Journal of Natural Products
Vol. 53, No. 3, pp. 623-629, May-Jun 1990

NEW NATURAL COLCHICINOIDS: INDICATIONS OF TWO POSSIBLE CATABOLIC ROUTES FOR THE COLCHICINE ALKALOIDS

TALEB H. AL-TEL, MUSA H. ABU ZARGA,[1,*] SALIM S. SABRI,[1,*] ALAN J. FREYER, and MAURICE SHAMMA*

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

ABSTRACT.—*Colchicum ritchii* of Jordanian origin has yielded the three non-nitrogenous colchicinoids colchicone [**1**], 3-demethylcolchicone [**2**], and cornigerone [**3**], as well as the amidic (−)-colchibiphenyline, which in $CDCl_3$ solution exists as a mixture of isomers **4a** and **4b**. Ketones **1–3** may exemplify one catabolic route for the colchicine alkaloids, while (−)-colchibiphenyline [**4a**,**4b**], and the accompanying and previously known (−)-androbiphenyline [**5a**,**5b**] may exemplify another.

Five *Colchicum* species (Liliaceae) are native to Jordan. These are *Colchicum crocifolium* Boiss., *Colchicum decaisnei* Boiss., *Colchicum triphyllum* G. Kuntze, *Colchicum steveni* Kunth, and *Colchicum ritchii* R. Br. (1). The last of these, namely *C. ritchii*, has been the subject of an investigation that has revealed the presence of a number of diphenolic phenethyltetrahydroisoquinoline-, androcymbine-, and colchicine-type alkaloids (2).

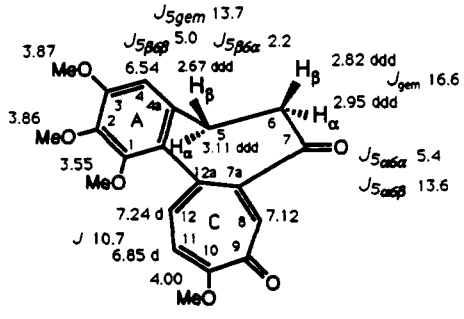
The present study was focused on the acid-insoluble components of *C. ritchii*. Extensive chromatography of the acid-insoluble extracts furnished three closely related ketonic and non-nitrogenous compounds, which also incorporate a tropolone system.

The first of these, colchicone [**1**], $C_{20}H_{20}O_6$, had a mass spectrum showing a molecular ion peak *m/z* 356 (54%) and base peak *m/z* 328 $[M-CO]^+$. The presence of two carbonyls was indicated by the ir spectrum, which included a strong band at 1610 cm^{-1} for the tropolonic carbonyl and another at 1710 cm^{-1} for the ketonic group of ring B.

The existence of these two carbonyls was confirmed by the ^{13}C-nmr spectrum, which displayed downfield singlets for the carbonyl carbons at δ 179.37 (ring C) and at 205.66 (ring B).

Extensive ^1H-nmr spin decoupling and nOe experiments resulted in the detailed ^1H-nmr values summarized around structure **1**. Four methoxyl singlets were in evidence with the most upfield, at δ 3.55, assigned to the highly hindered 1-OMe, while the most downfield, at δ 4.00, represented the tropolonic 10-OMe.

It was even possible to differentiate between the two remaining methoxyl singlets at δ 3.86 and 3.87, with the former due to 2-OMe and the latter to 3-OMe. Four aromatic proton signals, two appearing as two singlets and the two others as two dou-



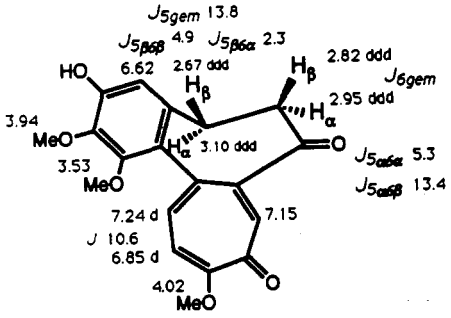
1

[1]Permanent address: Department of Chemistry, The University of Jordan, Amman, Jordan.

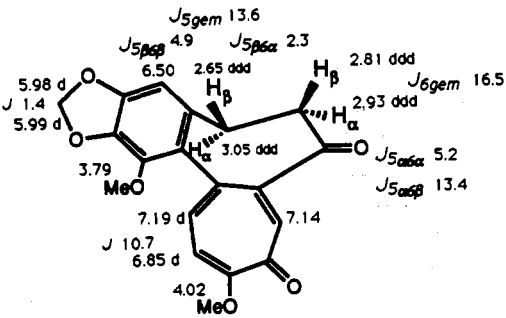
blets with J_{vic} = 10.7 Hz, could readily be assigned to H-4 and H-8, and to H-11 and H-12.

The most interesting part of the ^{1}H-nmr spectrum concerned the aliphatic region, whose features could be separated and analyzed at 500 MHz. Each of the four aliphatic protons appeared as doublets of doublets of doublets, with chemical shifts and coupling constants which could best be explained by a boat-like conformation for ring B as indicated in structure **1**.

The pseudo-equatorial H-5β (δ 2.67) showed reciprocating nOe's with the aromatic H-4 (δ 6.54). Significantly, the coupling constant between the pseudo-axial H-5α (δ 3.11) and H-6β (2.82) is large, 13.6 Hz, denoting a dihedral angle of about 170°. On the other hand, the coupling constant between H-5β and H-6β is rather small, 5.0 Hz, reflecting a dihedral angle of approximately 38°. It is interesting to note that the pseudo-equatorial H-6α (δ 2.95) showed an nOe with the aromatic H-8.



2



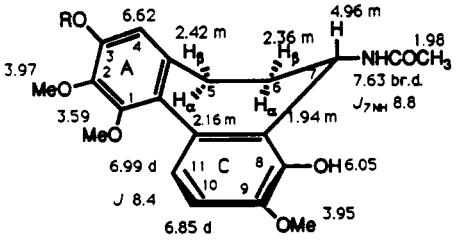
3

The boat-like conformation of ring B of colchicone [**1**] is also in accord with the X-ray data recorded in the literature for the structurally related ketone 7-oxodeacetamidocolchiceine, which had been obtained by laboratory chemical manipulation of (−)-colchicine (3). It should also be mentioned that compound **1** itself had been obtained in vitro as a degradative product of (−)-colchicine (3,4).

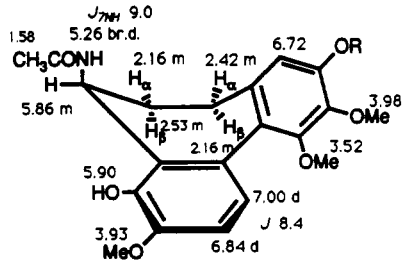
Reductive amination of colchicone [**1**] using methylamine and $NaBH_4$ provided (±)-demecolcine [**8**], $C_{21}H_{25}NO_5$, which is known as a natural product in its levorotatory form (2,5). In fact, (−)-demecolcine is also present as an alkaloid in *C. ritchii* (2).

Alternatively, $NaBH_4$ reduction of colchicone [**1**] led to the secondary alcohol colchicol [**6**], $C_{20}H_{22}O_6$, which was acetylated using Ac_2O in pyridine to supply the corresponding acetate **7**, $C_{22}H_{24}O_7$. It is worth pointing out that H-7 in acetate **7** appears in the ^{1}H-nmr spectrum at δ 5.32, 0.84 ppm further downfield than the corresponding signal for colchicol [**6**] which is found at δ 4.48.

An attempt was also made to introduce an extra double bond in ring B of colchicone [**1**] between carbons 5 and 6. If successful, we would then have had on hand a molecule that would have incorporated a benzene ring fused to a tropone ring, which in turn would have been fused to a tropolone. An effort was made, therefore, to brominate colchicone [**1**] at the benzylic C-5 site using *N*-bromosuccinimide and light, a reaction which would have been followed by elimination of HBr. However, the product turned out to be 4-bromocolchicone [**12**], $C_{20}H_{19}O_6Br$. Clearly, electrophilic aromatic substitution had prevailed over radical benzylic bromination. The mass spectrum of the product exhibited molecular ion *m/z* 434 (87%) and base peak *m/z* 406 $[M-CO]^+$, while the ir spectrum still retained the characteristic carbonyl absorptions at 1710 and 1615 cm^{-1}. The most salient feature of the nmr spectrum was the absence of an H-4 signal that usually appears near δ 6.6.



4a R=H (^{1}H nmr)
5a R=Me



4b R=H (^{1}H nmr)
5b R=Me

The mass spectrum of the second ketone, 3-demethylcolchicone [**2**], $C_{19}H_{18}O_6$, displayed molecular ion peak *m/z* 342 (75%) and base peak *m/z* 314 $[M-CO]^+$. Both peaks are 14 daltons less than the analogous peak for colchicone [**1**], indicating replacement of a methoxyl by hydroxyl. In line with this conclusion, the ir spectrum exhibited a broad phenolic hydroxyl band around 3300 cm^{-1} in addition to the two strong carbonyl absorptions at 1610 and 1710 cm^{-1}. The carbonyl carbons were also detectable in the ^{13}C-nmr spectrum, which exhibited two downfield singlets at δ 205.68 (ring B) and 179.40 (ring C).

The ^{1}H-nmr spectrum of 3-demethylcolchicone [**2**] at 360 MHz has been outlined around structure **2**. Indeed, only two ring-A methoxyls were present, at δ 3.53 and 3.94, with the former value assignable to 1-OMe. Irradiation of the H-4 signal (δ 6.62) produced no enhancement of any of the methoxyls. However, irradiation of 2-OMe (δ 3.94) and subsequently of 1-OMe (δ 3.53) effected strong mutual nOe's, thus fixing the phenolic function at C-3. The remaining features of the spectrum were similar to those of colchicone [**1**] and clearly indicated that in 3-demethylcolchicone [**2**] ring B was again in a boat-like conformation.

Acetylation of **2** gave rise to 3-demethylcolchicone acetate [**9**], $C_{21}H_{20}O_7$, whose ^{1}H-nmr spectrum included an acetyl methyl singlet at δ 2.36 and an H-4 singlet at δ 6.74. The ^{1}H-nmr data for 3-demethylcolchicone acetate has been summarized around structure **9**.

The third ketone, cornigerone [**3**], $C_{19}H_{16}O_6$, was also the least prevalent in the plant. The mass spectrum displayed molecular ion *m/z* 340 (79%) and base peak 312 $[M-CO]^+$, i.e., two daltons less than the corresponding peaks in 3-demethylcolchicone [**2**], implying that the 2-methoxy-3-hydroxy substitution of **3** had been replaced by a methylenedioxy. Along these lines, the ir spectrum was devoid of the broad phenolic hydroxyl band around 3300 cm^{-1} that characterized the spectrum of **2** but still retained the two strong carbonyl absorptions at 1607 and 1705 cm^{-1}.

Much more instructive was the 360 MHz ^{1}H-nmr spectrum, whose numerical values circle structure **3**. The most prominent novel feature was the two close doublets at δ 5.98 and 5.99 (J = 1.4 Hz) representing the 2,3-methylenedioxy substituent. In accordance with the decrease in steric hindrance around 1-OMe, the signal for that substituent had shifted downfield to δ 3.79, reflecting a greater degree of resonance with the aromatic ring A. The rest of the spectrum paralleled those for analogues **1** and **2**.

Besides the above three ketones, two amidic, non-ketonic alkaloids were also obtained. The first proved to be the known monophenolic (−)-androbiphenyline [**5a**,**5b**], which had recently been found for the first time in *Androcymbium palaestinum* (Boiss.) Bak. (Liliaceae), also of Jordanian origin (6).

(−)-Androbiphenyline had been determined to exist in $CDCl_3$ solution as a mix-

ture of conformers **5a** and **5b** in almost equal amounts. Upon heating, conformer **5b** became dominant. Additionally, upon *O*-acetylation, only conformer **5b** was in evidence.

Presently, because we were able to isolate (−)-androbiphenyline [**5a**,**5b**] from *C. ritchii* in a relatively large amount, we were able to crystallize it for the first time as white needles.

Our second amidic alkaloid was the new diphenolic (−)-colchibiphenyline [**4a**,**4b**], $C_{20}H_{23}NO_6$, which is structurally close to (−)-androbiphenyline [**5a**,**5b**]. The mass spectrum of (−)-colchibiphenyline featured molecular ion *m/z* 373 (32%) and base peak *m/z* 314 due to loss of the acetamide residue from the molecular ion.

The ir spectrum displayed an amidic carbonyl band at 1660 cm^{-1} overlapping with an NH band. It was not surprising to find that, just like (−)-androbiphenyline, (−)-colchibiphenyline existed as a mixture of isomers **4a** and **4b** in almost equal amounts in $CDCl_3$ solution.

All of the signals in the 500 MHz nmr spectrum had their close twins. However, a total of six aromatic methoxyl singlets were present for the two conformers, while the spectrum of (−)-androbiphenyline exhibited eight such peaks. This indicated that (−)-colchibiphenyline [**4a**,**4b**] possessed only three methoxyls.

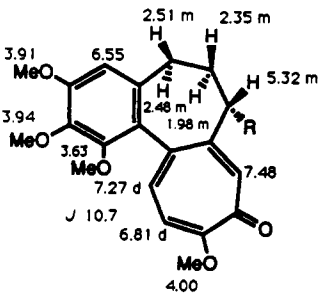
Through the use of homonuclear nmr shift-correlated 2D (COSY) experiments (7), selective spin decouplings, and comparisons with the ^{1}H-nmr spectrum of (−)-androbiphenyline [**5a**,**5b**], it was possible to differentiate between the twin sets of signals for (−)-colchibiphenyline and make specific assignments.

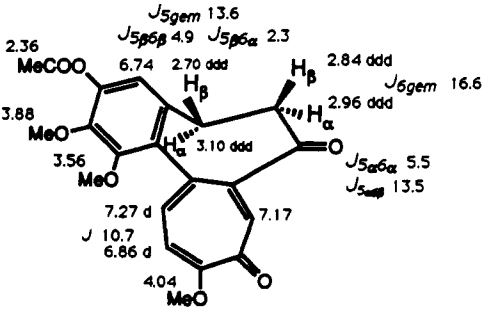
In particular, it appeared as if, by analogy with (−)-androbiphenyline, one phenolic hydroxyl in (−)-colchibiphenyline [**4a**,**4b**] was at C-8, while the other hydroxyl was probably at C-3. In order to establish more firmly the positions of the hydroxyls, a series of nmr nOe experiments were performed.

Irradiation of H-4 (δ 6.62 or 6.72) in conformations **4a**,**4b** had no detectable effect on the methoxyl singlets, indicating that the phenolic function was at C-3. In contrast, irradiation of H-10 (δ 6.85 or 6.84) resulted in enhancement of 9-OMe (δ 3.95 or 3.93) (see Experimental), pointing to the presence of another phenolic function at C-8.

CH_2N_2 *O*-methylation of either (−)-androbiphenyline [**5a**,**5b**] or (−)-colchibiphenyline [**4a**,**4b**] provided the pentamethoxylated derivative **11**, (−)-*O*-methylandrobiphenyline, $C_{22}H_{27}NO_6$. The mass spectrum of **11** had molecular ion *m/z* 401 (51%) and base peak *m/z* 328 $[M - NHAc - CH_2]^+$.

Alternatively, treatment of (−)-colchibiphenyline [**4a**,**4b**] with Ac_2O in pyridine supplied (−)-3,8-diacetylcolchibiphenyline [**10**], $C_{24}H_{27}NO_8$, with mass spectral molecular ion *m/z* 457 (4%) and base peak *m/z* 314 $[M - NHAc - 2\ Ac]^+$.

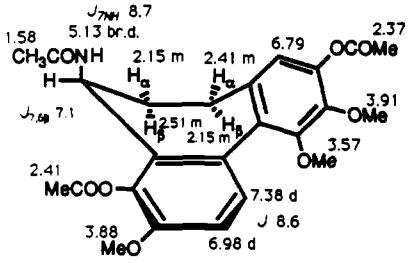




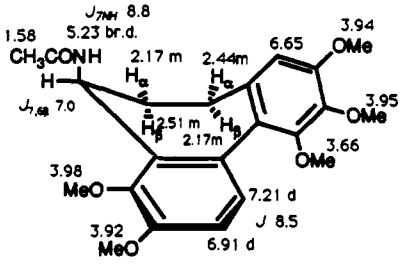
6 R=OH
7 R=OAc (^{1}H nmr) (OAc δ 2.12)
8 R=NHMe

9

The chemical shift of the *N*-acetyl methyl group serves as a ready indicator of the conformation of (−)-androbiphenyline [**5a**,**5b**] and (−)-colchibiphenyline [**4a**,**4b**]. In conformation **a**, this group falls near δ 1.98, while it is around 1.58 in **b**. Interestingly, ^{1}H-nmr spectroscopy indicated that both the pentamethoxy derivative and the diacetate ester existed in only one conformation, with the acetyl methyl appearing at δ 1.58, so that both compounds exist solely in conformation **b**. A simple explanation for this fact is that introduction of any bulky group at C-8 forces the molecule into conformation **b**, in which the acetamido group at C-7 is pseudo-axial and as distant as possible from the C-8 substituent.



10



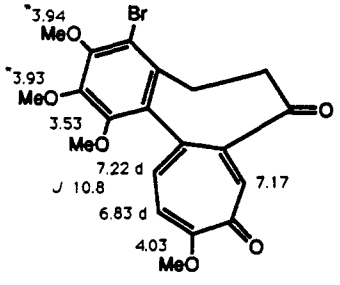
11

With the characterization of colchicone [**1**], 3-demethylcolchicone [**2**], and cornigerone [**3**] on the one hand, and (−)-androbiphenyline [**5a**,**5b**] and (−)-colchibiphenyline [**4a**,**4b**] on the other, it is possible to delineate at least the outlines of two possible catabolic routes for the colchicine-type alkaloids.

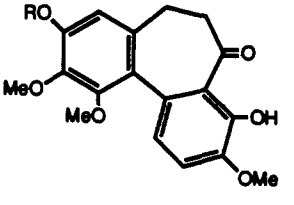
In the first, hydrolysis of the acetamido function followed by oxidation of the resulting amine and hydrolysis of the imine (>C-N-$COCH_3$↦-C-NH_2↦>$\overset{|}{C}$=NH↦>C=O) would lead to ketones **1**–**3**. In the second, decarbonylation of the tropolone ring with accompanying oxidation would supply biphenyline-type alkaloids.

It may be more than idle speculation to suggest that the existence of a ketonic biphenyline such as **13** may be demonstrated in the future. In such a species, the two possible catabolic routes for the colchicines would seem to converge, with both deamination and oxidative decarbonylation having taken place.

It should be cautioned, however, that the above possible catabolic pathways will be firmly established only through the use of properly labeled precursors fed to live plants.



12



13

EXPERIMENTAL

PLANT COLLECTION AND EXTRACTION, AND ISOLATION OF COMPOUNDS.—The bulbs and aerial parts of *C. ritchii* (19 kg, dry wt) were collected in April 1988, in southern Jordan, near the Petra archaeological site. A specimen was deposited in The University of Jordan herbarium. The dried plant was

powdered, defatted with light petroleum ether, and repeatedly extracted with cold MeOH. The combined extracts were concentrated under vacuum at room temperature. The residue was dissolved in H_2O and $CHCl_3$. The organic layer was separated, and the solvent was evaporated. The residue was redissolved in $CHCl_3$ and then extracted with 5% HCl. The $CHCl_3$-soluble material was fractionated using Si gel cc. EtOAc gradually enriched with MeOH was the eluent. Final purification of the compounds was by tlc on Si gel glass plates, using any of the following systems: Me_2CO-C_6H_6-$CHCl_3$ (2:6:2), C_6H_6-$CHCl_3$-MeOH (7:2:1), EtOAc-$CHCl_3$-EtOH (7:2:1).

Nmr spectra are in $CDCl_3$ at either 360 or 500 MHz. Chemical shifts are on the δ scale, and coupling constants are in Hz. Melting points are uncorrected.

COLCHICONE [**1**].—Yield 60 mg; mp 232° (EtOAc); uv (MeOH) λ max 229, 343, 349 nm (log ε 4.51, 4.05, 3.78); ir ($CHCl_3$) ν max 3000, 1710, 1610, 1480, 1410, 1290, 1245 cm^{-1}; eims *m/z* 356 (54), 328 (100), 313 (18), 300 (19), 285 (16), 269 (8). Significant nmr nOe's are H-4 to 3-OMe, 15%; H-4 to H-5β, 10%; H-5β to H-4, 16%; 3-OMe to H-4, 33%; 2-OMe to 3-OMe, 8%; H-11 to H-12, 35%; H-12 to H-11, 20%; H-11 to 10-OMe, 14%; 10-OMe to H-11, 40%; H-6α to H-8, 6%. ^{13}C nmr δ 150.16 (C-1), 141.80 (C-2), 153.70 (C-3), 106.96 (C-4), 132.00 (C-4a), 29.27 (C-5), 47.33 (C-6), 205.66 (C-7), 151.83 (C-7a), 132.80 (C-8), 179.37 (C-9), 164.10 (C-10), 112.40 (C-11), 135.31 (C-12), 136.45 (C-12a), 124.50 (C-12b), 61.12 (1-OMe), 61.07 (2-OMe), 56.44 (3-OMe), 55.96 (10-OMe).

COLCHICOL [**6**].—Colchicone (5 mg) was treated with excess $NaBH_4$ in MeOH. Workup, including tlc, afforded amorphous colchicol (2.4 mg): ^1H nmr δ 6.55 (H-4, s), 4.48 (H-7, m), 7.90 (H-8, s), 6.80 (H-11, d, J = 10.8 Hz), 7.19 (H-12, d, J = 10.8 Hz), 1.80–2.45 (CH_2CH_2, m), 3.62 (MeO-1, s), 3.91* (2-OMe, s), 3.92* (3-OMe, s), 3.99 (10-OMe, s); eims *m/z* 358 (86), 340 (1), 330 (100), 312 (5), 297 (12), 281 (10), 269 (9). Values marked with an asterisk may be interchanged.

COLCHICOL ACETATE [**7**].—Colchicol (2.3 mg) was treated with excess Ac_2O in pyridine at room temperature. Workup provided **7**, amorphous (2.1 mg): uv (MeOH) λ max 215, 241, 351 nm (log ε 4.20, 4.25, 3.97); ir ($CHCl_3$) ν max 3000, 1740, 1615, 1500, 1400; eims *m/z* 400 (92), 372 (100), 312 (65), 297 (75), 281 (55), 269 (27).

(±)-DEMECOLCINE [**8**].—Colchicone (5 mg) was dissolved in MeOH (2 ml). Methylamine (5 ml) was added, and the mixture was refluxed gently for 40 min. $NaBH_4$ (2 mg) was added, and the mixture was stirred for 15 min. Workup generated amorphous **8** (2.2 mg): uv (MeOH) 241, 351 nm (log ε 3.90, 3.60); ir ($CHCl_3$) ν max 3680, 3470, 1620, 1560, 1400 cm^{-1}; eims *m/z* 371 (27), 340 (9), 312 (48), 297 (14), 269 (8), 207 (100); ^1H nmr δ 6.50 (s, H-4), 3.22 (m, H-7), 3.42 (m, H-5β), 2.30 (m, H-5α), 2.50 (m, H-6β), 1.63 (m, H-6α), 7.64 (s, H-8), 6.77 (d, J = 10.9 Hz, H-11), 7.20 (d, J = 10.9 Hz, H-12), 2.20 (s, Me), 3.55 (s, 1-OMe), 3.89 (s, 2-OMe), 3.87 (s, 3-OMe), 3.95 (s, 10-OMe).

4-BROMOCOLCHICONE [**12**].—Colchicone (5 mg) and NBS (2.5 mg) were dissolved in CCl_4 (15 ml). The flask was flushed with N_2, and the mixture was stirred for 2 h under a 100 W light source. Workup gave rise to **12** (4.5 mg): amorphous; uv (MeOH) λ max 231, 348, 366 nm (log ε 4.30, 3.93, 3.80); ir ($CHCl_3$) ν max 1710, 1615, 1485, 1400, 1280 cm^{-1}; eims *m/z* 434 (87), $[M-CO]^+$ 406 (100), 393 (14), 380 (24), 363 (19), 349 (20), 312 (15), 297 (17), 269 (17).

3-DEMETHYLCOLCHICONE [**2**].—Yield 15 mg; mp 260–262° (MeOH); uv (MeOH) λ max 248, 348 nm (log ε 4.60, 4.44); uv (MeOH-OH^-) λ max 250, 320, 398 nm (log ε 4.60, 4.10, 3.98); ir ($CHCl_3$) ν max 3300 br, 3000, 1710, 1610, 1500, 1215 cm^{-1}; eims *m/z* 342 (75), 314 (100), 299 (17), 286 (23), 271 (17), 255 (8); hreims *m/z* $[M]^+$ 342.1092, calcd 342.1103. Significant nmr nOe's are: 2-OMe to 1-OMe, 7%; 1-OMe to 2-OMe, 10%; H-12 to H-11, 17%; H-11 to H-12, 17%; H-11 to 10-OMe, 8%; 10-OMe to H-11, 36%. ^{13}C nmr δ 149.90 (C-1), 140.00 (C-2), 150.20 (C-3), 110.00 (C-4), 132.00 (C-4a), 29.04 (C-5), 47.35 (C-6), 205.68 (C-7), 150.84 (C-7a), 133.01 (C-8), 179.40 (C-9), 164.90 (C-10), 112.30 (C-11), 136.00 (C-12), 136.24 (C-12a), 124.10 (C-12b), 61.20 (1-OMe), 60.08 (2-OMe), 56.52 (10-OMe).

3-DEMETHYLCOLCHICONE ACETATE [**9**].—Compound **2** (3 mg) was treated with excess Ac_2O in pyridine. Workup gave **9** (2 mg): amorphous; uv (MeOH) λ max 214, 241, 339 nm (log ε 4.53, 4.55, 4.26); uv (MeOH-OH^-) λ max 216, 239, 243, 247, 400 nm (log ε 4.65, 4.62, 4.62, 4.60, 4.26); ir ($CHCl_3$) ν max 3000, 1720, 1660, 1580, 1400 cm^{-1}; eims *m/z* 384 (34), 342 (22), 314 (100), 299 (15), 286 (16), 271 (9), 257 (14).

CORNIGERONE [**3**].—Yield 7 mg; amorphous; uv (MeOH) λ max 214, 222, 348, 402 nm (log ε 4.44, 4.40, 4.16, 4.00); ir ($CHCl_3$) ν max 3000, 1705, 1607, 1500, 1460, 1400 cm^{-1}; eims *m/z* 340 (79), 312 (100), 297 (9), 284 (69), 269 (37), 253 (16). Significant nmr nOe's are: H-4 to H-5β, 18%; H-12 to H-11, 45%; 10-OMe to H-11, 56%.

(−)-ANDROBIPHENYLINE [**5a**,**5b**].—Yield 0.142 g; mp 140–106° (EtOAc/C_6H_6); $[\alpha]_D$ −27.0° (c = 0.47, MeOH).

(−)-COLCHIBIPHENYLINE [**4a**,**4b**].—Yield 2.5 mg; amorphous; $[\alpha]_D$ −25.5° (c = 0.094, MeOH); uv (MeOH) λ max 214, 224, 226, 276, 303 nm (log ε 4.45, 4.40, 4.37, 3.93, 3.94); uv (MeOH-OH^-) λ max 222, 274, 303 nm (log ε 4.41, 3.93, 3.94); ir ($CHCl_3$) ν max 3520, 3000, 1660, 1595, 1170, 640 cm^{-1}; eims *m/z* 373 (32), 314 (100), 299 (50), 283 (11), 267 (27). Significant nmr nOe's for **4a** are: 1-OMe to H-11, 9%; H-5β to H-4, 33%; H-6β to H-7, 18%; 9-OMe to H-10, 69%; H-11 to H-10, 69%; H-10 to H-11, 81%; H-10 to 9-OMe, 69%; MeCO to H-6β, 30%; NH to H-7, 18%; H-6β to H-7, 21%. Significant nmr nOe's for **4b** are: 1-OMe to H-11, 13%; H-5α to H-4, 21%; H-6β to H-7, 19%, 9-OMe to H-10, 77%; H-10 to 9-OMe, 21%; H-10 to H-11, 68%; H-11 to H-10, 81%; H-6α to H-5α, 43%; H-5α to H-6α, 25%; H-6β to H-5β, 26%; MeCO to NH, 21%; NH to H-7, 20%.

(−)-3,8-DIACETYLCOLCHIBIPHENYLINE [**10**].—(−)-Colchibiphenyline (1 mg) was treated with excess Ac_2O in pyridine. Workup produced amorphous **10** (1 mg): $[\alpha]_D$ −21.3° (c = 0.56, MeOH); uv (MeOH) λ max 219, 260 nm (log ε 4.30, 4.10); uv (MeOH-OH^-) λ max 218, 286 nm (log ε 4.30, 4.00); ir ($CHCl_3$) ν max 3420, 1760, 1660, 1460 cm^{-1}; hreims *m/z* $[M]^+$ 457.1738, calcd 457.1737; eims *m/z* 457 (4), 415 (38), 373 (11), 356 (22), 314 (100), 299 (13), 287 (6), 267 (6).

(−)-*O*-METHYLANDROBIPHENYLINE [**11**].—(−)-Colchibiphenyline (1 mg) and (−)-androbiphenyline (5 mg) were treated separately with excess ethereal CH_2N_2 in the presence of MeOH for 13 h. Workup provided **11** (1.5 mg and 4 mg, respectively): amorphous; $[\alpha]_D$ −15.0° (c = 0.2, MeOH); uv (MeOH) λ max 214, 216, 262 nm (log ε 4.65, 4.62, 4.10); ir ($CHCl_3$) ν max 3410, 3000, 1660, 1470 cm^{-1}; eims *m/z* 401 (51), 358 (19), 342 (55), 328 (100), 313 (35), 297 (20), 281 (17), 269 (13). Significant nmr nOe's are: H-4 to 3-OMe, 22%; 2-OMe to 1-OMe, 23%; H-11 to 1-OMe, 11%; 1-OMe to H-11, 17%; H-11 to H-10, 48%; H-10 to H-11, 44%; H-10 to 9-OMe, 22%; 9-OMe to H-10, 51%; 8-OMe to H-7, 8%; H-7 to 8-OMe, 10%; MeCO to NH, 11%; NH to MeCO, 20%; H-6β to H-7, 15%; H-6β to H-5β, 50%; H-5α to H-4, 23%.

ACKNOWLEDGMENTS

This research was supported by National Science Foundation grant INT-8805184. T.H. Al-T. was the recipient of a travel grant from the College of Science and Technology in Jerusalem.

LITERATURE CITED

1. D.M. Al-Eisawi, *Mitt. Bot. Staatssamm. Münch.*, **18**, 79 (1982).
2. A.J. Freyer, Musa H. Abu Zarga, S. Firdous, H. Guinaudeau, and M. Shamma, *J. Nat. Prod.*, **50**, 684 (1987).
3. M.A. Iorio and A. Brossi, *Helv. Chim. Acta*, **61**, 1213 (1978).
4. B. Danieli, G. Palmisano, and G. Severini Ricca, *Gazz. Chim. Ital.*, **110**, 351 (1980).
5. C.D. Hufford, H.-G. Capraro, and A. Brossi, *Helv. Chim. Acta*, **63**, 50 (1980).
6. E. Tojo, M.H. Abu Zarga, A.J. Freyer, and M. Shamma, *J. Nat. Prod.*, in press.
7. J.K.M. Sanders and B.K. Hunter, "Modern NMR Spectroscopy," Biddles, London, 1988, p. 108.

Received 27 October 1989