HETEROCYCLES, Vol. 57, No. 2, 2002, pp. 259-267, Received, 12th November, 2001

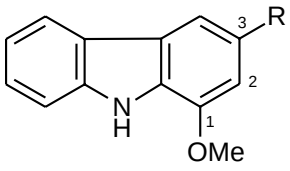
A CONCISE SYNTHESIS OF THE NATURAL CARBAZOLE MUKONINE

Alejandra Zempoalteca and Joaquin Tamariz*

Departamento de Química Orgánica, Escuela Nacional de Ciencias Biológicas, I.P.N. Prol. Carpio y Plan de Ayala, 11340 México, D.F., Mexico. E-mail: jtamariz@woodward.encb.ipn.mx

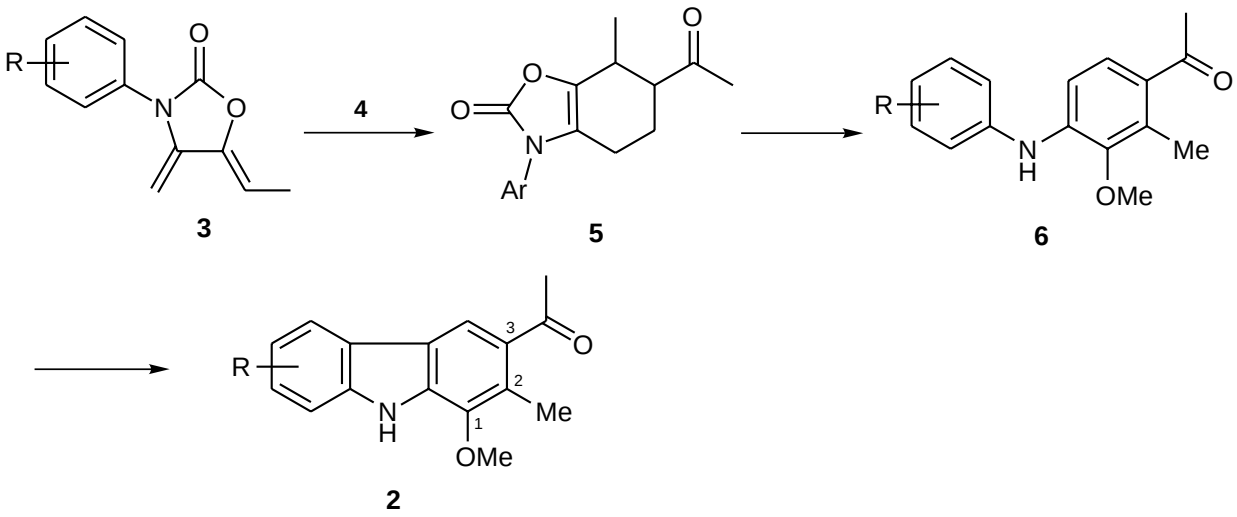
Abstract - A short and total synthesis of the natural carbazole mukonine (**1**) is described, based on a regioselective Diels-Alder reaction of *N*-phenyl 4,5-dimethylidene-2-oxazolidinone (**9**) with methyl propiolate (**10**). Successive transformation of the cycloadduct in one step to the corresponding phenylaryl-amine (**16**), and palladium promoted cyclization of the latter provided carbazole (**1**).

Given the biological importance of natural carbazole alkaloides,[1] an intensive effort has been directed toward their isolation,[2] and total synthesis.[1c,3] Among them, mukonine (**1**) has been isolated from *Murraya koenigii*[4] and *Clausena excavata*.[2c,2f] From a biogenetical viewpoint, carbazole (**1**) probably arises from *in vivo* oxidation of the 3-methyl precursor called murrayafoline A.[1j,4,5] Several synthetic routes have been reported for its preparation.[4,6]



R = CO_2Me, mukonine (**1**)
R = Me, murrayafoline A

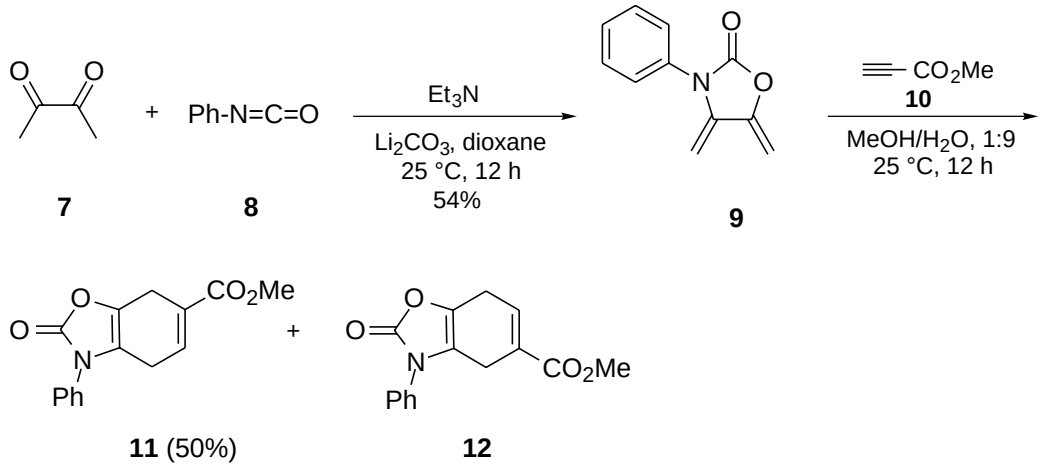
Recently, we described a straightforward synthesis of substituted carbazoles (**2**), taking advantage of the regioselective Diels-Alder addition of a series of novel *N*-substituted 5-ethylidene-4-methylidene-2-oxazolidinones (**3**) toward methyl vinyl ketone (**4**).[7] Dienes (**3**) were readily prepared from an α-diketone and the corresponding isocyanates.[8] Thus, the obtained adducts (**5**) were transformed to diarylamine intermediates (**6**) by a one-pot procedure, and they were converted to the desired carbazoles (**2**) *via* palladium-promoted cyclization (Scheme 1). As an extension of this synthetic strategy, and with the aim of testing it as an efficient methodology for the synthesis of natural carbazoles, hereby we describe a short synthesis of mukonine (**1**).



Scheme 1

RESULTS AND DISCUSSION

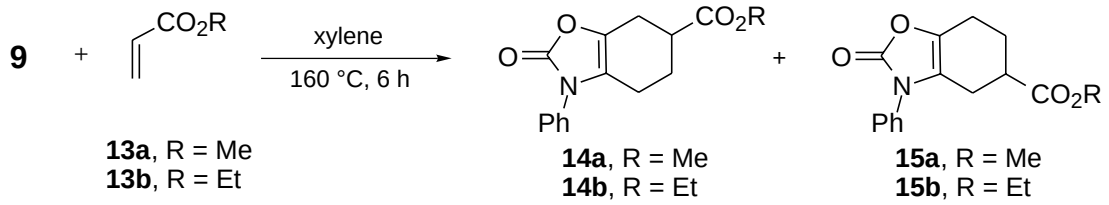
Following the synthetic pathway of Scheme 1, the preparation of **1** should include as a key step the regioselective Diels-Alder addition of diene (**9**) toward methyl propiolate (**10**) as the dienophile (Scheme 2). Diene (**9**) has been previously prepared in 54% yield from the condensation reaction of 2,3-butanedione (**7**) with phenyl isocyanate (**8**).[8a] Even though the cycloaddition between **9** and **10** has proven to be highly regioselective in the presence of Lewis acid catalysts to give preferentially adduct (**11**),[8a] the reaction was not suitable on a larger scale, since the formation of a byproduct was preferred. The latter corresponded to the byproduct isolated during the preliminary investigation on Diels-Alder additions of these dienes, and tentatively attributed to a bicycle structure.[8b]



Scheme 2

Accordingly, we carried out the reaction under a series of new conditions in order to improve the low selectivity provided by the thermal reaction conditions (Table 1, Entry 1). Thus, methyl and ethyl

acrylates (**13a**) and (**13b**), were reacted at the same temperature, giving better proportions of the *para* (PhN/CO_2R) regioisomers (**14a**) and (**14b**), respectively (Table 1, Entries 2 and 3) (Scheme 3). The structure of these adducts was established by NMR spectroscopy, and confirmed by X-Ray crystallographic analysis of adduct (**14b**) (Figure 1).[9]



Scheme 3

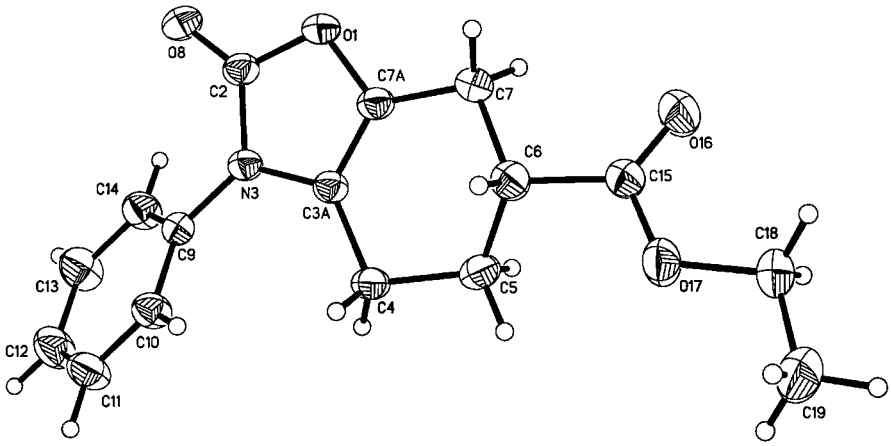


Figure 1. ORTEP Structure of **14b**.

Table 1. Cycloaddition of Diene (9) with Dienophiles (10, 13a, and 13b).[a]

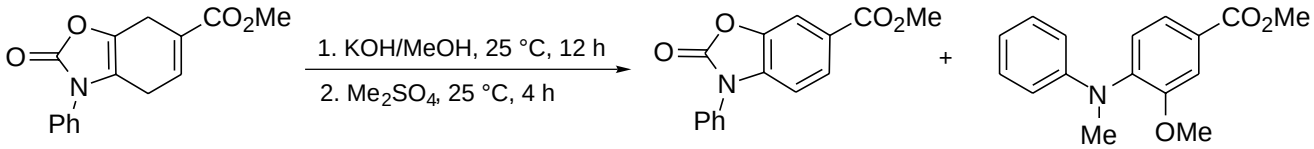
Entry	Dienophile	Solvent	Temp. (°C)	Time (h)	Products (ratio)[b]	Yield (%)[c]
1	**10**	xylene	160	6	**11**/**12** (60:40)	32
2	**13a**	xylene	160	6	**14a**/**15a** (72:28)	63
3	**13b**	xylene	160	6	**14b**/**15b** (69:31)	54
4	**10**	MeOH/H_2O (1:9)	25	12	**11**/**12** (78:22)	50
5	**10**	MeOH/H_2O (4:6)	25	72	**11**/**12** (75:25)	42
6	**13a**	MeOH/H_2O (1:9)	25	12	**14a**/**15a** (81:19)	57

[a]In all entries, 2.67 mmol of diene and 5.35 mmol of dienophile were used. Reactions were carried out under N_2, and in the dark.[b] Determined by ^{1}H NMR spectroscopy from the crude mixture. [c] Of the major isomer after recrystallization

Considering the effect of the polarity of the medium on the enhancement of the reactivity and selectivity in Diels-Alder cycloadditions,[10] the reaction with **10** was carried out in mixtures of MeOH/H_2O as

solvent to furnish the desired adduct (**11**) in moderate yield after separation and recrystallization (Table 1, Entries 4 and 5). It is noteworthy that diene (**9**) was stable under aqueous conditions, and the cycloaddition was sensitive to the catalytic effect of the polarity of the solvent. These conditions were also applied for olefin (**13a**), and the proportion of the major adduct (**14a**) was improved (Table 1, Entry 6).

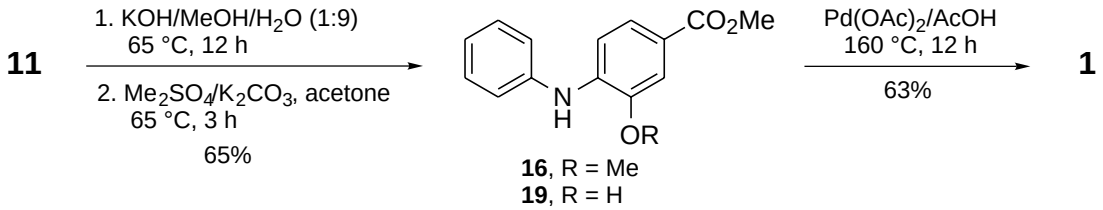
Basic hydrolysis (NaOH/MeOH) of adduct (**11**), followed by methylation with dimethyl sulfate in the same flask, in accord with the previous report,[7] failed to provide the expected phenylarylamine (**16**), and only side products (**17**) and (**18**) were isolated in low yields (Scheme 4). Besides, the ratio of these compounds depended on the temperature and reaction time, along with the presence of additional polar byproducts. In particular, the structure of **17** indicates that the aromatization of the cyclohexadiene ring is a favorable and, probably, faster process than the hydrolysis of the 2-oxazolidinone ring.



11 **17** (20%) **18** (15%)

Scheme 4

Optimized conditions were found when the hydrolysis of **11** was carried out under more drastic reaction conditions (65 °C, 12 h), including up to 30% of water in the solvent, and by isolating the phenol precursor (**19**) before methylation. Moreover, the latter reaction was carried out by treatment with dimethyl sulfate and potassium carbonate in acetone at 65 °C for 3 h,[11] to give the desired product (**16**) in 65% yield (Scheme 5). Unfortunately, these and further investigated conditions were not efficient in transforming isomer (**14a**) into the amine (**16**), since only decomposition of starting material was observed. This was probably due to the unfavorable oxidation state of the cyclohexene ring, since **14a**, in contrast to **11**, possesses only one unsaturation.



Scheme 5

Mukonine (**1**) was then prepared by oxidative coupling cyclization of the phenyl and aryl rings of **16** promoted by stoichiometric $Pd(OAc)_2$ in acetic acid.[7] Although the reported reaction conditions (110 °C, 3 h) were unable to consume the starting material, even at longer reaction time, by increasing both temperature and time, the target product (**1**) was isolated in fair yield (Scheme 5).

In conclusion, we have described a new and concise synthesis of mukonine (**1**), by using the novel approach that involves a regioselective Diels-Alder addition of the exo-heterocyclic diene (**9**), as a building block of the functionalized A-ring of the carbazole. With the preparation of **1**, a formal synthesis of other related carbazoles may be considered, such as koenoline,[1j,5a] murrayanine,[5,6a,12] murrayafoline A,[6a,12] and mukoeic acid.[5b,6a]

EXPERIMENTAL

General. Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. NMR spectra were recorded at 300 MHz for ^{1}H, and at 75.4 MHz for ^{13}C, on a Varian Gemini-300, using TMS as internal standard. MS and HRMS spectra were obtained, in electron impact (EI) (70 eV) and fast atom bombardment (FAB) modes, on a Hewlett-Packard 5971A, and on a Jeol JMS-AX 505 HA spectrometers. X-Ray analyses were collected on a P-4 Siemens diffractometer, using Mo Ka radiation (graphite crystal monochromator, λ = 0.71073 Å). Microanalyses were performed by M-H-W Laboratories (Phoenix, AZ). Analytical TLC was carried out using E. Merck silica gel 60 F_{254}, 0.25 mm coated plates, visualizing by long- and short-wavelength UV lamp. All air moisture sensitive reactions were carried out under nitrogen using oven-dried glassware. Dioxane and xylene were freshly distilled from sodium, and methylene chloride from calcium hydride, prior to use. Li_2CO_3 was dried overnight at 120 °C before using. Triethylamine was freshly distilled from NaOH. All other reagents were used without further purification. Preparation of diene (**9**) was reported elsewhere.[8a]

General Procedures for the Diels-Alder Reaction of Dienophiles Methyl Propiolate (10), Methyl Acrylate (13a), and Ethyl Acrylate (13b), with Diene (9). Method A. A mixture of **9** (0.500, 2.67 mmol), dienophile (5.35 mmol), and hydroquinone (0.003 g) in dry xylene (3 mL) was placed in a threaded ACE glass pressure tube with a sealed Teflon screw cap, under N_2 atmosphere, and in the dark. The mixture was stirred and heated to 160 °C for 6 h. The solvent was removed under vacuum and the residue purified by column chromatography (hexane/EtOAc, 8:2) on silica gel (30 g/g of crude) to give the corresponding adducts. **Method B**. To a solution of diene (**9**) (0.500 g, 2.67 mmol) in a mixture of MeOH/H_2O (1:9, 20 mL) the olefin (5.35 mmol) was added at rt, under N_2 atmosphere, and in the dark. The mixture was stirred at the same temperature for 12 h, and the solvent was removed under vacuum. The crude was extracted with CH_2Cl_2 (3 x 20 mL), and the combined organic phase was dried (Na_2SO_4), and the solvent was removed under vacuum. The crude was purified by column chromatography (hexane/EtOAc, 8:2) on silica gel (30 g/g of crude) to give the corresponding adducts.

6-Methoxycarbonyl-3-phenyl-2,3,4,7-tetrahydrobenzoxazol-2-one (11). 5-Methoxycarbonyl-3-phenyl-2,3,4,7-tetrahydrobenzoxazol-2-one (12). Method A. With 0.45 g of methyl propiolate (**10**), gave a mixture of **11**/**12** (60:40) as a pale yellow powder, which was recrystallized (hexane/CH_2Cl_2, 8:2) to yield 0.235 g (32%) of **11** as a white powder. **Method B**. With 0.45 g of **10**, gave a mixture of **11**/**12**

(78:22) as a pale yellow powder, which was recrystallized (hexane/CH_2Cl_2, 8:2) to yield 0.36 g (50%) of **11** as a white powder: mp 175-176 °C [lit.,[8a] 175-176 °C].

6-Methoxycarbonyl-3-phenyl-2,3,4,5,6,7-hexahydrobenzoxazol-2-one (14a). 5-Methoxycarbonyl-3-phenyl-2,3,4,5,6,7-hexahydrobenzoxazol-2-one (15a). Method A. With 0.46 g of methyl acrylate (**13a**), gave a mixture of **14a**/**15a** (72:28), which was purified by column chromatography to yield 0.46 g (63%) of **14a** as a white powder. **Method B**. With 0.46 g of **13a**, gave a mixture of **14a**/**15a** (81:19), which was purified by column chromatography to yield 0.42 g (57%) of **14a** as a white powder: mp 111-112 °C (hexane/CH_2Cl_2, 8:2). R_f 0.53 (hexane/EtOAc, 1:1). IR (KBr) 1757, 1730, 1598, 1500, 1407, 1331, 1171 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85-1.95 (m, 1H, H-5), 2.14-2.24 (m, 1H, H-5), 2.32-2.50 (m, 2H, H-4), 2.74-2.82 (m, 2H, H-7), 2.82-2.95 (m, 1H, H-6), 3.74 (s, 3H, CO_2CH_3), 7.28-7.38 (m, 3H, PhH), 7.40-7.49 (m, 2H, PhH); signals attributed to minor isomer (**15a**): 3.70 (s, CO_2CH_3); ^{13}C NMR ($CDCl_3$) δ 19.6 (C-4), 23.6 (C-7), 24.7 (C-5), 38.9 (C-6), 52.1 (CO_2CH_3), 120.4 (C-3a), 125.0 (C-11), 127.6 (C-13), 129.3 (C-12), 133.6 (C-7a), 133.9 (C-10), 154.3 (C-2), 173.9 (CO_2CH_3); MS (70 eV) 273 (M^+, 98), 258 (1), 242 (3), 228 (4), 213 (60), 187 (25), 171 (34), 158 (100), 143 (61), 130 (66), 117 (42), 77 (74). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.95; H, 5.49; N, 5.13. Found: C, 66.05; H, 5.56; N, 5.27.

6-Ethoxycarbonyl-3-phenyl-2,3,4,5,6,7-hexahydrobenzoxazol-2-one (14b). **5-Ethoxycarbonyl-3-phenyl-2,3,4,5,6,7-hexahydrobenzoxazol-2-one (15b)**. **Method A**. With 0.535 g of ethyl acrylate (**13b**), gave a mixture of **14b**/**15b** (69:31), which was purified by column chromatography to yield 0.415 g (54%) of **14b** as a white powder: mp 103-104 °C (hexane/CH_2Cl_2, 7:3). R_f 0.70 (hexane/EtOAc, 1:1). IR (KBr) 1757, 1730, 1709, 1597, 1502, 1397, 1326, 1187, 1162, 1022 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (t, J = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.86-2.00 (m, 1H, H-5), 2.14-2.24 (m, 1H, H-5), 2.32-2.45 (m, 2H, H-4), 2.73-2.81 (m, 2H, H-7), 2.81-2.92 (m, 1H, H-6), 4.20 (q, J = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 7.27-7.41 (m, 3H, PhH), 7.42-7.54 (m, 2H, PhH); signals attributed to minor isomer (**15b**): 1.29 (t, J = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$) δ 14.2 ($CO_2CH_2CH_3$), 19.7 (C-4), 23.6 (C-7), 24.7 (C-5), 39.0 (C-6), 61.0 ($CO_2CH_2CH_3$), 120.4 (C-3a), 125.0 (C-12), 127.6 (C-14), 129.4 (C-13), 133.7 (C-7a), 133.9 (C-11), 154.4 (C-2), 173.5 ($CO_2CH_2CH_3$); MS (70 eV) 287 (M^+, 100), 272 (73), 256 (12), 241 (63), 198 (13), 170 (16), 154 (13), 115 (15), 77 (14). Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.87. Found: C, 66.79; H, 5.79; N, 4.89.

6-Methoxycarbonyl-3-phenyl-2,3-dihydrobenzoxazol-2-one (17). **Methyl 3-Methoxy-4-(*N*-methyl-*N*-phenylamino)benzoate (18)**. A mixture of compound (**11**) (0.50 g, 1.84 mmol) in methanol (95%) (10 mL) and NaOH (0.29 g, 7.3 mmol) was stirred at rt for 12 h. The solution was concentrated under vacuum, water (2 mL) added, cooled to 0 °C, and methyl sulfate (1.16 g, 9.19 mmol) was added dropwise. The mixture was stirred at 5 °C for 4 h, and then at rt for 4 h. The mixture was extracted with CH_2Cl_2 (2 x 20 mL), washed with a saturated solution of NH_4Cl (2 x 20 mL) and dried (Na_2SO_4). The solvent was removed under vacuum, and the crude purified by column chromatography on silica gel (hexane/EtOAc, 9:1) to give 0.1 g (20%) of **17**, and 0.09 g (15%) of **18** as white powders. Data of **17**: mp 128-129 °C

(hexane/EtOAc/CH_2Cl_2, 8:1:1). R_f 0.60 (hexane/EtOAc, 1:1). IR (KBr) 1722, 1607, 1482, 1242 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.95 (s, 3H, CO_2CH_3), 7.11 (d, J = 8.8 Hz, 1H, H-4), 7.45-7.63 (m, 5H, PhH), 7.93-7.98 (m, 2H, H-5, H-7); ^{13}C NMR ($CDCl_3$) δ 52.4 (CO_2CH_3), 108.7 (C-4), 111.4 (C-7), 125.1 (C-11), 125.4 (C-6), 126.5 (C-5), 128.8 (C-13), 130.0 (C-12), 132.9 (C-3a or C-10), 135.0 (C-10 or C-3a), 142.2 (C-7a), 153.0 (C-2), 166.1 (CO_2CH_3); MS (70 eV) 269 (M^+, 99), 238 (100), 194 (28), 166 (24), 154 (39), 127 (8), 77 (34). HRMS (FAB$^+$, *m*NBA) Calcd for $C_{15}H_{11}NO_4$: 269.0689. Found: 269.0688. Data of **18**: mp 194-195 °C (hexane/CH_2Cl_2, 7:3). R_f 0.67 (hexane/EtOAc, 1:1). IR (KBr) 1713. 1597, 1500, 1438, 1337, 1270, 1233, 1122, 1024 cm^{-1}. ^1H NMR ($CDCl_3$) δ 3.23 (s, 3H, NCH_3), 3.83 (s, 3H, CO_2CH_3 or OCH_3), 3.86 (s, 3H, OMe or CO_2CH_3), 6.63 (d, J = 7.8 Hz, 2H, H-8), 6.75 (t, J = 7.3 Hz, 1H, H-10), 7.00 (d, J = 8.4 Hz, 1H, H-5), 7.15-7.20 (m, 2H, H-9), 7.90 (d, J = 2.4 Hz, 1H, H-2), 7.95 (dd, J = 8.4, 2.4 Hz, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ 39.1 (NCH_3), 51.9 (CO_2CH_3), 55.8 (OCH_3), 111.7 (C-2), 113.6 (C-8), 117.6 (C-5), 123.2 (C-1), 128.8 (C-9), 129.0, 130.5, 136.5, 149.0, 159.8, 166.5 (CO_2CH_3); MS (70 eV) 271 (M^+, 100), 256 (19), 240 (13), 208 (14), 196 (38), 181 (27), 168 (29), 104 (16), 91 (37). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.57; H, 6.46; N, 4.97.

Methyl 3-Methoxy-4-phenylaminobenzoate (16). A mixture of compound (**11**) (0.50 g, 1.85 mmol) in a mixture of methanol/H_2O (5:2) (10 mL) and KOH (0.31 g, 5.55 mmol) was stirred and heated to 65 °C for 12 h. The solution was concentrated under vacuum, CH_2Cl_2 (20 mL) was added, and washed with a 10% aqueous solution of HCl until pH = 5. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL), and the combined organic layers were dried (Na_2SO_4). The solvent was removed under vacuum, and the brown solid crude was dissolved in acetone (5 mL). To this solution, dimethyl sulfate (0.35 g, 2.77 mmol) and potassium carbonate (0.38 g, 2.77 mmol) were added at rt, and the mixture was heated to 65 °C for 3 h. The mixture was filtered, the solvent was removed under vacuum, and the crude purified by column chromatography on silica gel treated with 10% of triethylamine in hexane (hexane/EtOAc, 8:2) to give 0.31 g (65%) of **16** as a white powder: mp 179-180 °C (hexane/CH_2Cl_2, 6:4). R_f 0.63 (hexane/EtOAc, 1:1). IR (KBr) 3344, 1696, 1592, 1523, 1297, 1231 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.88 (s, 3H, OCH_3), 3.95 (s, 3H, CO_2CH_3), 6.55 (br s, 1H, NH), 7.02-7.09 (m, 1H, H-10), 7.19-7.40 (m, 2H, H-5, H-8), 7.34 (dd, J = 8.2, 7.6 Hz, 2H, H-9), 7.51 (d, J = 1.8 Hz, 1H, H-2), 7.59 (dd, J = 8.2, 1.8 Hz, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ 51.8 (CO_2CH_3), 56.7 (OCH_3), 110.7 (C-5), 110.8 (C-2), 119.9 (C-1), 120.7 (C-8), 122.9 (C-10), 123.8 (C-6), 129.4 (C-9), 138.1 (C-4 or C-7), 140.6 (C-7 or C-4), 146.4 (C-3), 167.1 (CO_2CH_3); MS (70 eV) 257 (M^+, 100), 242 (5), 226 (25), 208 (7), 181 (17), 154 (30), 128 (9), 107 (14), 91 (26), 77 (41). HRMS (FAB$^+$, *m*NBA) Calcd for $C_{15}H_{15}NO_3$: 257.1052. Found: 257.1052.

Mukonine (1).[6a] A mixture of **16** (0.30 g, 1.17 mmol) and palladium acetate (0.39 g, 1.75 mmol) in glacial acetic acid (5 mL) was placed in a threaded ACE glass pressure tube with a sealed Teflon screw cap, under N_2 atmosphere. The mixture was stirred and heated to 160 °C for 12 h. The mixture was filtered, diluted with water (20 mL), neutralized with an aqueous saturated solution of $NaHCO_3$, and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phase was dried (Na_2SO_4), and the solvent was removed under vacuum. The crude was purified by column chromatography on silica gel treated with

10% of triethylamine in hexane (100 g, hexane/EtOAc, 8:2) to give 0.19 g (63%) of **1** as a white solid: mp 197-198 °C [lit.,[4] 195 °C]. R_f 0.78 (hexane/EtOAc, 1:1). IR (KBr) 3339, 1676, 1610, 1591, 1496, 1448, 1356, 1265, 1032, 747 cm^{-1}. ^1H NMR (acetone-d_6) δ 3.92 (s, 3H, CO_2CH_3), 4.07 (s, 3H, OCH_3), 7.26 (dd, J = 7.6, 7.0 Hz, 1H, H-6), 7.46 (dd, J = 8.2, 7.0 Hz, 1H, H-7), 7.59 (s, 1H, H-2), 7.65 (d, J = 8.2 Hz, 1H, H-8), 8.21 (d, J = 7.6 Hz, 1H, H-5), 8.48 (s, 1H, H-4), 10.84 (br s, 1H, NH); ^{13}C NMR (acetone-d_6) δ 52.2 (CO_2CH_3), 56.3 (OCH_3), 107.3 (C-2), 112.8 (C-8), 116.8 (C-4), 120.9 (C-6), 121.5 (C-5), 122.6 (C-3), 124.5 (Cq), 124.55 (Cq), 127.3 (C-7), 134.2 (Cq), 141.5 (Cq), 146.5 (C-1), 168.2 (CO_2CH_3); MS (70 eV) 255 (M^+, 100), 240 (48), 224 (46), 212 (13), 196 (19), 181 (31), 153 (43), 139 (10), 126 (33), 87 (7), 63 (14).

X-Ray Structure Determination of 14b. Crystal data: $C_{16}H_{17}NO_4$; M = 287.31; triclinic; space group P-1; a = 7.2018 (9), b = 8.487 (2), c = 12.202 (2) Å; α = 105.56 (2)°, β = 90.064 (12)°, γ = 91.001 (14)°; V = 718.3 (2) $Å^3$, Z = 2; D = 1.328 mg/m^3; absorption coefficient: 0.096 mm^{-1}; No. of reflections collected: 3865; No. of independent reflections: 3107; No. of observed reflections: 3089; R = 0.0545, R_w = 0.0839; goodness of fit on F^2 = 1.033.[9]

ACKNOWLEDGEMENTS

We are grateful to Dr. Hugo A. Jiménez-Vázquez for reviewing the manuscript. We thank Fernando Labarrios for his help in spectrometric measurements. J.T. acknowledges CGPI/IPN (Grants 200410 and 32.14) and CONACYT (Grant 32273-E) for financial support. A.Z. thanks CONACYT for a graduate scholarship awarded, and the Ludwig K. Hellweg Foundation for a scholarship complement.

REFERENCES AND NOTES

1. a) A. Chakraborty, B. K. Chowdhury, and P. Bhattacharyya, *Phytochemistry*, 1995, **40**, 295. b) M. Kaneda, T. Naid, T. Kitahara, S. Nakamura, T. Hirata, and T. Suga, *J. Antibiot.*, 1988, **41**, 602. c) A. Chakraborty, C. Saha, G. Podder, B. K. Chowdhury, and P. Bhattacharyya, *Phytochemistry*, 1995, **38**, 787. d) G. Bringmann, A. Ledermann, and G. François, *Heterocycles*, 1995, **40**, 293. e) M. R. TePaske, J. B. Gloer, D. T. Wicklow, and P. F. Dowd, *J. Org. Chem.*, 1989, **54**, 4743. f) K. Sakano, K. Ishimaru, and S. Nakamura, *J. Antibiot.*, 1980, **33**, 683. g) K. Sakano and S. Nakamura, *J. Antibiot.*, 1980, **33**, 961. h) C.-J. Mo, K. Shin-ya, K. Furihata, A. Shimazu, Y. Hayakawa, and H. Seto, *J. Antibiot.*, 1990, **43**, 1337. i) D. J. Hook, J. J. Yacobucci, S. O'Connor, M. Lee, E. Kerns, B. Krishnan, J. Matson, and G. Hesler, *J. Antibiot.*, 1990, **43**, 1347. j) M. Fiebig, J. M. Pezzuto, D. D. Soejarto, and A. D. Kinghorn, *Phytochemistry*, 1985, **24**, 3041.
2. For recently isolated carbazoles: a) M. Tanaka, K. Shin-ya, K. Furihata, and H. Seto, *J. Antibiot.*, 1995, **48**, 326. b) D. J. Faulkner, *Nat. Prod. Rep.*, 1997, **14**, 259. c) T.-S. Wu, S.-C. Huang, P.-L. Wu, and C.-M. Teng, *Phytochemistry*, 1996, **43**, 133; d) M. Toyota and M. Ihara, *Nat. Prod. Rep.*, 1998,

15, 327. e) C. Saha and B. K. Chowdhury, *Phytochemistry*, 1998, **48**, 363. f) T.-S. Wu, S.-C. Huang, P.-L. Wu, and C.-S. Kuoh, *Phytochemistry*, 1999, **52**, 523. g) S. Hibino and T. Choshi, *Nat. Prod. Rep.*, 2001, **18**, 66.

3. T. Choshi, T. Sada, H. Fujimoto, C. Nagayama, E. Sugino, and S. Hibino, *J. Org. Chem.*, 1997, **62**, 2535, and references cited therein; T. Choshi, T. Sada, H. Fujimoto, C. Nagayama, E. Sugino, and S. Hibino, *Tetrahedron Lett.*, 1996, **37**, 2593; H.-J. Knölker and G. Schlechtingen, *J. Chem. Soc., Perkin Trans. 1*, 1997, 349, and references cited therein; T. Choshi, H. Fujimoto, E. Sugino, and S. Hibino, *Heterocycles*, 1996, **43**, 1847; Z, Bouaziz, P. Nebois, A. Poumarou, and H. Fillion *Heterocycles*, 2000, **52**, 977; Y. Nonaka, T. Kawasaki, and M. Sakamoto *Heterocycles*, 2000, **53**, 1681.
4. D. P. Chakraborty, P. Bhattacharyya, S. Roy, S. P. Bhattacharyya, and A. K. Biswas, *Phytochemistry*, 1978, **17**, 834.
5. a) B. K. Choudhury and D. P. Chakraborty, *Phytochemistry*, 1971, **10**, 1967. b) B. K. Chowdhury and D. P. Chakraborty, *Chem. Ind.*, 1969, 549.
6. a) G. Bringmann, S. Tasler, H. Endress, K. Peters, and E.-M. Peters, *Synthesis*, 1998, 1501. b) H.-J. Knölker and M. Bauermeister, *Tetrahedron*, 1993, **49**, 11221, and references cited therein. c) E. Brenna, C. Fuganti, and S. Serra, *Tetrahedron*, 1998, **54**, 1585.
7. A. B. Mandal, F. Delgado, and J. Tamariz, *Synlett*, 1998, 87.
8. (a) A. B. Mandal, A. Gómez, G. Trujillo, F. Méndez, H. A. Jiménez, M. J. Rosales, R. Martínez, F. Delgado, and J. Tamariz, *J. Org. Chem.*, 1997, **62**, 4105. (b) R. Hernández, J. M. Sánchez, A. Gómez, G. Trujillo, R. Aboytes, G. Zepeda, R. W. Bates, and J. Tamariz, *Heterocycles*, 1993, **36**, 1951.
9. The authors have deposited the atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.
10. (a) R. Breslow and U. Maitra, *Tetrahedron Lett.*, 1984, **25**, 1239. (b) P. A. Grieco, *Aldrichimica Acta*, 1991, **24**, 59. (c) W. Blokzijl, M. J. Blandamer, and J. B. F. N. Engberts, *J. Am. Chem. Soc.*, 1991, **113**, 4241.
11. Y. Tagawa, H. Yamashita, M. Nomura, and Y. Goto, *Heterocycles*, 1998, **48**, 2379.
12. D. P. Chakraborty, B. K. Barman, and P. K. Bose, *Tetrahedron*, 1965, **21**, 681; D. P. Chakraborty and B. K. Chowdhury, *J. Org. Chem.*, 1968, **33**, 1265.