5. ^{13}C- and ^{1}H-NMR. Assignments for Colchicine Derivatives

by **Charles D. Hufford**

Department of Pharmacognosy, School of Pharmacy, University of Mississippi, University, MS 38677 USA

and **Hans-Georg Capraro** and **Arnold Brossi**

Section on Medicinal Chemistry, Laboratory of Chemistry, NIAMDD, National Institutes of Health, Bethesda, Maryland 20205, USA

(25.IX.79)

Summary

The ^{13}C-NMR. spectra of a number of colchicine derivatives are given comprising examples of the normal series (**4** → **10**), iso series (**11** → **16**) and colchiceine series (**17**), which were either reported in the literature or obtained by partial synthesis or degradation reactions. The ^{13}C-NMR. assignments were made by comparisons with known compounds and selective single-frequency off-resonance decoupling experiments. Selective proton decoupling experiments have also allowed assignments of the H–C(11) and H–C(12) protons of the iso and colchiceine series.

In a recent publication, the results of a study of the microbial transformation of colchicine (**1**) were reported [1]. With the aid of the proton-coupled ^{13}C-NMR. data, selective single-frequency off-resonance decoupling experiments and by comparison of the data with those of **1** and its hydrolysis products 10-*O*-demethylcolchicine (colchiceine, **18**) and trimethylcolchicinic acid (**19**), the correct structure to the metabolites obtained, 2-*O*-demethylcolchicine (**2**) and 3-*O*-demethylcolchicine (**3**) was assigned.

We have now examined the ^{13}C-NMR. spectra of other colchicine derivatives comprising examples from the normal series (**4** → **10**), iso series (**11** → **16**) and colchiceine series (**17**). The ^{13}C-NMR. spectra offer an excellent way to distinguish between derivatives of each series. These compounds are natural products (*e.g.* **2**, **3**, **6**, **7**) [2], or obtained by partial synthesis (*e.g.* **8**, **9**, **11**–**15**, **17**) [3–7], or by degradations (*e.g.* **4**, **5**, **10**, **16**, **18**, **19**) [8–11][1]), and have recently been prepared again in connection with another project [7].

1-*O*-Demethylcolchicine (**4**) was reported to be a microbial metabolite of colchicine (**1**) [12], although only 2-*O*-demethylcolchicine (**2**) and 3-*O*-demethylcolchicine (**3**) were identified as microbial metabolites using the fermentation

[1]) The isomeric *O*-methyl ethers **10** and **16** were obtained by methylation of *Woodward*'s dehydrodeacetylaminocolchiceine, an intermediate in *Eschenmoser*'s total synthesis of colchicine (**1**) [11] with CH_2N_2. The position of the double bond in ring B of **10** and **16** is not firmly established and may well have to be assigned to the 5,6-position.

0018-019X/80/1/0050-07$01.00/0 © 1980 Schweizerische Chemische Gesellschaft

Table 1. *^{13}C-NMR. spectral data of colchicine derivatives of the normal series*[a])

C-Atom assignments[b])	**4**[c])	**5**	**6**	**7**	**8**	**9**	**10**
1	150.8[1]	142.1*s*	150.6*s*	150.6*s*	151.4*s*	150.9*s*	151.8*s*
2	135.9[2]	140.1*s*	141.6*s*	141.6*s*	142.2*s*	141.6*s*	141.7*s*
3	147.0[1]	153.8*s*	153.5*s*	153.4*s*	153.6*s*	153.6*s*	152.9*s*
4	103.3	110.0*d*	107.5*d*	107.5*d*	107.6*d*	107.4*d*	107.1*d*
5	29.5	30.1*t*	30.4*t*	30.6*t*	30.0*t*	30.7*t*	39.0*t*
6	–	37.1*t*	38.7*t*	36.3*t*	34.0*t*	40.6*t*	130.5*d*
7	50.8	52.2*d*	62.8*d*	68.5*d*	57.2*d*	53.8*d*	129.7*d*
8	130.7	131.3*d*	132.3*d*	134.2*d*	130.9*d*	132.0*d*	133.7*d*
9	178.0	179.7*s*	179.8*s*	180.1*s*	179.5*s*	179.8*s*	178.5*s*
10	163.3	164.4*s*	164.1*s*	164.1*s*	164.2*s*	164.0*s*	164.1*s*
11	112.3	112.3*d*	111.9*d*	111.7*d*	112.0*d*	111.9*d*	111.4*d*
12	135.5[2]	134.0*d*	134.6*d*	133.8*d*	133.9*d*	135.3*d*	136.1*d*
13	168.2	169.3*s*[1]	–	–	171.1*s*	–	–
14	22.5	22.9*qa*	–	–	22.4*qa*	–	–
1a	119.4	125.7*s*	126.0*s*	125.9*s*	126.4*s*	125.9*s*	128.2*s*
4a	134.4[2]	134.4*s*	135.3*s*	134.8*s*	133.9*s*	134.5*s*	133.1*s*
7a	152.2	151.8*s*	150.9*s*	152.0*s*	151.4/153.6	154.5*s*	154.1*s*
12a	134.0[2]	136.3*s*	137.2*s*	137.5*s*	136.2*s*	136.5*s*	135.4*s*
CH_3O–C(1)	–	60.8*qa*[2]	60.8*qa*[1]	60.6*qa*[1]	61.3*qa*[1]	61.0*qa*[1]	61.1*qa*[1]
CH_3O–C(2)	60.2	60.4*qa*[2]	61.2*qa*[1]	61.2*qa*[1]	61.6*qa*[1]	61.1*qa*[1]	61.3*qa*[1]
CH_3O–C(3)	55.7[3]	56.5*qa*[3]	56.2*qa*[2]	56.1*qa*[2]	56.2*qa*[2]	56.3*qa*[2]	56.1*qa*[2]
CH_3O–C(10)	55.9[3]	56.3*qa*[3]	56.2*qa*[2]	56.1*qa*[2]	56.3*qa*[2]	56.3*qa*[2]	56.2*qa*[2]
CH_3–N	–	–	34.5*qa*	43.7*qa*	33.8*qa*	–	–
CH_3COO	–	169.8*s*[1]	–	–	–	–	–
CH_3COO	–	20.0*qa*	–	–	–	–	–

[a]) Measured in $CDCl_3$ except for **4**.

[b]) Assignments are based on predicted chemical shifts, comparisons with literature data, single-frequency off-resonance decoupling, and selective proton decoupling. Assignments bearing the same numerical superscript in any one column may be reversed.

[c]) This compound was extremely insoluble in all solvents and was measured as a saturated solution in (D_6) DMSO (~ 10 mg). Only the PND spectrum was recorded. The C(6) signal was obscured by (D_6) DMSO.

conditions reported previously [1]. However, 1-*O*-demethylcolchicine (**4**) is now easily accessible by an elegant selective *O*-demethylation of colchicine (**1**) [8] [9]. The proton noise-decoupled ^{13}C-NMR. spectrum of **4** was obtained and the assignments made (see *Table 1*) by analogy to **1, 2** and **3** [1]. The ^{13}C-NMR. spectra of several other colchicine derivatives of the normal series *(Table 1)*, demecolcine (**6**), *N*-methyldemecolcine (**7**), *N*-acetyldemecolcine (**8**), *N*-deacetylcolchicine (**9**) and dehydrodeacetylaminocolchicine (**10**) were recorded. The C-atom C(7a) can be differentiated from C(1) and C(3) by carrying out a selective single-frequency off-resonance decoupling experiment at low decoupling power [1]. If the decoupling frequency is centered near $\delta_H = 3.9$ (OCH_3) the signals for C(1) and C(3) appear as sharp singlets, whereas C(7a) is coupled[2]).

[2]) Three-bond coupling in aromatic and olefinic systems is much larger than two or four-bond coupling. C(7a) is three-bond coupled to H–C(12) and appears as a doublet in this experiment, whereas C(1) and C(3) are only three-bond coupled to the protons of the methoxyl group and this coupling has been eliminated.

Specific assignments for C(1) and C(3) in colchicine (**1**) were not made [1] but by comparing these signals with those of 1-demethyl-1-acetylcolchicine (**5**) definite assignments are now possible. The signals for C(1) and C(3) appear at 153.8 and 151.4 ppm in **1** and 153.6 and 142.1 in **5**. Since C(3) is located *meta* to the substituent at C(1), then its chemical shift should be relatively unaffected in going from **1** to **5**. Thus, the signal at 153.8 ppm in **1** and 153.6 ppm in **5** can be assigned to C(3). C(4a) can be differentiated from C(12a) by centering the decoupling frequency at $\delta_H = 2.5$ (H–C(5) and H–C(6))[3]. The other assignments are based on those of colchicine (**1**) [1], single-frequency off-resonance decoupling (SFORD), and selective proton decoupling experiments.

Using similar techniques, the ^{13}C-NMR. assignments of some colchicine derivatives of the iso series *(Table 2)*, *N*-trifluoroacetyldeacetylisocolchicine (**11**), isodemecolcine (**12**), *N*-methylisodemecolcine (**13**), *N*-acetylisodemecolcine (**14**), *N*-deacetylisocolchicine (**15**), and dehydrodeacetylaminoisocolchicine (**16**), have been made. The chemical shifts of the carbon signals in the two series appear at

Table 2. *^{13}C-NMR. spectral data of colchicine derivatives of the iso and colchiceine series*[a])

C-Atom assignments[b])	**11**	**12**	**13**	**14**	**15**	**16**	**17**
1	151.2*s*	150.7*s*	151.5*s*	150.9*s*	150.6*s*	151.5*s*	150.6*s*
2	142.1*s*	141.1*s*	141.6*s*	141.8*s*	141.8*s*	141.4*s*	141.6*s*
3	154.2*s*	153.6*s*	153.7*s*	153.9*s*	153.7*s*	152.9*s*	153.7*s*
4	108.0*d*	107.5*d*	107.6*d*	107.6*d*	107.4*d*	106.8*d*	107.7*d*
5	30.1*t*	30.4*t*	30.7*t*	30.1*t*	30.7*t*	38.6*t*	30.3*t*
6	37.6*t*	40.1*t*	37.7*t*	36.5*t*	42.4*t*	131.0*d*	39.8*t*
7	53.7*d*	63.0*d*	68.9*d*	58.9*d*	53.0*d*	129.6*d*	39.8*t*
8	110.4*d*	111.2*d*	112.4*d*	109.4*d*	111.1*d*	115.9*d*	118.3*d*
9	164.1*s*	164.1*s*	163.9*s*	164.0*s*	163.9*s*	162.8*s*	173.0*s*
10	179.5*s*	179.6*s*	179.8*s*	179.4*s*	179.6*s*	179.4*s*	168.2*s*
11	133.9*d*	133.8*d*	133.8*d*	134.0*d*	133.6*d*	132.0*d*	124.5*d*
12	141.8*d*	141.4*d*	140.7*d*	141.0*d*	141.3*d*	142.1*d*	141.8*d*
13	157.5*qa*[c])	–	–	171.5*s*	–	–	–
14	116.4*qa*[d])	–	–	22.2*qa*	–	–	–
1a	125.9*s*	126.0*s*	126.2*s*	125.6*s*	125.9*s*	128.4*s*	126.3*s*
4a	134.8*s*	135.7*s*	135.4*s*	134.7*s*[1]	135.9*s*	133.2*s*	135.5*s*
7a	143.1*s*	145.4*s*	146.1*s*	143.6*s*	147.2*s*	144.4*s*	151.3*s*
12a	135.4*s*	135.2*s*	135.4*s*	134.3*s*[1]	134.2*s*	132.6*s*	136.5*s*
CH_3O–C(1)	61.1*qa*[1]	61.0*qa*[1]	60.6*qa*[1]	61.2*qa*[2]	60.9*qa*[1]	61.0*qa*[1]	61.0*qa*[1]
CH_3O–C(2)	61.4*qa*[1]	61.2*qa*[1]	61.3*qa*[1]	61.4*qa*[2]	61.1*qa*[1]	61.3*qa*[1]	61.2*qa*[1]
CH_3O–C(3)	56.1*qa*[2]	56.1*qa*[2]	56.1*qa*[2]	55.8*qa*[3]	56.2*qa*[2]	51.6*qa*[2]	56.2*qa*
CH_3O–C(10)	56.3*qa*[2]	56.1*qa*[2]	56.1*qa*[2]	56.2*qa*[3]	56.2*qa*[2]	56.1*qa*[2]	–
CH_3–N	–	35.2*qa*	44.2*qa*	36.5*qa*	–	–	35.0*qa*

[a]) Measured in $CDCl_3$.

[b]) Assignments are based on predicted chemical shifts, comparisons with literature data, single-frequency off-resonance decoupling, and selective proton decoupling. Assignments bearing the same numerical superscript in any one column may be reversed.

[c]) J_{CCF} 38.0.

[d]) J_{CF} 289.0.

[3]) C(4a) appears as a singlet (no three-bond coupling; eliminated long range coupling to H–C(5) and H–C(6) whereas C(12a) is three-bond coupled to H–C(8) and H–C(11).

similar values except for C(7a), which appears 7–9 ppm downfield in the normal series (**4–10**). In the iso series, C(8) appears between 110–116 ppm (*cf.* C(11) in **4**→**10**, 111–112 ppm) while C(11) appears between 132–134 ppm (*cf.* C(8) in **4**→**10**, 131–134 ppm). The assignment of the most downfield doublet to C(12) (141–142 ppm), and the signal near 134 ppm to C(11) in the iso series, would seem appropriate, since C(12) is the β-carbon of an α,β-unsaturated ketone system[4]). It is also interesting to note that changes in the substituent on the nitrogen atom at C(7) cause very little change in the chemical shifts of C(8) in **4–9** *(Table 1)* and **11–15** *(Table 2)* while H–C(8) is changed considerably *(Table 3)*.

^{13}C-NMR. signals of demecolceine (**17**) are easily assigned by analogy to the other derivatives, particularly for the C-atoms in rings A and B. The major differences between **17** and **4–16** occur in the tropolone ring (ring C). C(8) can be assigned by selective SFORD experiments (δ_H = 8.07, H–C(8)). Since the proton assignments for H–C(11) and H–C(12) are not unambiguously known [14] [15] selective SFORD cannot be used to assign C(11) and C(12). However, C(11) can be assigned to the signal at 124.5 ppm and C(12) to the signal at 141.8, based upon the following argument. The signals for C(11) and C(12) of demecolcine (**6**) appear at 111.9 and 134.6 ppm, respectively. Assuming that the most downfield of the signals of **17** is assigned to C(12) (141.8 ppm) and the more upfield to C(11) (124.5 ppm), then this would represent a change of 7.2 ppm downfield for C(12) and 12.6 ppm downfield for C(11), in going from **6** to **17**. Should the assignments for C(11) and C(12) be reversed in **17**, then a change of 29.9 ppm downfield for

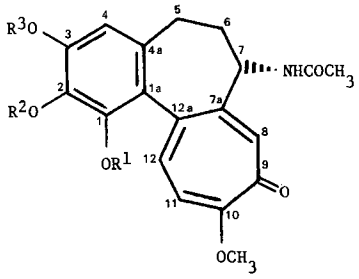
Table 3. *^{1}H-NMR. spectral data of colchicine derivatives*[a])

Compound	H–C(4)	H–C(8)	H–C(11)	H–C(12)
4	6.40	7.06	6.92	7.16
5	6.58	7.50	6.86	7.18
6	6.55	7.71	6.79	7.25
7	6.53	8.11	6.78	7.27
8	6.56	7.11	6.79	7.29
9	6.54	7.74	6.77	7.04
11	6.64	7.44	7.13	7.56
12	6.59	7.90	7.13	7.42
13	6.57	7.92	7.12	7.42
14	6.61[b])	6.67[b])	7.10	7.44
15	6.58	7.99	7.11	7.30

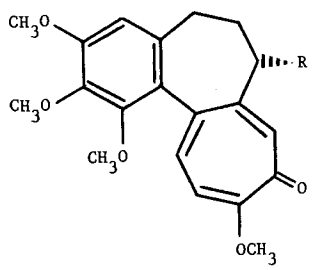
[a]) Chemical shifts (δ) in $CDCl_3$ except for **4** (D_6) DMSO at 60 MHz (TMS internal standard). The more downfield AB doublet in the iso series (**11**→**15**) has been assigned to H–C(12) (see footnote 3).

[b]) May be reversed.

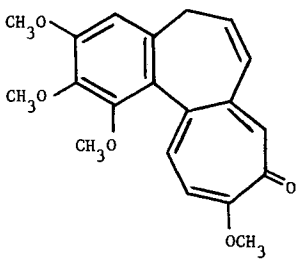
[4]) Even though the proton assignments for H–C(11) and H–C(12) in colchicine and derivatives of the normal series seem well established, these assignments in the iso series have not been as clear [14]. Again, it would seem logical to assign H–C(12) to the most downfield doublet based on the well established principle that the β-proton always resonates at lower field than the α-proton in an α,β-unsaturated system. Selective single-frequency off-resonance decoupling has correlated the carbon signals near 141 ppm with proton signals occurring between δ_H = 7.3–7.4 (lowest field *AB* doublet). Thus, this evidence suggests that in the normal series and iso series, H–C(12) always appears further downfield than H–C(11).



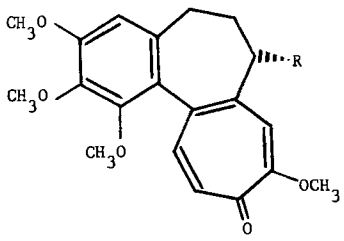
1 $R^1=R^2=R^3=CH_3$
2 $R^1=R^3=CH_3$; $R^2=H$
3 $R^1=R^2=CH_3$; $R^3=H$
4 $R^2=R^3=CH_3$; $R^1=H$
5 $R^2=R^3=CH_3$; $R^1=COCH_3$



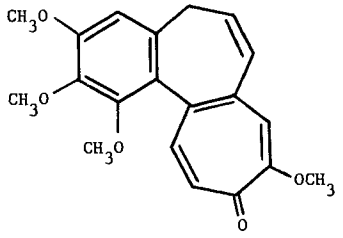
6 $R=NHCH_3$
7 $R=N(CH_3)_2$
8 $R=NCH_3COCH_3$
9 $R=NH_2$



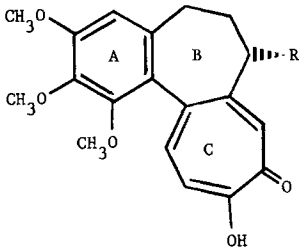
10



11 $R=NHCOCF_3$
12 $R=NHCH_3$
13 $R=N(CH_3)_2$
14 $R=NCH_3COCH_3$
15 $R=NH_2$



16



17 $R=NHCH_3$
18 $R=NHCOCH_3$
19 $R=NH_2$

C(11) and 10.1 ppm upfield for C(12) would be the result; a situation that would seem unlikely. The signal at 173.0 ppm was assigned to C(9) and the signal at 168.2 ppm to C(10). These two C-atoms come at almost identical chemical shifts in 10-*O*-demethylcolchiceine (**18**) [1], reflecting the tautomerism possible in the colchiceine series. In **17** (as well as **18** and **19** [1]) C(7a) occurs at a chemical shift value similar to that in the normal series (**4**–**10**) whereas C(12) occurs at a chemical shift value similar to that in the iso series (**11**–**16**).

Since selective proton decoupling experiments involving C(11) and C(12) were performed, and since these have now been assigned independently of the proton assignments, then H–C(12) in **17** can be assigned to the more downfield *AB*-doublet in the colchiceine series; the same situation exists in the normal series [14] and iso series (see footnote 3).

Note added in proof: Recently, a publication has appeared regarding ^{13}C-NMR. assignments of colchicine [*A. Bladé-Font, R. Muller, J. Elhuero, R. Faure* and *E.-J. Vincent*, Chemistry Letters *1979*, 233]. These assignments agree with those reported in [1] and with those listed here except for C(8) and C(12). The selective proton decoupling experiments [1] in colchicine clearly identify C(8) with the signal at 130.7 ppm and C(12) with the signal at 134.5 ppm.

Experimental Part

General remarks. The ^{13}C-NMR. and ^{1}H-NMR. were recorded on a *JEOL*-FX60 *Fourier*-transform NMR. spectrometer with TMS as internal standard. The ^{13}C-NMR. spectra (15.03 MHz) were obtained using a 45° pulse and repetition rate of 10 s. The selective SFORD experiments were carried out by centering the decoupler on the appropriate proton resonance and then recording the spectra on several different power settings. Melting points (m.p.) are corrected. UV. spectra: in EtOH, λ_{max} in nm, ε in parentheses. IR. spectra in $CHCl_3$, data in cm^{-1}; abbreviations: *s* strong, *m* medium, *w* weak, br. broad. Mass spectra (MS.) *m/z*, electron impact 70 eV, relative intensity in parentheses. Optical rotations were measured in $CHCl_3$ solution, concentration in parentheses.

N-*Acetyldemecolcine* (**8**). Demecolcine (**6**, 1.88 mmol, 0.7 g) was stirred overnight in a mixture of pyridine (3 ml) and acetic anhydride (2 ml). The excess solvent was evaporated at high vacuum and the crude product filtered on SiO_2 ($CHCl_3$/MeOH 95:5) to yield 724 mg (93%) of **8**. Double m.p. at 199–200° and 233–235°; $[a]_D^{20} = -251°$ ($c = 1.17$). – UV.: 350 (19400), 242 (31000). – IR.: 1645*s*, 1619*s*, 1593*s*, 1570*s*, 1505*m*, 1490*s*, 1467*s*, 1448*m*, 1435*m*, 1409*m*, 1353*m*, 1328*s*, 1296*m*, 1287*m*, 1181*m*, 1141*s*, 1098*s*, 1085*m*, 1046*w*, 1022*m*, 1003*m*, 986*m*, 922*w*, 899*w*, 869*w*, 843*m*. – MS.: 413 (M^+, 88), 398 (9), 386 (18), 370 (57), 356 (16), 342 (18), 340 (18), 312 (100).

$C_{23}H_{27}NO_6$ (413.44) Calc. C 66.81 H 6.57 N 3.38% Found C 66.72 H 6.46 N 3.27%

Dehydrodeacetylaminocolchicine (**10**) *and dehydrodeacetylaminoisocolchicine* (**16**). Dehydrodeacetylaminocolchiceine [11] was dissolved in MeOH and treated with an excess of ethereal CH_2N_2. After the solvent was evaporated, the residue was filtered on SiO_2 ($CHCl_3$, then $CHCl_3$/MeOH 97:3). The fractions were examined on HPLC. and those enriched with **10** and **16** combined. Pure **10** and **16** (one peak on HPLC.; sharp m.p.) were obtained by repeated fractional crystallization from ethyl acetate/ether and MeOH/ether; **16** was much easier to crystallize than **10**.

Dehydrodeacetylaminocolchicine (**10**). M.p.: 172–174°. – UV.: 246 (44200), 355 (15200). – IR.: 1613*s*, 1589*s*, 1511*s*, 1489*s*, 1416*m*, 1432*m*, 1399*m*, 1391*m*, 1378*s*, 1325*m*, 1287*m*, 1158*m*, 1149*s*, 1101*s*, 1089*s*, 1047*m*, 1015*m*, 1003*m*, 988*m*, 957*w*, 898*w*, 848*m*. – ^{1}H-NMR.: 3.06 (*d*, $J = 6.3$, H–C(5)); 3.58 and 3.92 (2*s*, 2×3 H, OCH_3); 3.96 (*s*, 2×3 H, OCH_3); 6.18 (*m*, 1 H–C(6)); 6.50 (*d*, $J = 8.5$, H–C(7)); 6.56 (*s*, H–C(4)); 6.69 (*d*, $J = 11.0$, H–C(11)); 7.22 (*d*, $J = 11.0$, H–C(12)); 7.30 (*s*, H–C(8)).

$C_{20}H_{20}O_5$ (340.355) Calc. C 70.57 H 5.91% Found C 70.51 H 5.89%

Dehydrodeacetylaminoisocolchicine (**16**). M.p.: 190–191°. – UV.: 285 sh. (10800), 237 (38000), 350 (19500). – IR.: 1619*s*, 1598*m*, 1524*s*, 1552*m*, 1491*s*, 1467*m*, 1458*m*, 1433*w*, 1405*m*, 1379*m*, 1338*m*, 1319*w*, 1261*s*, 1168*m*, 1155*s*, 1139*s*, 1099*s*, 1080*w*, 1043*w*, 1002*w*, 989*m*, 878*w*, 850*m*. – ^{1}H-NMR.: 2.64 (*d*×*d*, $J = 10.0$ and 6.0, H–C(5)); 3.10 (*d*×*d*, $J = 12.0$ and 8.0, H–C(5)); 3.66, 3.91, 3.94, and 3.98 (4*s*, 4×3 H, OCH_3); 6.24 (*m*, H–C(6)); 6.57 (*d*, $J = 9.0$, H–C(7)); 6.60 (*s*, H–C(4)); 6.90 (*s*, H–C(8)); 6.98 (*d*, $J = 13.0$, H–C(11)); 7.40 (*d*, $J = 13.0$, H–C(12)).

$C_{20}H_{20}O_5$ (340.355) Calc. C 70.57 H 5.91% Found C 70.43 H 6.11%

N-*Methylisodemecolcine* (**13**) was prepared following the procedure of *Ueno* [13]. The compound resisted all attempts at crystallization from different solvents or mixture of solvents. $[a]_D^{22} = -229°$ ($c = 1.00$). – UV.: 340 (17150), 246 (29450). – IR.: 1617*s*, 1600*s*, 1563*s*, 1488*s*, 1464*s*, 1455*s*, 1407*s*, 1357*m*, 1343*s*, 1330*m*, 1313*s*, 1303*m*, 1288*m*, 1163*s*, 1141*s*, 1095*s*, 1078*m*, 1043*m*, 1024*w*, 1001*m*, 986*m*, 920*w*, 903*w*, 853*w*, 837*w*. – MS.: 385 (M^+, 100), 370 (46), 368 (24), 354 (60), 342 (37), 341 (48), 340 (41), 326 (21), 312 (22).

N-*Acetylisodemecolcine* (**14**). Compound **14** was prepared in the same way as **8**. Yield 95%. M.p.: 173–174° (from MeOH/ether); $[a]_D^{20} = -308°$ ($c = 1.03$). – UV.: 343 (19050), 244 (30570). – IR.: 1653*s*, 1618*s*, 1599*m*, 1565*s*, 1492*s*, 1466*s*, 1455*s*, 1408*s*, 1351*m*, 1327*s*, 1312*m*, 1288*w*, 1167*m*, 1152*s*, 1141*s*, 1098*s*, 1063*w*, 1045*m*, 1003*m*, 985*m*, 921*w*, 873*w*, 844*w*. – ^{1}H-NMR. ($CDCl_3$, RT.): 1.56(*s*) and 2.15 (*s*, total 3 H, NCH_3COCH_3); 2.1–2.8 (*m*, 2 H–C(5) and 2 H–C(6)); 3.28 (*s*, NCH_3COCH_3); 3.71 (*s*, 3 H) and 3.90 (*s*, 9 H, 4×OCH_3); 4.46 (very br. *m*) and 4.88 (very br. *m*, H–C(7)); 6.57(*s*) and 6.63 (*s*, H–C(4) and H–C(8)); 7.12 (*d*, $J = 12.5$) and 7.40 (*d*, br. lines, $J = 12.5$, H–C(11) and H–C(12)). – MS.: 413 (M^+, 45), 398 (6), 385 (96), 370 (100).

$C_{23}H_{27}O_6N$ (413.442) Calc. C 66.81 H 6.57 N 3.38% Found C 67.07 H 6.60 N 3.27%

N-*Deacetylisocolchicine* (**15**). Trimethylcolchicinic acid (**19**) suspended in MeOH was treated with an excess of ethereal CH_2N_2. After evaporation of the solvent, the residue was chromatographed on SiO_2 ($CHCl_3$/acetone/ethanol 20:10:2.5). The first compound eluted was **15**, followed by a mixture of **9** and **15** (main fraction) and a small amount of **9**. M.p.: 177–180° (from ethanol/ether); $[\alpha]_D^{20} = -253°$ ($c = 1.14$). – UV.: 340 (18670), 243 (29450). – IR.: 1618*s*, 1595*s*, 1562*s*, 1490*s*, 1467*s*, 1458*s*, 1434*w*, 1406*m*, 1351*s*, 1340*m*, 1324*m*, 1315*m*, 1287*w*, 1181*w*, 1167*m*, 1142*s*, 1096*s*, 1054*w*, 1012*w*, 998*w*, 986*w*, 920*w*, 843*w*. – MS.: 357 (M^+, 100), 342 (25), 328 (27), 326 (42), 312 (49), 298 (57).

REFERENCES

[1] *C.D. Hufford, C.C. Collins & A.M. Clark,* J. pharm. Sci. *68,* 1239 (1979).
[2] *T. Kametani,* 'The Chemistry of the Isoquinoline Alkaloids', Elsevier Publishing Co., New York, p. 222, 1969.
[3] *F. Šantavý, R. Winkler & T. Reichstein,* Helv. *36,* 1319 (1953).
[4] *A. Uffer, O. Schindler, F. Šantavý & T. Reichstein,* Helv. *37,* 18 (1954).
[5] *Y. Ueno,* J. pharm. Soc. Japan *73,* 1232 (1953).
[6] *R.F. Raffauf, A.L. Farren & G.E. Ullyot,* J. Amer. chem. Soc. *75,* 5292 (1953).
[7] *H.G. Capraro & A. Brossi,* Helv. *62,* 965 (1979).
[8] *G. Muller, A. Bladé & R. Bardoneschi,* U.S. patent 3.410.899 (1968).
[9] *A. Bladé-Font,* Tetrahedron Letters *1979,* in press. We thank Dr. *Bladé-Font,* for having informed us on the results of his study.
[10] *J.W. Cook & J.D. Loudon,* in Manske's 'Alkaloids', Vol. II, Academic Press, New York and London, p. 269 and 270, 1952.
[11] *J. Schreiber, W. Leimgruber, M. Pesaro, P. Schudel, T. Threlfall & A. Eschenmoser,* Helv. *44,* 540 (1961).
[12] *L. Velluz & P. Bellet,* C.r. hebd. Séances Acad. Sci. *248,* 3453 (1959).
[13] *Y. Ueno,* J. pharm. Soc. Japan *73,* 1230 (1953).
[14] *W.C. Wildman & B.A. Pursey,* in Manske's 'Alkaloids', Vol. XI, Academic Press, New York and London, Chapter II, p. 19.
[15] *M.A. Iorio, A. Brossi & J.V. Silverton,* Helv. *61,* 1213 (1978).