(irradiation after the acquisition time) in order to minimize the crown ether signals.

Optical Purity Determinations. 1t (4 mg, 25 μmol) was acetylated in dry methanol (100 μL) with acetic anhydride (4 μL) at room temperature for 2 h. Following elimination of solvent under vacuum, the crude product was esterified by refluxing for 30 min in dry 2-propanol–hydrogen chloride (1.5 mol/L; 100 μL). Following elimination of solvent under vacuum, the crude product was analyzed by gas chromatography on a Chrompack-fused silica capillary column (50 m × 0.25 mm) coated with XE60-S–Valine (*S*)-phenylethylamide (175 °C helium (1.5 bar)).

Acknowledgment. We acknowledge R. Azerad for optical determinations and G. Cahiez for ^{19}F NMR spectra.

Action of Diazomethane on Methyl (*Z*(or *E*))-2-(Acylamino)cinnamates. A New Route to Methyl (*Z*)-2-(Acylamino)-3-methylcinnamates

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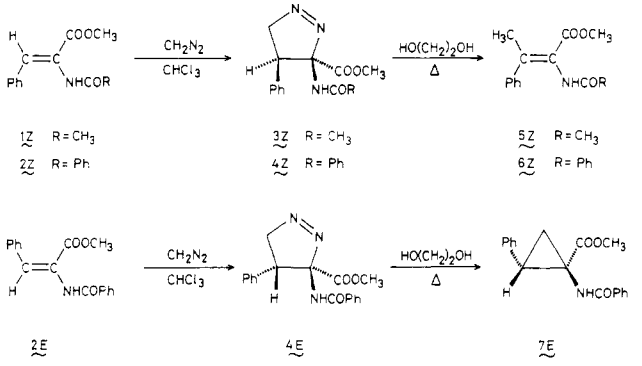
Diazomethane reacts with methyl (*Z*(or *E*))-2-acetamido(or benzamido)cinnamates (**1**, **2**) to afford regio- and stereospecifically (*Z*(or *E*))-4-phenyl-3-acetamido(or benzamido)-3-carbomethoxy-Δ^1-pyrazolines (**3**, **4**). **3Z** and **4Z** undergo pyrolysis to afford stereoselectively methyl (*Z*)-2-acetamido(or benzamido)-3-methylcinnamates (**5Z** and **6Z**). **4E** undergoes pyrolysis to afford stereoselectively methyl (*E*)-2-phenyl-1-benzamidocyclopropane-1-carboxylate (**7E**).

It has recently been reported[1] that ethyl *N*-acetyl-α,β-dehydroalaninate reacts with some 1,3-dipoles in 1,3-dipolar cycloadditions which have proved to proceed regiospecifically regardless of the presence of the acetamido group which exercises a strong directing effect on the addition of electrophilic reagents to the double bond,[2] to afford geminally functionalized heterocyclic amino carboxylic acids.

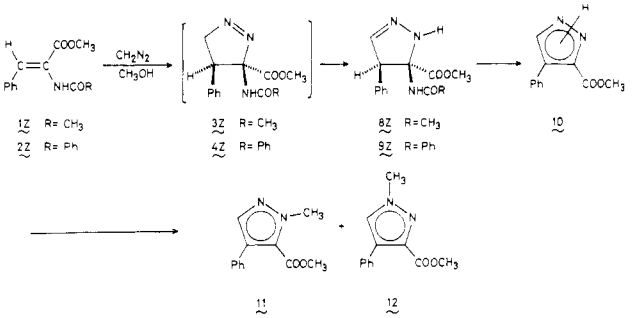
We have now tested the action of diazomethane on methyl (*Z*(or *E*))-2-acetamido(or benzamido)cinnamates[3] (**1**, **2**) and the pyrolysis of the pyrazolines obtained because of our interest in synthesizing prochiral enamides containing tetrasubstituted alkene moieties[4] in order to hydrogenate them.

We have found that diazomethane reacts regiospecifically with methyl (*Z*(or *E*))-2-acetamido(or benzamido)-cinnamates (**1**, **2**) in 1,3-dipolar cycloadditions to afford (*Z*(or *E*))-4-phenyl-3-acetamido(or benzamido)-3-carbomethoxy-Δ^1-pyrazolines (**3**, **4**) in quantitative yields without noticeable influence of the solvent polarity[5] on the cycloaddition rate,[6] as pointed out by Huisgen and others[7] (Scheme I). Furthermore, these cycloadditions have been shown to proceed stereospecifically, as expected,[8] since *Z* olefins gave *Z* pyrazolines and the *E* olefin gave *E* pyrazoline, as we verified by NOE by the irradiation of the hydrogen in the acylamino group in **3Z**, **4Z**, and **4E**.

Scheme I



Scheme II



Cycloaddition occurred without noticeable influence of the solvent polarity on the reaction rate to afford Δ^1-pyrazolines (**3**, **4**), but when methanol was used as a solvent the initially formed Δ^1-pyrazolines (**3**, **4**) underwent sub-

(1) Horikawa, H.; Nishitani, T.; Iwasaki, T.; Inoue, I. *Tetrahedron Lett.* **1983**, *24*, 2193.

(2) See for example: Love, A. L.; Olsen, R. K. *J. Org. Chem.* **1972**, *37*, 3431.

(3) Stereochemistry of all products was unambiguously determined by ^{13}C NMR couplings and NOE: (a) Cutolo, M.; Fiandanese, V.; Naso, F.; Sciacovelli, O. *Tetrahedron Lett.* **1983**, *24*, 4603. (b) Prokofev, E. P.; Karpeiskaya, E. I. *Tetrahedron Lett.* **1979**, 737. (c) Shimohigashi, Y.; Nitz, T. J.; Stammer, C. H. *Tetrahedron Lett.* **1982**, *23*, 3235.

(4) Oro, L. A.; Cabeza, J. A.; Cativiela, C.; Díaz de Villegas, M. D.; Meléndez, E. *J. Chem. Soc., Chem. Commun.* **1983**, 1383.

(5) We tested chloroform, tetrahydrofuran, and dimethylformamide, and for synthetic purposes we chose chloroform because it dissolves a great amount of the product in a few milliliters and it is easily removable.

(6) Although kinetics were not performed, a simultaneous experiment in the same conditions for the three solvents did not show noticeable differences in the disappearance of the departure products (tested by TLC). In all cases the reaction took place in about three days.

(7) See for example: Huisgen, R. *J. Org. Chem.* **1968**, *33*, 2291.

(8) Elguero, J. "Comprehensive Heterocyclic Chemistry"; Katritzky, A. R., Ed.; Pergamon Press: Oxford, 1984; Vol. 5, pp 277–284.

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sequent reactions, and 1-methyl-4-phenyl-5-carbomethoxypyrazole (**11**) and 1-methyl-4-phenyl-3-carbomethoxypyrazole (**12**) were obtained. We can assume that the initially formed Δ^1-pyrazoline (**3**, **4**) in methanol and in the presence of diazomethane in excess tautomerizes to the more stable Δ^2-pyrazoline (**8**, **9**), since the latter was isolated from the reaction solution (see the Experimental Section). The Δ^2-pyrazoline (**8**, **9**) in the reaction conditions slowly eliminates either acetamide or benzamide (which were isolated and identified) to afford 4-phenyl-3(5)-carbomethoxypyrazole (**10**). Reaction of **10** with an excess of diazomethane gives **11** and **12**, identification of which was made on the basis of their ^{1}H NMR spectral data,[9] in the ratio 4:1 as reported[10] for the methylation of pyrazole **10** (Scheme II).

The tautomerization was not observed with the reaction time used and at room temperature with the other solvents tested in the cycloaddition probably due to the aprotic character of these solvents. However when these conditions were varied (higher temperatures or longer periods of time) we noticed the appearance of Δ^2-pyrazoline.

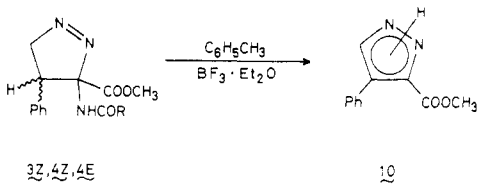
To the best of our knowledge 2-acetamido(or benzamido)-3-methylcinnamic esters have only been obtained by the stereospecific opening[11] of 2-methyl(or phenyl)-4-(α-arylethylidene)-5(4*H*)-oxazolones, difficult to obtain by condensation procedures;[12] for that reason we tested pyrolysis of the Δ^1-pyrazolines (**3**, **4**) obtained by the previous procedure in order to establish a route to these 2-(acylamino)-3-methylcinnamic esters and we found that pyrolysis of **3Z** carried out at about 90 °C in toluene for 40 h occurred with high stereoselectivity to afford methyl (*Z*)-2-acetamido-3-methylcinnamate (**5Z**) in good yield (80%), and pyrolysis of **4Z** in the same conditions afforded methyl (*Z*)-2-benzamido-3-methylcinnamate (**6Z**) in good yield (70%) and with high stereoselectivity but took 7 days. On the other hand pyrolysis of **4E** in the same conditions gave nitrogen extrusion in 7 days but methyl (*E*)-2-phenyl-1-benzamidocyclopropane-1-carboxylate[13] (**7E**) was the product obtained (Scheme I).

The reaction conditions were then varied in the pyrolysis of the pyrazolines (**3**, **4**) in order to diminish the reaction time and if possible to alter the reaction products to obtain methyl (*E*)-2-benzamido-3-methylcinnamate by pyrolysis of **4E**. We found that, under the same temperature conditions (90 °C) with some solvents, e.g., nitromethane, the results were not modified; but with others, e.g., dimethylformamide and 1,2-ethanediol, tautomerization to Δ^2-pyrazolines in these conditions was faster and pyrazole **10** was also obtained. Nevertheless, in 1,2-ethanediol at a higher temperature (200 °C), which accelerates nitrogen extrusion,[14] only one product was obtained by heating pyrazolines **3Z**, **4Z**, or **4E** for 10 min.

To sum up, pyrolysis of **3Z** and **4Z** in 1,2-ethanediol at 200 °C occurred in about 10 min to afford stereoselectively **5Z** and **6Z** respectively, in good yields; pyrolysis of **4E** in the same conditions occurred in about 10 min but **7E** was again the reaction product (Scheme I).

The high selectivity in the nitrogen extrusion reaction to afford alkenes as the only product from (*Z*)-Δ^1-pyrazolines (**3Z**, **4Z**) is remarkable since such selectivity is not usual in the pyrolysis of pyrazolines[15] to afford unsaturated compounds which usually appear as byproducts. In fact pyrazoline **4E** extrudes nitrogen to afford a cyclopropane **7E** as usual. These results can be explained by the recently discussed[12] mechanism for thermal decomposition of Δ^1-pyrazolines.

Scheme III



3Z,4Z,4E 10

We also tested the effect of boron trifluoride on the pyrolysis of pyrazolines **3Z**, **4Z**, and **4E** since it is known that boron trifluoride alters the product composition to a considerable extent, increasing in some cases the proportion of unsaturated compound.[16] We found that boron trifluoride in toluene caused aromatization of the pyrazoline to give the known pyrazole[10] **10** in about 75% yield in all cases (Scheme III). All attempts to alter reaction products to afford methyl (*E*)-2-benzamido-3-methylcinnamate from **4E** were unsuccessful.

Experimental Section

All melting points were taken on a Büchi 510 capillary melting point apparatus and are uncorrected. Fourier transform ^{1}H NMR spectra of **3** and **4** in Me_2SO-d_6 and **5**–**12** in $CDCl_3$ were recorded at 80 MHz on a Bruker WP-80-SY spectrometer, under ASPECT-2000 computer control, with Me_4Si as the internal standard. Chemical shifts are given in the δ scale, in ppm downfield from internal Me_4Si, and coupling constants are given in hertz. Chemical shifts and coupling constants for the ABX portion of the spectrum of **3** and **4** in Me_2SO-d_6 were obtained by simulation interaction with PANIC (the Bruker-adapted version of LAOCOON), and the final RMS error was 0.045. Overhauser enhancement factors were determined for undegassed 50 mM solutions of **3** and **4** in Me_2SO-d_6 by using the NOE difference technique, by gated irradiation of the amide NH proton (saturation time 10 s, decoupling power 45 dB below 0.2 W, decoupler bandwidth γB_2 = 2.5 Hz). NOE signal enhancements of approximately 3–15% were observed. Elemental analyses were measured on a Perkin-Elmer 240-B analyzer. All compounds showed spectra in total agreement with the proposed structure and only one spot by TLC.

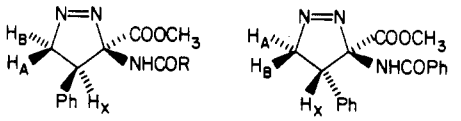
Methyl (*Z*)-2-acetamidocinnamate (**1Z**), methyl (*Z*)-2-benzamidocinnamate (**2Z**), and methyl (*E*)-2-benzamidocinnamate (**2E**) were prepared by stereospecific opening of the corresponding 5(4*H*)-oxazolones by a general procedure.[17]

(*Z*)-4-Phenyl-3-acetamido-3-carbomethoxy-Δ^1-pyrazoline (3Z). A total of 1 g (4.5 mmol) of **1Z** dissolved in 20 mL of chloroform was treated with an ethereal solution of diazomethane (from 2 g of *N*-methyl-*N*-nitrosourea in 20 mL of ether) in a stoppered and protected from light flask at room temperature for about 3 days until completion (TLC). The solution was treated with anhydrous $CaCl_2$ to get rid of excess diazomethane, filtered, and concentrated in vacuo. The resultant solid was dried over P_2O_5 to give a quantitative yield (1.19 g) of pure **3Z** as a white solid: mp 147–148 °C; NMR in Table I. Anal. Calcd for $C_{13}H_{15}N_3O_3$: C, 59.77; H, 5.74; N, 16.09. Found: C, 59.69; H, 5.60; N, 15.97.

(*Z*)-4-Phenyl-3-benzamido-3-carbomethoxy-Δ^1-pyrazoline (4Z). A total of 1 g (3.6 mmol) of **2Z** underwent diazomethane cycloaddition under exactly the same conditions used in the

(9) Elguero, J.; Jacquier, R.; Tien Duc, H. C. N. *Bull. Soc. Chim. Fr.* **1966**, 3727.
(10) Bastide, J.; Lematre, J. *Bull. Soc. Chim. Fr.* **1970**, 3543.
(11) Cativiela, C.; Meléndez, E. *Synthesis* **1980**, 901.
(12) Cativiela, C.; Díaz de Villegas, M. D.; Mayoral, J. A.; Meléndez, E. *J. Org. Chem.* **1984**, *49*, 1436 and references herein.
(13) Stereochemistry of this compound was unambigously determined by Stammer et al. See: King, S. W.; Riordan, J. M.; Holt, E. M.; Stammer, C. H. *J. Org. Chem.* **1982**, *47*, 3270.
(14) McGreer, D. E.; Masters, J. M. E. *Can. J. Chem.* **1969**, *47*, 3975.
(15) Engel, P. S. *Chem. Rev.* **1980**, *80*, 99 and references cited therein.
(16) McGreer, D. E.; Chiu, N. W. K.; Vinje, M. G. *Can. J. Chem.* **1965**, *43*, 1398.
(17) Arenal, T.; Bernabé, M.; Fernández-Alvarez, E. *An. Quim. Ser. C* **1981**, *77C*, 55.

Table I. ^{1}H NMR Spectral Data of (*Z*(or *E*))-4-Phenyl-3-acetamido(or benzamido)-3-carbomethoxy-Δ^1-pyrazolines (3, 4)



3Z, R=CH_3
4Z, R=Ph

4E

	chemical shift, δ									coupling constants,[a] H		
no.	H_o	$H_{m,p}$	PhCO	CH_3CO	H_{N-H}	H_A	H_B	H_X	$COOCH_3$	J_{AB}	J_{AX}	J_{BX}
3Z	6.75–6.90	7.10–7.30		1.45	9.00	5.09	4.96	4.06	3.67	−18.40	3.10	8.10
4Z	6.80–6.95	7.05–7.30	7.35–7.50		9.52	5.15	5.04	4.21	3.69	−19.5	2.71	8.29
4E	7.85–8.00	7.50–7.65	7.05–7.35		9.29	4.73	5.12	3.84	3.26	−17.81	7.30	8.31

[a] Theoretical ^{1}H NMR spectral data were generated by using the Panic Program (Bruker Instrument Corp.) which applies the LAOCOON III algorithm.

preparation of **3Z** to give a quantitative yield (1.14 g) of pure **4Z** as a white solid: mp 98–100 °C; NMR in Table I. Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.87; H, 5.26; N, 13.00. Found: C, 66.92; H, 5.12; N, 12.96.

(*E*)-4-Phenyl-3-benzamido-3-carbomethoxy-Δ^1-pyrazoline (4E). A total of 1 g (3.6 mmol) of **2E** underwent diazomethane cycloaddition under exactly the same conditions used in the preparation of **3Z** to give a quantitative yield (1.14 g) of pure **4E** as a white solid: mp 127–129 °C; NMR in Table I. Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.87; H, 5.26; N, 13.00. Found: C, 67.02; H, 5.09; N, 13.21.

1-Methyl-4-phenyl-5-carbomethoxypyrazole (11) and 1-Methyl-4-phenyl-3-carbomethoxypyrazole (12). A total of 4 mmol of olefin (**1Z**, **2Z**, or **2E**) dissolved in 20 mL of absolute methanol was treated with an excess of ethereal solution of diazomethane at room temperature as necessary for 4 days. The progress of the reaction was followed by noting the disappearance of starting olefin by TLC. The solution was treated with anhydrous $CaCl_2$ to get rid of excess diazomethane, filtered, and evaporated in vacuo. The resultant oil was dried over P_2O_5 and dissolved in a minimum amount of ether. The compounds of the mixture were separated by column chromatography (SiO_2, 70–280 mesh) with ether as an eluting agent to afford analytically pure samples of the following. First about 70% of 1-methyl-4-phenyl-5-carbomethoxypyrazole (**11**): mp 65–66 °C (lit.[10] mp 66 °C); NMR δ 3.70 (s, 3 H), 4.15 (s, 3 H), 7.35–7.45 (m, 5 H), 7.51 (s, 1 H). Secondly about 17% of 1-methyl-4-phenyl-3-carbomethoxypyrazole (**12**): mp 106–108 °C; NMR δ 3.87 (s, 3 H), 3.98 (s, 3 H), 7.40–7.55 (m, 6 H). Finally the corresponding amide (acetamide or benzamide).

When the reaction was allowed to stand at room temperature for only 2 days and treated under exactly the previous conditions, we were able to isolate by column chromatography Δ^2-pyrazolines. **8Z**: mp 141–142 °C; NMR δ 1.70 (s, 3 H), 3.85 (s, 3 H), 4.75 (d, 1 H, J = 1.5 Hz), 6.0 (br s, 1 H), 6.12 (br s, 1 H), 6.90 (d, 1 H, J = 1.5 Hz), 7.15–7.40 (m, 5 H). Anal. Calcd for $C_{13}H_{15}N_3O_3$: C, 59.77; H, 5.74; N, 16.09. Found: C, 59.82; H, 5.87; N, 16.03. **9Z**: mp 76–78 °C; NMR δ 3.80 (s, 3 H), 4.86 (d, 1 H, J = 1.5 Hz), 6.13 (br s, 1 H), 6.74 (br s, 1 H), 6.85 (d, 1 H, J = 1.5 Hz), 7.20–7.50 (m, 10 H). Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.87; H, 5.26; N, 13.00. Found: C, 66.69; H, 5.35; N, 12.87. **9E**: mp 77–79 °C; NMR δ 3.44 (s, 3 H), 4.62 (d, 1 H, J = 1.5 Hz), 5.26 (br s, 1 H), 5.42 (br s, 1 H), 6.93 (d, 1 H, J = 1.5 Hz), 7.20–7.50 (m, 8 H), 7.90–8.10 (m, 2 H). Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.87; H, 5.26; N, 13.00. Found: C, 66.73; H, 5.39; N, 12.88.

Methyl (*Z*)-2-Acetamido-3-methylcinnamate (5Z). A total of 1 g (3.8 mmol) of **3Z** dissolved in 10 mL of 1,2-ethanediol was heated at about 200 °C for 10 min. The solution was cooled and water added until the solution became cloudy. Crystallization at room temperature afforded 720 mg (80%) of pure **5Z**: mp 141–142 °C; NMR δ 1.84 (s, 3 H), 2.28 (s, 3 H), 3.82 (s, 3 H), 6.90 (br s, 1 H), 7.30–7.50 (m, 5 H). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.95; H, 6.43; N, 6.00. Found: C, 67.08; H, 6.25; N, 5.88.

Methyl (*Z*)-2-Benzamido-3-methylcinnamate (6Z). A total of 1 g (3.1 mmol) of **3Z** underwent pyrolysis under the same conditions used in the preparation of **5Z** to give 695 mg (76%) of **6Z**: mp 147–149 °C; NMR δ 2.33 (s, 3 H), 3.82 (s, 3 H), 7.30–7.65 (m, 11 H). Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.22; H, 5.76; N, 4.74. Found: C, 73.01; H, 5.58; N, 4.92.

Methyl (*E*)-2-Phenyl-1-benzamidocyclopropane-1-carboxylate (7E). A total of 1 g (3.1 mmol) of **3E** underwent pyrolysis under exactly the same conditions used in the preparation of **5Z** to give 750 mg (82%) of **7E**: mp 194–195 °C (lit.[13] mp 193–195 °C); NMR δ 1.71 (dd, 1 H, J = −5.3 Hz, J = 10 Hz), 2.33 (dd, 1 H, J = −5.3 Hz, J = 8.5 Hz), 3.04 (dd, 1 H, J = 10 Hz, J = 8.5 Hz), 3.40 (s, 3 H), 6.85 (br s, 1 H), 7.30–7.60 (m, 8 H), 7.90–8.10 (m, 2 H).

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Registry No. **1Z**, 60676-51-9; **2Z**, 21462-02-2; **2E**, 13257-30-2; **3Z**, 96791-17-2; **4Z**, 96791-18-3; **4E**, 96791-19-4; **5Z**, 89141-15-1; **6Z**, 89141-16-2; **7E**, 87378-72-1; **8Z**, 96791-20-7; **9Z**, 96791-21-8; **9E**, 96791-22-9; **10**, 5932-28-5; **11**, 23097-85-0; **12**, 96256-54-1; CH_2N_2, 334-88-3.