DMAD.-

We found that vinylpyrazoles **1** or **2** react with DMAD under microwave irradiation within 6 and 30 min, affording the products indicated in the scheme in 72 and 45% overall yield, respectively. Reaction of **1** was performed on a teflon vessel in a domestic oven, whereas the reaction of **2** was carried out at atmospheric pressure in a focused microwave reactor with measurement and control of power and temperature. However, further experiments with both irradiation sources did not show any dependence of the yield or product ratio with the system employed.

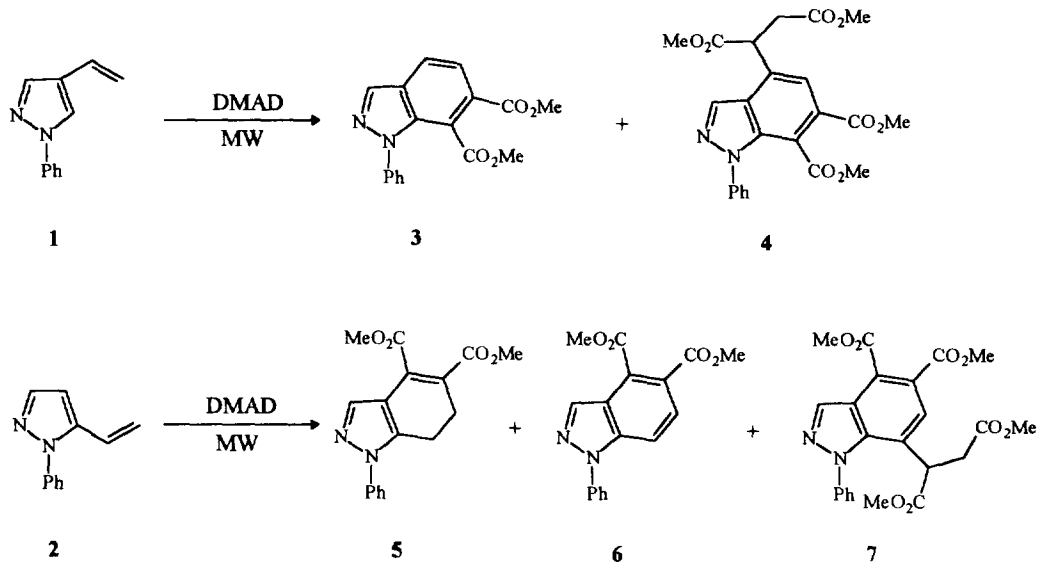
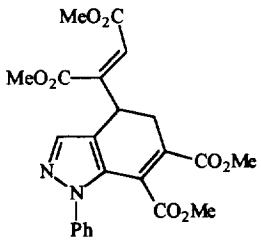


Table 1. Comparison of the Reaction of **1** or **2** with DMAD by Classical Heating or under Microwave Irradiation.

Vinylpyrazole	Reaction conditions	Products [yield(%)]
1	CH_2Cl_2, 150 °C, 8-10 atm[ref. 2]	**3** + **4** (18% overall yield)
1	MW, 780 W, 130 °C, 6 min	**3** (10) + **4** (62)
2	CH_2Cl_2, 140 °C, 3 days[ref. 4c]	**5** (53)
2	MW, 75 W, 160 °C, 30 min	**5** (10) + **6** (6) + **7** (29)

All these products were easily isolated by flash chromatography on silica gel. Indazoles **4** and **7** resulted from a further ene reaction of the primary Diels-Alder adduct with a second molecule of DMAD followed by two [1,3]-sigmatropic hydrogen shifts.[2] At shorter times, the intermediate products **8** from the vinylpyrazole **1**, and **9** from the compound **2** were isolated. These intermediates rearranged spontaneously in a few minutes to **4** and **7**, respectively, at the indicated reaction temperature. Contrary to the data reported by classical heating, ene reactions were also observed for compound **2**.[4c] All these compounds were characterized by their spectroscopic data.



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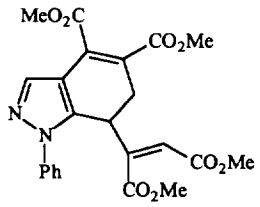

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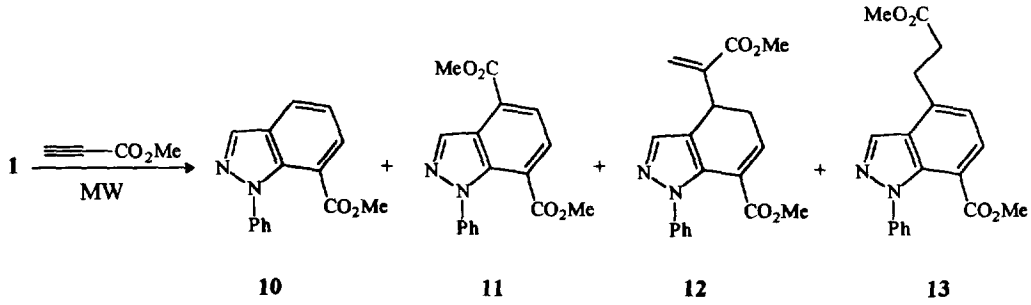
As Table 1 shows, microwave irradiation reduced dramatically the reaction times and improved the yield of the indazoles **3** and **4** respect to classical heating. Moreover, it permited the characterization of several products, such are **6**, **7** and **9**, not detected before.[4c]

Cycloadditions with methyl or ethyl propiolate.-

Microwave irradiation of vinylpyrazole **1** and methyl propiolate for 20 min afforded compounds **10**, **11** and a non-separable mixture of **12** and **13** (products ratio 3:1) in 39% overall yield. Irradiation of

vinylpyrazole **2** and ethyl propiolate for 25 min gave the cycloadduct **14**, as the sole product, in 22% yield. Both reactions were performed in a closed teflon vessel with a domestic oven.



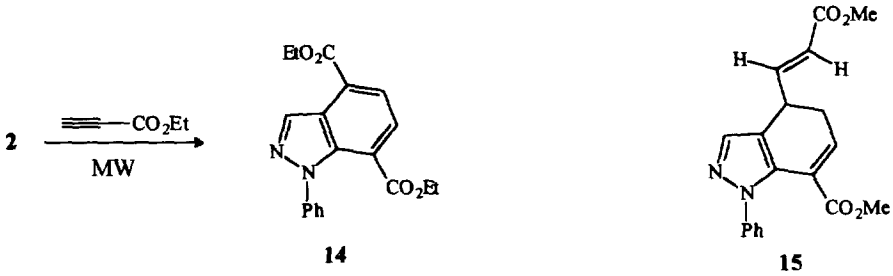


Table 2. Comparison of the Reaction of **1** or **2** with Methyl (or Ethyl) Propiolate by Classical Heating or under Microwaves

Vinylpyrazole	Dienophile	Reaction conditions	Products [yield(%)]
1	MP	CH_2Cl_2, 150 °C, 5 days[ref. 4b]	**10** (0.65) + **12,13** (5.2)
1	MP	MW, 780 W, 170 °C, 20 min	**10** (12) + **11** (6) + **12,13** (21)
2	MP	CH_2Cl_2, 140 °C, 7 days[ref. 4c]	**11** (7)
2	ethyl propiolate	MW, 780 W, 186 °C, 25 min	**14** (22)

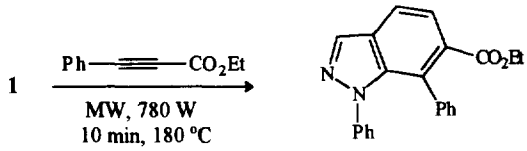
Indazoles **11** and **14** resulted from a double Diels-Alder reaction with subsequent extrusion of ethene.[2] When the reaction of compound **1** and MP was stopped at 10 min, we could isolate the intermediate product **15**, which spontaneously rearranged to **13** at 170 °C. The ^{1}H-NMR spectra of the intermediate **15** showed two signals at 5.90 and 7.02 ppm with a vicinal coupling constant of 15.5 Hz, that were assigned to the exocyclic double bond protons, having an E configuration.

The short reaction times under microwave irradiation reduced polymerization, therefore, produced the cycloaddition in higher yields and permited the isolation of the products with high purity by a single flash chromatography.

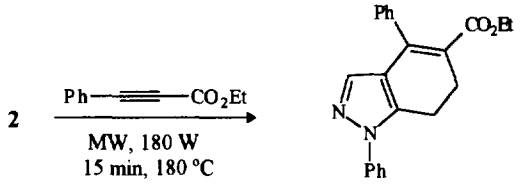
Cycloadditions with ethyl phenylpropiolate.-

Cycloaddition of **1** with ethyl phenylpropiolate under microwave irradiation at 780 W for 10 min in a domestic oven gave the aromatic adduct **16** in 12% yield. Cycloaddition of **2** with the same dienophile in a focused microwave reactor at 180 W for 15 min afforded the non aromatic product **17** (19%).

These reactions had not been previously described under classical conditions, perhaps owing to the low reactivity of ethyl phenylpropiolate. In order to compare, we performed the reaction of **1** or **2** with ethyl phenylpropiolate by classical heating in a sealed vessel at 140 °C for 6 days, however, we only detected polymerization or decomposition products.



16 (12%)



17 (19%)

The regiochemistry of cycloadditions with ethyl phenylpropiolate was inferred by NOE difference experiments (see Figure 1), in dimethylsulfoxide-d_6 with **16** and benzene-d_6 with **17** to observe separately the signals corresponding to the aromatic protons, although this was not possible with **16** in the tested solvents.

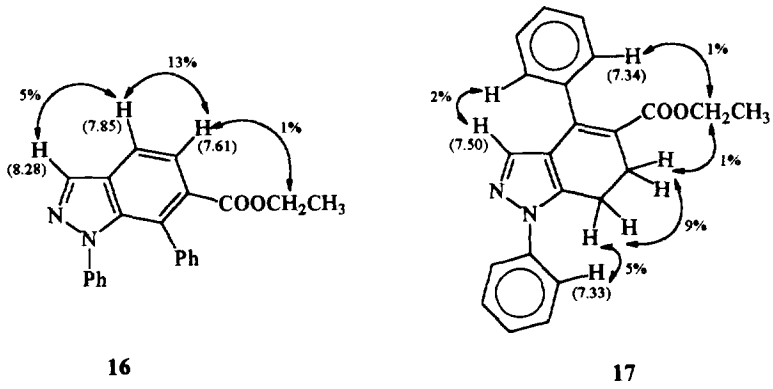


Figure 1. Selected NOEs for compounds **16** and **17**. Values in parentheses are chemical shifts (ppm)

Calculations

In order to explain the reactivity of **1** with DMAD, MP and ethyl phenylpropiolate, and particularly, to justify the regioselectivity in the last case, semiempirical molecular orbital calculations were performed with the program Hyperchem[7] using the PM3 method and complete (RHF) geometry optimization. The Polak-Riviere conjugated-gradient algorithm was employed, and all calculations converged successfully and had gradients less than 0.1. Input structures for these calculations were generated by molecular mechanics procedures using the MM+ force field in Hyperchem.

Table 3 shows that the reaction is in all cases a normal electron demand one, and a smaller energy-gap for ethyl phenylpropiolate, and consequently a faster reaction, than for MP; so the lower yield of cycloaddition products in the reaction with ethyl phenylpropiolate may be, perhaps, due to a faster polymerization process.[8]

Table 3. HOMO-LUMO Energies of 4-Vinylpyrazole **1**, DMAD, MP and Ethyl Phenylpropiolate (EPP) and Energy-gaps.

Compound	E_{HOMO} (eV)	E_{LUMO} (eV)	E_{LUMO} **1**- E_{HOMO}	E_{LUMO}- E_{HOMO} **1**
1	-8.70	-0.56		
DMAD	-11.78	-1.03	11.22	7.67
MP	-11.56	0.16	11.00	8.86
EPP	-9.71	-0.66	9.15	8.04

Figure 2 represents the coefficients of the frontier orbitals of **1** and ethyl phenylpropiolate (left) as well as **1** and methyl propiolate (right) ; coefficients show in both cases, a regioselectivity according with the experimental results, and inferred by NOE difference experiments in the case of **16**.

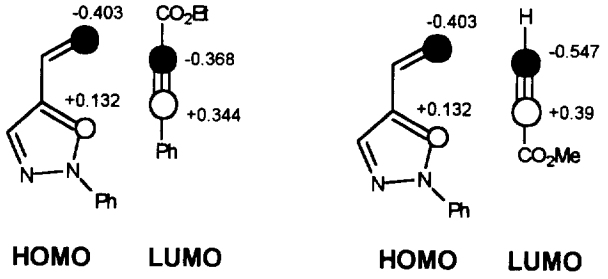


Figure 2

CONCLUSIONS

Synergy between microwave irradiation and solvent-free conditions induces vinylpyrazoles to undergo Diels-Alder cycloadditions with acetylenic dienophiles within a few minutes avoiding the drastic reaction conditions described by classical heating. With this methodology, yields were improved remarkably, disminishing the polymerization process and increasing the purity of the products. It is possible to employ a low reactive dienophile, such as ethyl phenylpropiolate, whose cycloaddition with vinylpyrazoles have not been described under classical conditions. Regiochemistry in the latter reactions were inferred by NOE difference experiments, and confirmed by molecular orbital calculations. Finally, under these conditions, intermediates and products not described by classical heating were isolated. All these results are coherent with a remark of Lewis[9] stating that 'slower reacting systems tend to show a greater effect under microwave irradiation than reacting systems'.

EXPERIMENTAL

General.- All mp's were determined on a Gallenkamp apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 299.94 MHz on a Varian Unity 300 spectrometer. ^{13}C NMR spectra were recorded at 75.429 MHz on a Varian Unity 300 machine. Chemical shifts are reported in ppm (δ) using Me_4Si as

standard, and coupling constants *J* are given in Hz. Percentage NOE enhancements were obtained by integrating the affected resonance relative to the irradiated resonance in the difference spectrum in each case. Column chromatography was carried out with SiO_2 (silica gel, Merck type 60 230-400 mesh). Microwave irradiations were conducted in a Miele Electronic M720 domestic oven or a focused microwave reactor Prolabo MX350 with measurement and control of power and temperature by infrared detection. Elemental analysis were determined on a Perkin-Elmer PE2400 CHN apparatus. Mass spectra were obtained on a VG Autospec instrument (70 eV). Reagents were purchased from commercial suppliers or prepared by literature methods.

General Procedures.- **Method A**: A teflon vessel was charged with the vinylpyrazole (1 equiv.) and the acetylenic ester (3 equiv.) and then closed and the reaction mixture irradiated in a domestic oven at 780 W for the indicated time. The crude reaction was purified by flash chromatography on silica gel.

Method B: A mixture of the vinylpyrazole (1 equiv.) and the acetylenic ester (3 equiv.) was irradiated in a focused microwave reactor Prolabo for the time and at the power indicated. The crude reaction was purified by flash chromatography on silica gel.

Reaction of 1-phenyl-4-vinylpyrazole (1) with DMAD.- (Method A) From 1-phenyl-4-vinylpyrazole[10,3a] (170 mg, 1 mmol) and DMAD (426 mg, 3 mmol) with irradiation for 6 min (final temperature 130 °C). Flash chromatography (hexane-ethyl acetate 2:1) afforded the products **3** (31 mg, 10%) and **4** (281 mg, 62%). Irradiation of the reaction mixture for 3 min permited the isolation of the intermediate **8** (95 mg, 21%).

Data for **3**: m.p. 118-119 °C (from carbon tetrachloride-hexane); ^{1}H-NMR ($CDCl_3$) δ (ppm) 3.31 and 3.90 (2 x s, 6 H, 2 x OCH_3), 7.44-7.52 (m, 5 H, Ph), 7.79 (d, *J* 8.5, 1 H, H-4), 7.90 (d, *J* 8.5, 1 H, H-5), 8.27 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 52.7 and 58.1 (OCH_3), 121.8, 122.2, 126.9, 127.0, 127.7, 128.9, 129.0, 134.8, 139.4 (C_{arom}), 166.4 and 166.5 (COO). Anal. calcd. for $C_{17}H_{14}N_2O_4$: C, 65.8; H, 4.55; N, 9.05. Found: C, 65.7; H, 4.6; N, 9.15%.

Data for **4**: yellow oil; ^{1}H-NMR ($CDCl_3$) δ (ppm) 2.78 (dd, *J* 17.1 and 5.5, 1 H, CH_2), 3.40 (dd, *J* 17.1 and 9.5, 1 H, CH_2), 3.23, 3.63, 3.64 and 3.82 (4 x s, 12 H, 4 x OCH_3), 4.55 (dd, *J* 9.5 and 5.5, 1 H, C*H*CH_2), 7.34-7.45 (m, 5 H, Ph), 7.62 (s, 1 H, H-5), 8.34 (s, 1H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 36.5 and 44.8 (*C*HCH_2), 52.1, 52.2, 52.7 and 52.8 (OCH_3), 120.6, 126.6, 127.0, 127.2, 128.9, 129.1, 129.3, 132.3, 132.4, 139.1 (C_{arom}), 166.0, 166.1, 171.4 and 172.1 (COO). Anal. calcd. for $C_{23}H_{22}N_2O_8$: C, 60.8; H, 4.9; N, 6.15. Found: C, 60.95; H, 4.85; N, 6.1%.

Data for the intermediate **8**: yellow oil; ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.89 (dd, *J* 16.9 and 6.0, 1 H, CH_2), 3.02 (dd, *J* 16.9 and 7.6, 1 H, CH_2), 3.10, 3.64, 3.68 and 3.70 (4 x s, 12 H, 4 x OCH_3), 4.15 (t, *J* 6.4, 1 H, C*H*CH_2), 5.86 (d, *J* 1.2, 1 H, =CH), 7.32-7.59 (m, 5 H, Ph), 7.70 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ

(ppm) 30.4 and 35.1 (*C*HCH$_2$), 51.8, 51.2, 52.3 and 52.4 (OCH$_3$), 118.9, 121.2, 125.9, 128.0, 128.7, 128.8, 129.2, 132.7, 137.2, 138.7 and 149.2 (others), 164.6, 164.9, 165.8 and 167.9 (COO).

Reaction of 1-phenyl-5-vinylpyrazole (2) with DMAD.- (Method B) From 1-phenyl-5-vinylpyrazole[4c] (200 mg, 1.17 mmol) and DMAD (499 mg, 3.51 mmol) with irradiation at 75 W for 30 min (final temperature 160 °C). Flash chromatography (hexane-ethyl acetate 2:1) permited the isolation of **5** (36 mg, 10%), **6** (22 mg, 6%) and **7** (154 mg, 29%). Irradiation of the reaction mixture for 12 min permited to isolate the intermediate **9** (79 mg, 15%).

Data for **5**: m.p. 102-103 °C (from carbon tetrachloride) (Lit.[4c] 116 °C); ^{1}H-NMR (CDCl$_3$) δ (ppm) 2.86 (t, *J* 8, 2 H, CH$_2$), 3.00 (t, *J* 8, 2 H, CH$_2$), 3.80, 3.94 (2 x s, 6 H, 2 x OCH$_3$), 7.40-7.51 (m, 5 H, Ph), 7.67 (s, 1 H, H-3); ^{13}C-NMR (CDCl$_3$) δ (ppm) 20.5 and 24.8 (CH$_2$), 52.2 and 52.5 (OCH$_3$), 123.3, 127.8, 129.3, 137.4, 139.5 (others), 166.7 and 166.9 (COO). Anal. calcd. for $C_{17}H_{16}N_2O_4$: C, 65.4; H, 5.15; N, 9.0. Found: C, 65.3; H, 5.1; N, 9.1%.

Data for **6**: m.p. 164-165 °C (from diethyl ether) (Lit.[4c] 128 °C); ^{1}H-NMR (CDCl$_3$) δ (ppm) 3.94 and 4.06 (2 x s, 6 H, 2 x OCH$_3$), 7.42-7.89 (m, 7 H, H$_{arom}$), 8.37 (s, 1 H, H-3); ^{13}C-NMR (CDCl$_3$) δ (ppm) 52.7 and 53.0 (OCH$_3$), 112.3, 123.1, 124.1, 127.6, 129.6, 137.7, 139.3, 139.8 (C$_{arom}$), 167.2 and 167.3 (COO). Anal. calcd. for $C_{17}H_{14}N_2O_4$: C, 65.8; H, 4.55; N, 9.05. Found: C, 65.95; H, 4.55; N, 9.0%.

Data for **7**: yellow oil; ^{1}H-NMR (CDCl$_3$) δ (ppm) 2.55 (dd, *J* 17.1 and 5.6, 1 H, CH$_2$), 3.05 (dd, *J* 17.1 and 9.3, 1 H, CH$_2$), 3.54, 3.59, 3.92 and 4.05 (4 x s, 12 H, 4 x OCH$_3$), 4.21 (dd, *J* 9.3 and 5.6, 1 H, C*H*CH$_2$), 7.41-7.57 (m, 5 H, Ph), 7.66 (s, 1 H, H-6), 8.35 (s, 1 H, H-3); ^{13}C-NMR (CDCl$_3$) δ (ppm) 36.9 and 40.0 (*C*HCH$_2$), 51.8, 52.5, 52.7 and 52.9 (OCH$_3$), 123.8, 126.0, 127.9, 129.3, 129.9, 135.4, 139.4, 140.2 (C$_{arom}$), 166.7, 167.2, 170.6 and 171.9 (COO). Anal. calcd. for $C_{23}H_{22}N_2O_8$: C, 60.8; H, 4.9; N, 6.15. Found: C, 60.9; H, 4.85; N, 6.2%.

Data for the intermediate **9**: yellow oil; ^{1}H-NMR (CDCl$_3$) δ (ppm) 2.87 (dd, *J* 17.6 and 8.6, 1 H, CH$_2$), 3.26 (dd, *J* 17.6 and 1.7, 1 H, CH$_2$), 3.69, 3.80, 3.84 and 3.95 (4 x s, 12 H, 4 x OCH$_3$), 4.07 (dd, *J* 8.6 and 1.2, 1 H, H-7), 5.40 (d, *J* 1.2, 1 H, =CH), 7.41-7.51 (m ,5 H, Ph), 7.77 (s, 1 H, H-3); ^{13}C-NMR (CDCl$_3$) δ (ppm) 30.2 and 34.3 (*C*HCH$_2$), 52.0, 52.3, 52.6 and 52.7 (OCH$_3$), 117.1, 122.1, 123.4, 128.4, 129.4, 137.0, 137.5, 138.3, 146.2 (others), 164.7, 166.1, 166 8 and 167.5 (COO).

Reaction of 1-phenyl-4-vinylpyrazole (1) with MP.- (Method A) From 1-phenyl-4-vinylpyrazole (510 mg, 3 mmol) and MP (756 mg, 9 mmol) with irradiation for 20 min (final temperature 170 °C). Through a flash chromatography (hexane-ethyl acetate 4:1) **10** (91 mg, 12%), **11** (56 mg, 6%) and a non-separable mixture of **12** and **13** (213 mg, 21%) were isolated. Irradiation of the reaction mixture for 12 min permited the isolation of the intermediate **15** (30 mg, 3%).

Data for **10**: m.p. 84-85 °C (from carbon tetrachloride); ^{1}H-NMR ($CDCl_3$) δ (ppm) 3.24 (s, 3 H, OCH_3), 7.28 (dd, *J* 8.0 and 7.3, 1 H, H-5), 7.38-7.50 (m, 5 H, Ph), 7.87 (dd, *J* 7.3 and 1.2, 1 H, H-6), 7.96 (dd, *J* 8.0 and 1.2, 1 H, H-4), 8.29 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 51.5 (OCH_3), 116.4, 120.9, 124.1, 125.3, 126.6, 127.4, 129.0, 129.7, 135.9, 142.1 (C_{arom}), 166.7 (COO). Anal. calcd. for $C_{15}H_{12}N_2O_2$: C, 71.4; H, 4.8; N, 11.1. Found: C, 71.5; H, 4.8; N, 11.05%.

Data for **11**: m.p. 72-73 °C (from methanol); ^{1}H-NMR ($CDCl_3$) δ (ppm) 3.25 and 4.07 (2 x s, 6 H, 2 x OCH_3), 7.42-7.55 (m, 5 H, Ph), 7.85 (d, *J* 7.6, 1 H, H-6), 8.01 (d, *J* 7.6, 1 H, H-5), 8.83 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 51.9 and 52.5 (OCH_3), 120.9, 123.9, 124.3, 126.0, 127.8, 128.5, 129.1, 129.2, 136.5 (C_{arom}), 165.7 and 166.2 (COO). Anal. calcd. for $C_{17}H_{14}N_2O_4$: C, 65.8; H, 4.55; N, 9.05. Found: C, 65.75; H, 4.5; N, 9.05%.

Data for **12**: ^{1}H-NMR ($CDCl_3$) δ (ppm) 2.65 (ddd, *J* 17.3, 7.1 and 5.6, 1 H, H-5), 2.78 (ddd, *J* 17.3, 6.8 and 4.4, 1 H, H-5), 3.09 and 3.80 (2 x s, 6 H, 2 x OCH_3), 4.15 (dd, *J* 7.1 and 6.8, 1 H, C*H*CH_2), 5.50 (s, 1 H, =CH), 6.28 (s, 1 H, =CH), 6.81 (dd, *J* 5.6 and 4.4, 1 H, H-6), 7.28-7.51 (m, 6 H, Ph and H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 30.9 and 32.1 (*C*HCH_2), 51.2 and 52.0 (OCH_3), 121.0-141.3 (others), 165.2 and 166.9 (COO).

Data for **13**: ^{1}H-NMR ($CDCl_3$) δ (ppm) 2.81 (t, *J* 7.6, 2 H, =C-CH_2), 3.21 and 3.68 (2 x s, 6 H, 2 x OCH_3), 3.36 (t, *J* 7.6, 2 H, CH_2COO), 7.09 (d, *J* 7.3, 1 H, H-5), 7.28-7.51 (m, 5 H, Ph), 7.79 (d, *J* 7.3, 1 H, H-6), 8.33 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 28.1 and 34.4 (CH_2), 51.4 and 51.7 (OCH_3), 121.0-141.3 (others), 166.5 and 172.9 (COO).

Data for the intermediate **15**: yellow oil; ^{1}H-NMR ($CDCl_3$) δ (ppm) 2.56 (ddd, *J* 17.0, 8.3 and 4.9, 1 H, H-5), 2.72 (ddd, *J* 17.0, 7.3 and 4.9, 1 H, H-5), 3.10 and 3.75 (2 x s, 6 H, 2 x OCH_3), 3.70 (ddd, *J* 8.3, 7.3 and 1.2, 1 H, C*H*CH_2), 5.90 (dd, *J* 15.5 and 1.2, 1 H, =CHCOO), 6.88 (t, *J* 4.9, 1 H, H-6), 7.02 (dd, *J* 15.5 and 7.3, 1 H, =C*H*CH), 7.33-7.48 (m, 5 H, Ph), 7.52 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 30.4 and 34.0 (*C*HCH_2), 51.3 and 51.7 (OCH_3), 118.7, 119.1, 121.9, 123.3, 127.4, 129.1, 129.3, 136.0, 137.7, 148.1 (others), 165.1 and 166.6 (COO).

Reaction of 1-phenyl-5-vinylpyrazole (2) with ethyl propiolate.- (Method A) From 1-phenyl-5-vinylpyrazole (200 mg, 1.17 mmol) and ethyl propiolate (344 mg, 3.51 mmol) with irradiation for 25 min (final temperature 186 °C). Flash chromatography (hexane-ethyl acetate 20:1) afforded the adduct **14** (87 mg, 22%), m.p. 77-78 °C (from methanol); ^{1}H-NMR ($CDCl_3$) δ (ppm) 0.92 and 1.51 (2 x t, *J* 7.1, 6 H, 2 x CH_3), 3.75 and 4.53 (2 x q, *J* 7.1, 4 H, 2 x OCH_2), 7.41-7.54 (m, 5 H, Ph), 7.85 (d, *J* 7.5, 1 H, H-6), 8.02 (d, *J* 7.5, 1 H, H-5), 8.85 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 13.6 and 14.3 (CH_3), 61.5 and 61.7 (OCH_2),

121.1, 124.0, 124.1, 125.3, 126.3, 127.7, 128.4, 129.2, 136.6, 141.7 (C_{arom}), 165.3 and 166.0 (COO). Anal. calcd. for $C_{19}H_{18}N_2O_4$: C, 67.45; H, 5.35; N, 8.3. Found: C, 67.45; H, 5.3; N, 8.35%.

Reaction of 1-phenyl-4-vinylpyrazole (1) with ethyl phenylpropiolate.- (Method A) From 1-phenyl-4-vinylpyrazole (510 mg, 3 mmol) and ethyl phenylpropiolate (1566 mg, 9 mmol) with irradiation for 10 min (final temperature 180 °C). Flash chromatography (hexane-ethyl acetate 9:1) gave the adduct **16** (123 mg, 12%), m.p. 103-104 °C (from methanol); ^{1}H-NMR ($CDCl_3$) δ (ppm) 0.87 (t, *J* 7.1, 3 H, CH_3), 4.00 (q, *J* 7.1, 2 H, OCH_2), 6.90-7.10 (m, 10 H, 2 x Ph), 7.61 (d, *J* 8.6, 1 H, H-5), 7.86 (d, *J* 8.6, 1 H, H-4), 8.28 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 13.5 (CH_3), 61.0 (OCH_2), 120.1, 121.9, 126.4, 126.6, 127.0, 127.2, 128.0, 129.4, 130.0, 134.7 (C_{arom}), 169.1 (COO). Anal calcd. for $C_{22}H_{18}N_2O_2$: C, 77.15; H, 5.3; N, 8.2. Found: C, 77.25; H, 5.35; N, 8.2%.

Reaction of 1-phenyl-5-vinylpyrazole (2) with ethyl phenylpropiolate.- (Method B) From 1-phenyl-5-vinylpyrazole (200 mg, 1.17 mmol) and ethyl phenylpropiolate (610 mg, 3.51 mmol) with irradiation at 180 W for 15 min (final temperature 180 °C). Flash chromatography (hexane-ethyl acetate 9:1) afforded the adduct **17** (76 mg, 19%) as a yellow oil; ^{1}H-NMR (C_6D_6) δ (ppm) 0.63 (t, *J* 7.1, 3 H, CH_3), 2.37 (t, *J* 8.7, 2 H, H-7), 2.76 (t, *J* 8.6, 2 H, H-6), 3.84 (q, *J* 7.1, 2 H, OCH_2), 6.93-7.31 (m, 10 H, 2 x Ph), 7.45 (s, 1 H, H-3); ^{13}C-NMR ($CDCl_3$) δ (ppm) 13.5 (CH_3), 21.1 and 26.6 (CH_2), 60.0 (OCH_2), 119.2, 121.4, 123.2, 127.5, 127.9, 128.0, 129.2, 138.6, 138.9, 139.0, 142.1 (others), 168.5 (COO). Anal calcd. for $C_{22}H_{20}N_2O_2$: C, 76.7; H, 5.85; N, 8.15. Found: C, 76.75; H, 5.9; N, 8.1%.

ACKNOWLEDGEMENTS

Financial support by the Comisión Interministerial de Ciencia y Tecnología of Spain (DGICyT, PB94-0742) and a grant (Junta de Comunidades de Castilla-La Mancha) are gratefully acknowledged. We thank to Dr. Fernando Cossio (Univ. Pais Vasco) the calculation of coeficients in the frontier orbitals.

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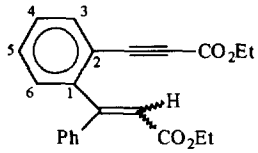
7. Hyperchem is a product of Autodesk Inc.
8. In fact, we isolated the following dimer (ca. 14%) during the cycloaddition of **1** or **2** with ethyl phenylpropiolate:



M.p. 129-130 °C (from methanol); ^{1}H-NMR (DMSO-d_6) δ (ppm) 0.90 and 1.36 (2 x t, *J* 7.1, 6 H, 2 x CH_3), 3.96 and 4.37 (2 x q, *J* 7.1, 4 H, 2 x OCH_2), 7.29 and 7.52 (m, 5 H, Ph), 7.44 (dd, *J* 7.8 and 1.3, 1 H, H-6), 7.65 and 7.71 (2 x td, *J* 7.8, 7.3 and 1.3, 2 H, H-4 and -5), 8.26 (dd, *J* 7.3 and 1.3, 1 H, H-3), 8.67 (s, 1 H, =CH); ^{13}C-NMR ($CDCl_3$) δ (ppm) 13.6 and 14.2 (CH_3), 61.1 and 61.6 (OCH_2), 124.8, 126.9, 127.3, 127.9, 128.8, 129.2, 130.3, 131.3, 132.3, 134.0, 136.7, 138.5 (others), 165.9 and 168.7 (COO); MS (EI) m/z 348 (M^+), 303, 275.

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(*Received in UK* 18 *April* 1996; *revised* 13 *May* 1996; *accepted* 16 *May* 1996)