F_i consisted of a single pure isomer 1_i.

Equilibrium Mixture of 1. In a 25-mL flask was dissolved 11.6 mg of I_2 in 1 mL of CH_2Cl_2 and brought to 25 mL with *o*-dichlorobenzene.[15] This solution was transferred into an open reacting tube and placed in an oil bath thermostated at 393 K. After several reaction times, every 15–30 min at the beginning and every 40–60 min later on, aliquots of 0.5-mL were removed, quenched to room temperature, and analyzed by HPLC in the conditions of the preparative separation. After 5.5 h the peak areas of all isomers remained constant within experimental error, indicating that equilibrium was reached. After 7.5 h the remaining reaction mixture was quenched. The solvent was removed at 1 mmHg and at room temperature on a rotavapor. The solid residue was dissolved in 0.5 mL of CD_2Cl_2; the methoxy region of the ^1H NMR spectrum of this solution is shown in Figure 1. An analogous experiment starting from pure 1_1 resulted in the same final mixture.

Preparative Separation of 2. The separated[5] sample of 175 mg of 2 was prepurified by gravitational LC on silica (Woelm 63-200) using hexane/benzene (50:50 v/v) as an eluent. In a first HPLC separation with hexane/CH_2Cl_2 (85:15 v/v) as eluent, three fractions of 2 were collected: 64 mg of F_1' ($k' = 1.5$), 52 mg of F_2' ($k' = 1.8$), and about 2 mg of F_3' ($k' = 2.1$). In a second HPLC separation with hexane:$CHCl_3$ (97:3 v/v) fraction F_1' was separated into 8 mg of F_{11}' ($k' = 1.1$) and 42 mg of F_{12}' ($k' = 1.2$); no further separation of F_2' was detected. These four fractions exhibited identical mass spectra: as base peak the parent peak at *m/e* 618 with the expected isotopic distribution and no other peaks with intensities larger than 5%. From the methyl region of their ^1H NMR spectra, it was deduced that F_{11}' consisted of 2_1, F_{12}' of 2_2 and 2_3, F_2' of 2_4–2_6, and F_3' of 2_7.

Equilibrium Mixture of 2. In a 50-mL reaction flask was dissolved 16 mg of 2 (containing all isomers) in 10 mL of kerosene (Fluka purum), redistilled before use [bp 100–108 °C (11 mmHg)]. The flask was equipped with a water condensor, flushed with argon, and heated in a metal bath. The reaction mixture was refluxed during 44 h at 487 K. The kerosene was distilled off in a bulb-to-bulb apparatus [95–100 °C (13 mmHg)]. The solid residue was purified by TLC on silica (Merck Kieselgel 60 F_{254}) with hexane/benzene (50:50 v/v). The methyl region of the ^1H NMR spectrum of the 16 mg of recovered 2 is shown in Figure 2.

Registry No. 1, 86933-45-1; 2, 86933-46-2.

Diazafulvenones. Thermal Isomerizations and Eliminations in Alkoxycarbonyl and Anilinocarbonyl Derivatives of Imidazole

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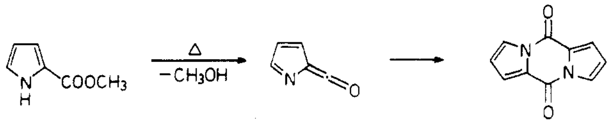
Received June 19, 1985

4-Carbonyl-4*H*-imidazole (**10**) and 2-carbonyl-2*H*-imidazole (**11**) are formed by flash vacuum pyrolysis of methyl 4- and 2-imidazolecarboxylates, respectively. **10** and **11** dimerize to diketopiperazines **14** and **16**, respectively. The same products are also obtained from 4- and 2-(anilinocarbonyl)imidazoles, respectively. Methyl imidazole-1-carboxylate (**4**) on pyrolysis gives a ca. 1:1 mixture of the same ketenes **10** and **11**, which dimerizes to a 1:2:1 ratio of diketopiperazines **14**–**16**. In contrast, ethyl imidazole-1-carboxylate gave CO_2, ethylene, and imidazole as the major products. The pyrolysis reactions were monitored by low-temperature infrared and high-temperature mass spectrometry.

The formation of 2-carbonyl-2*H*-pyrrole (1-azafulven-6-one, **2**) by flash vacuum pyrolysis of pyrrole-2-carboxylic acid or its methyl ester (**1**) was reported recently.[2] The ketene **2** was directly observed by IR[2] and mass spectrometry,[3] trapped with methanol to regenerate the starting material (**1**), and isolated in the form of the dimer **3**.



1 2 3

We now wish to report the formation of diazafulvenones **10** and **11** on pyrolysis of the imidazole derivatives **4**, **8**, **9**, **12**, and **13**, their direct detection by IR and mass spectrometry, and their dimerization to give diketopiperazine derivatives **14**–**16**.

The pyrolysis of methyl imidazole-4-carboxylate (**8**) at 750–820 °C (10^{-4} torr) with isolation of the products on a KBr window at −196 °C resulted in the formation of two new species, absorbing at 2245 and 2150 cm^{-1}. The latter absorption disappeared on warming to −40 °C and is ascribed to 4-carbonyl-4*H*-imidazole (**10**) because in a preparative experiment (see Experimental Section) carried out at the same temperature (750 °C) the dimer **14** was isolated in 20% yield. The strucutre of **14** is based on the IR, ^1H NMR, mass and high-resolution mass spectra, and elemental analysis.

The same IR results were obtained on pyrolysis of the anilide **9** at 800 °C. Here, too, the dimer **14** was isolated in 20% yield after a preparative pyrolysis. Thus, the ketene **10** is formed by elimination of methanol from **8**,

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[1] (a) Université Mons. (b) Universidad Complutense. (c) CSIC. (d) AKZO. (e) Marburg. (f) Permanent address: University of Queensland.

[2] (a) Gross, G.; Wentrup, C. *J. Chem. Soc., Chem. Commun.* **1982**, 360. (b) Wiersum, U. E. *Recl.: J. R. Neth. Chem. Soc.* **1982**, *101*, 365.

[3] Gross, G.; Wentrup, C.; Maquestiau, A.; Flammang, R., unpublished results. Gross, G. Ph.D. Thesis, University of Marburg, 1983.

0022-3263/86/1951-0306$01.50/0

and of aniline from **9**. The additional absorption at 2245 cm^{-1}, observed in both cases, disappeared on warming and is ascribed to a nitrile of unknown structure, presumably formed by opening of the imidazole ring. Ring opening of other nitrogen heterocycles, such as indole and pyrazole, is known to occur.[4]

The pyrolysis of methyl imidazole-2-carboxylate (**12**) at 750–820 °C also resulted in the formation of a ketene absorbing at 2150 cm^{-1}, as well as nitrile absorptions at 2280, 2245, and 2210 cm^{-1}. Again, a similar spectrum was obtained on pyrolysis of the anilide **13**, and preparative pyrolyses of **12** and **13** gave the ketene dimer **16** in 20% and 10% yield, respectively (Scheme I).

We next turned our attention to methyl imidazole-1-carboxylate (**4**). This compound, too, gave rise to a ketene absorption at 2150 cm^{-1}, as well as nitrile absorptions at 2245 and 2210 cm^{-1}, on pyrolysis at 820 °C. A preparative pyrolysis of **4** gave a mixture of the three dimers **14**, **15**, and **16** (20% combined yield) in a 1:2:1 ratio. This implies that **4** decomposes to give the two ketenes **10** and **11** in a 1:1 ratio. Statistical dimerization of the ketenes leads to the observed formation of "pure" and "mixed" dimers. The first step in the pyrolysis of **4** is assumed to be a 1,5-sigmatropic shift, giving a 1:1 mixture of the 2*H*-imidazole derivatives **5** and **6**. The elimination of methanol appears to be a direct process (**5** → **10** and **6** → **11**), taking place faster than further 1,5-sigmatropic shifts that would convert **5** to **8** and **6** to **12**, because no trace of **8** and/or **12** could be detected by ^{1}H NMR spectroscopy of the pyrolysates obtained from **4** at 300–720 °C. These ^{1}H NMR spectra did, however, demonstrate the presence of 1-methylimidazole (**7**), formed by an independent route.

The results described above were corroborated with mass spectrometric monitoring of the pyrolyses. The normal (70-eV electron impact) mass spectra of **4**, **8** and **12** without pyrolysis (150 °C inlet temperature) are given in Table I, as are the results of pyrolysis of **4** at 400–900 °C. It is immediately seen that the three isomers give different spectra, and this is even more obvious from the MIKE (mass analyzed ion kinetic energy) spectra of the molecular ions of **4**, **8**, and **12** (Table II). The MIKE spectrum of **4** is characterized by loss of CO_2 to give the molecular ion of 1-methylimidazole (m/z 82) (Scheme II). The MIKE spectra of **8** and **12** are characterized by losses of $CH_3O\cdot$ and CH_2O, to give m/z 95 and 96, respectively. There is precedent for such fragmentation pathways of esters.[5,6] Most importantly, the insensitivity of the MIKE spectrum of the molecular ion of **4** to a rise in temperature confirms that **4** does not isomerize to **8** and/or **12**.

The pyrolysis mass spectra of **4** (Table I) demonstrate that, at temperatures above 400 °C, two thermal reactions set in: (i) loss of CO_2 (m/z 44) to give 1-methylimidazole (**7**; m/z 82) which was identified by comparison of its collision activation (CA) mass spectrum with that of authentic **7** and (ii) loss of methanol (m/z 32) to give the ketenes **10** and **11** (m/z 94). The latter dimerize, in part, already in the gas phase prior to ionization, as attested by the observation of a weak signal for the dimers at m/z 188. Ketene formation reaches a maximum at a pyrolysis temperature of ca. 800 °C.

Also ethyl imidazole-1-carboxylate (**17**) was examined by pyrolysis–mass spectrometry (Table III). Here, the

Table I. Mass Spectral Data of 4, 8, and 12 at Various Temperatures

compd	T, °C	relative abundance at m/z 188	126	96	95	94	82	81	68	67	66	59	55	54	44	42	41	40	39	38	32	31	29	28	27	26
4	150		100		15		22	29	15	8	4	55	29	27	8	33	22	78	15	7		4	11	22	9	
	400		100		13		33	27	15	8	4	46	29	31	26	35	26	100	21	11		4	16	41	13	11
	600	0.7	100		14	11	40	30	17	18	7	44	27	29	29	32	24	91	28	13	11	16	25	48	16	13
	800	1.5	3		7	65	63	21	12	99	40	6	12	37	100	28	24	36	96	48	41	57	50	78	38	27
	900	0.7			3	43	39	8	8	65	29	3	8	24	100	18	22	24	65	35	33	48	38	60	43	23
8	150		65	11	100	11	5	5	62	36	5	4	5	4	4	7	33	55	15	8	4	6	10	23	7	4
12	150		28	26	41	10	6	15	100	20	6	15	11	15	8	17	35	52	22	11	4	6	21	40	16	7

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[4] Wentrup, C. *Tetrahedron*, **1971**, *27*, 367. Wentrup, C.; Crow, W. D. *Ibid.* 1971, *27*, 361. It is not possible at present to quantify nitrile formation in the present work. The nature of the nitriles is the subject of continuing investigation.

[5] Iwasaki, S. *Helv. Chim. Acta* **1976**, *59*, 2738.

[6] Roberts, D. T.; Little, W. F.; Bursey, M. M. *J. Am. Chem. Soc.* **1967**, *89*, 4917.

Scheme I

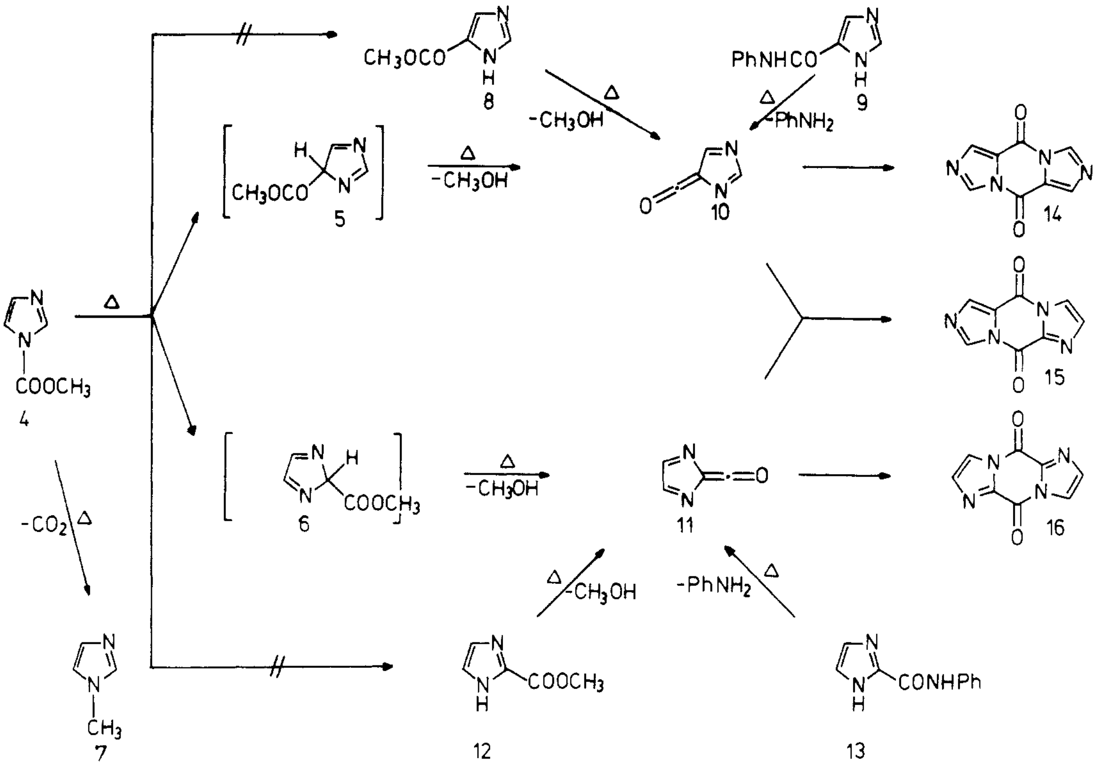


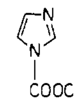
Table II. MIKE Spectral Data of the Molecular Ions (m/z 126) of 4, 8, and 12

compd	T, °C	125	108	88	96	95	82	81	69	68
		relative abundance at m/z								
4	150						100			
	600						100			
8	430	57	17	7	9	100		4		3
12	430				100		2		2	

Table III. Mass Spectral Data of 17 at Various Temperatures

T, °C	188	140	96	95	94	81	69	68	67	44	41	40	39	29	28	27	26
	relative abundance at m/z																
150		26	4	12		21	7	78	10	4	28	34	8	100	14	27	5
500		26	4	12		22	8	99	11	15	33	32	9	100	25	29	10
700	0.5	1	1	1	2	1	7	100	13	72	52	30	13	6	68	35	30

classical β elimination[7] is the predominant reaction, giving ethylene, CO_2, and imidazole, whereas only traces of the ketenes **10** and **11** (m/z 94) and their dimers (m/z 188) are formed at 700 °C. These results are quite similar to



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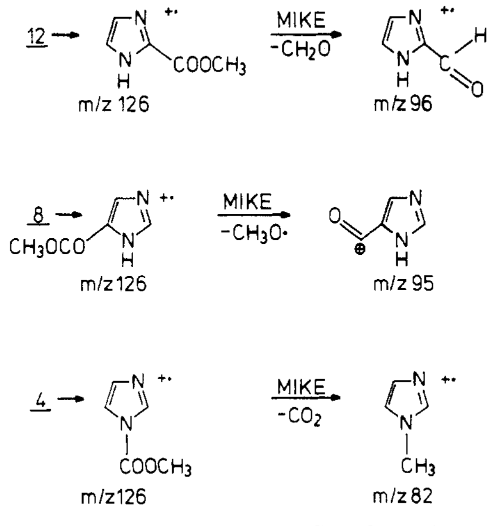
those obtained on pyrolysis of methyl and ethyl benzotriazole-1-carboxylate: whereas the former eliminates CO_2 and gives a mixture of 1- and 2-methylbenzotriazole, the latter undergoes fragmentation to ethylene, CO_2, and the pyrolysis products of benzotriazole.[8]

Experimental Section

General. Pyrolyses for IR observation were carried out at ca. 10^{-4} torr in a reactor employing a 5 × 0.8 cm (i.d.) quartz tube. The products were collected on KBr windows mounted on Air

Scheme II



Products liquid N_2 cryostats at −196 °C, and reactions occuring on warmup were monitored with a Perkin-Elmer 281 IR spectrometer with a working resolution of 2 cm^{-1} in the 2300–2000-cm^{-1} region. A similar reactor was used for mass spectrometric detection, coupled with a modified triple sector AEI MS 902 mass

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[7] See, e.g.: Brown, R. F. C. "Pyrolytic Methods in Organic Chemistry"; Academic Press: New York, 1980; pp 85–89.

[8] Wentrup, C. Ph.D. Thesis, Australian National University, Canberra, 1969.

spectrometer[9] operating at an accelerating voltage of 8 kV. Electron ionization was carried out at 70 eV at a current of 100–500 μA. Other details have been described.[10] The preparative pyrolysis apparatus consisted of an electrically heated tubular oven, employing a 25 × 2 cm quartz tube, pumped at ca. 10^{-3} torr. In this case, the products were isolated in liquid N_2 traps. Melting points are uncorrected.

Diimidazo[3,4-*a*:3′,4′-*d*]pyrazine-5,10-dione (14). 5-(Anilinocarbonyl)imidazole (**9**) (250 mg) was sublimed at 130 °C and pyrolyzed at 800 °C (10^{-3} torr) in the course of 3 h. A yellow solid (20% yield) condensed at the exit of the oven, in the air-cooled part of the cold trap, and was identified as **14** on the basis of the following data: mp 250–253 °C (from dimethoxyethane) (lit.[11] mp 254–255 °C); IR (KBr) 3080 (m), 1730 (s), 1550 (s), 1450 (m), 1360 (s), 1320 (w), 1270 (s), 1210 (s), 1145 (w), 1100 (m), 1090 (m), 1015 (w), 880 (m), 730 (m), 630 (m) cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 8.87 (d, J = 0.7 Hz, 2 H), 8.23 (d, J = 0.7 Hz, 2 H); mass spectrum, m/z (relative intensity) 188 ($M^{+\cdot}$, 100), 160 (15), 95 (40), 94 (41), 93 (57), 68 (60); high-resolution mass spectrum, $M^{+\cdot}$ 188.0336 (calcd for $C_8H_4N_4O_2$ 188.0334), 189.0339 (calcd for $^{12}C_7{}^{13}C_1H_4N_4O_2$ 189.0311). Anal. Calcd for $C_8H_4N_4O_2$: C, 51.07; H, 2.14; N, 29.78. Found: C, 51.03; H, 2.13; N, 29.49.

The same compound was obtained in 20% yield on pyrolysis of methyl imidazole-4-carboxylate (**8**) at 750 °C and identified as above.

Diimidazo[3,2-*a*:3′,2′-*d*]pyrazine-5,10-dione (16). Methyl imidazole-2-carboxylate (**12**) (50 mg) was sublimed at 100 °C and pyrolyzed at 750 °C in the course of 3 h. The yellow solid (20% yield) deposited in the air-cooled part of the cold trap was identified as **16** on the basis of the following data: mp 265–268 °C (from dimethoxyethane); IR (KBr) 3120 (m), 1740 (s), 1520 (m), 1445 (s), 1390 (s), 1330 (w), 1275 (s), 1160 (m), 1060 (m), 1020 (m), 800 (m), 750 (w), 700 (w), 650 (m) cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 8.14 (d, J = 1.5 Hz, 2 H), 7.50 (d, J = 1.5 Hz, 2 H); mass spectrum, m/z (relative intensity) 188 ($M^{+\cdot}$, 8), 94 (55), 68 (100); high-resolution mass spectrum, $M^{+\cdot}$ 188.0332 (calcd for $C_8H_4N_4O_2$ 188.0334).

The same compound was obtained in 10% yield on pyrolysis of 2-(anilinocarbonyl)imidazole (**13**) at 700 °C and identified as above. In addition, *N,N′*-diphenylurea was isolated from the cold trap in 46% yield. No dimer **16** was isolable after pyrolysis of **13** at 800 °C; instead, the majority of the material polymerized at the exit of the pyrolysis tube.

Pyrolysis of Methyl Imidazole-1-carboxylate (4). (a) This was carried out at 750 °C (10^{-3} torr). The yellow substance condensing in the air cooled part of the cold trap was identified as a 1:2:1 mixture (20% yield) of **14**, **15**, and **16** by comparison of the IR and ^1H NMR spectra with those of **14** and **16** described above. Diimidazo[3,2-*a*:3′,4′-*d*]pyrazine-5,10-dione (**15**) had the following ^1H NMR spectrum: ($(CD_3)_2SO$) δ 8.90 (d, J = 0.7 Hz, 1 H), 8.20 (d, J = 0.7 Hz, 1 H), 8.13 (d, J = 1.5 Hz, 1 H), 7.54 (d, J = 1.5 Hz, 1 H). The dimers were virtually insoluble in all ordinary solvents of low and medium polarity and did not elute on thin-layer chromatography except when highly polar solvents (CH_3OH) were used. Therefore, a chromatographic separation of the dimers was not feasible.

(b) **4** was pyrolyzed at various temperatures between 300 and 720 °C. The IR and NMR spectra of the pyrolysate obtained at 630 °C demonstrated the presence of the starting material as well as 1-methylimidazole (**7**). The abovementioned mixture of dimers was obtained in 10% yield at 700 °C. At this temperature **4** was still detectable, but in none of these experiments was **8** or **12** detectable by ^1H NMR.

Registry No. **4**, 61985-23-7; **5**, 99560-58-4; **6**, 99560-59-5; **7**, 616-47-7; **8**, 17325-26-7; **9**, 13189-13-4; **10**, 99560-56-2; **11**, 99560-57-3; **12**, 17334-09-7; **13**, 63678-16-0; 14, 53525-65-8; **15**, 99560-60-8; **16**, 79711-73-2; ethyl imidazole-1-carboxylate, 19213-72-0.

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[9] Maquestiau, A.; Van Haverbeke, Y.; Flammang, R.; Abrassart, M.; Finet, D. *Bull. Soc. Chim. Belg.* **1979**, *87*, 765.

[10] Maquestiau, A.; Flammang, R.; Pauwels, P. *Org. Mass Spectrom.* **1983**, *18*, 547.

[11] Kasina, S.; Nematollahi, J. *Synthesis*, **1975**, *162*.

Nitrone Cycloaddition in the Stereoselective Synthesis of β-Carbolines from *N*-Hydroxytryptophan

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The cycloaddition chemistry of nitrone **6**, obtained by treatment of *N*-hydroxytryptophan ester **4** with methyl orthoformate, has been evaluated. 1,3-Dipolar cycloadditions with alkenes proceed with high or complete regioselectivity to yield 4′- or 5′-substituted isoxazolidines (Scheme II). Complete C(3) → C(1) trans induction as well as high or complete stereoselectivity at the other newly introduced chiral center C(4′) or C(5′) is observed. The regiochemical course of these reactions is as predicted by frontier molecular orbital theory.

Tryptophan derivatives having a functionality in addition to the amino and carboxy group in the α-amino acid fragment have been found as characteristic structural elements of several natural products.[1] Recently, we reported[2] a scheme in which *N*-hydroxytryptophan **4** links L-tryptophan to α- and/or β-functionalized tryptophan derivatives.

Here we wish to report a reaction sequence that features the conversion of *N*-hydroxytryptophan **4** into the nitrone **6** which is used in a regio- and stereoselective cycloaddition to alkenes. The utility of the resulting cycloadducts for

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[‡] Department of Crystallography.

[1] E.g.: (a) Sporidesmin F: Jamieson, W. D.; Rahman, R.; Taylor, A. *J. Chem. Soc. C* **1969**, 1564. (b) TR-2: Cole, R. J.; Kirksey, J. W.; Cox, R. H.; Clardy, J. J. *J. Agric. Food Chem.* **1975**, *23*, 1015. (c) Neoechinulin B: Marchelli, R.; Dossena, A.; Pochini, A.; Dradi, E. *J. Chem. Soc., Perkin Trans. 1*, **1977**, 713. (d) Astechrome: Arai, K.; Sato, S.; Shimizu, S.; Nitta, K.; Yamamoto, Y. *Chem. Pharm. Bull.* **1981**, *29*, 1510.

[2] Ottenheijm, H. C. J.; Plate, R.; Noordik, J. H.; Herscheid, J. D. M. *J. Org. Chem.* **1982**, *47*, 2147.

[3] Sundberg, R. I., Ed. "The Chemistry of Indoles"; Academic Press: New York, 1970; p 236.

[4] In some cases small amounts of **9** were formed as side product.

0022-3263/86/1951-0309$01.50/0