Tetrahedron Vol. 42, No. 13, pp. 3579 to 3586, 1986
Printed in Great Britain.

0040-4020/86 $3.00 + .00
Pergamon Journals Ltd.

ANTIBIOTICS FROM BASIDIOMYCETES. Part 23.[1] MERULIDIAL, AN ISOLACTARANE DERIVATIVE FROM MERULIUS TREMELLOSUS

BRUNO M. GIANNETTI, BERT STEFFAN and WOLFGANG STEGLICH*

Institut für Organische Chemie und Biochemie der Universität Bonn,
Gerhard-Domagk-Straße 1, D-53 Bonn, F.R.G.

WOLFRAM QUACK and TIMM ANKE

Abteilung Biotechnologie der Universität Kaiserslautern,
Paul-Ehrlich-Str. 22, D-675 Kaiserslautern, F.R.G.

(*Received in Germany* 24 *March* 1986)

Abstract- The structure of merulidial (**1a**), a sesquiterpenoid antibiotic produced by cultures of Merulius tremellosus has been elucidated by spectral investigations and conversion into several derivatives.

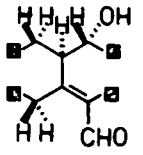
INTRODUCTION

Some time ago we reported on the isolation and characterization of merulidial, a sesquiterpenoid antibiotic from culture fluids of Merulius tremellosus (Fr.).[2] The compound exhibits strong antibiotic effects against several bacteria and fungi and possesses cytotoxic activity against the ascitic form of Ehrlich carcinoma. According to the Ames test merulidial is strongly mutagenic.[2,3] From fruit-bodies of the same fungus merulinic acid A and two related aromatic polyketides with antibacterial and haemolytic activity have been isolated.[4] In the present publication we describe the structural elucidation of merulidial.[5]

RESULTS AND DISCUSSION

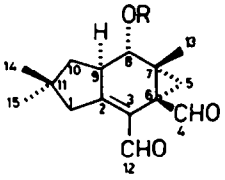
Merulidial, $C_{15}H_{20}O_3$, shows IR bands (KBr) at 3375 (OH), 1699 (CHO) and 1693, 1656 cm^{-1} (α,β-Δ-CHO). The two aldehyde groups give rise to singlets at δ 9.58 and 9.81 in the ^1H NMR spectrum (Table 1). Singlets at δ 1.06, 1.14 and 1.17 can be assigned to three quarternary methyl groups, and the components of an AB quartet (J = 5.5 Hz) at δ 1.17 and 1.76 are due to the protons of an isolated cyclopropane methylene group. Four well resolved multiplets at δ 1.39, 2.05, 2.54 and 3.67 indicate the presence of the sequence (C)-CH_2-CH(C)-CHOH-(C). The multiplet at δ 2.54 is connected by long range coupling (^4J = 3 Hz) with the A part of an AB-system at δ 2.66 and 2.75 (J = 18.5 Hz). The chemical shifts of these protons suggest that the ^4J-coupling occurs across the β-carbon of the unsaturated aldehyde unit, which

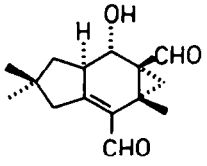
leads to partial structure A.



A

The UV maximum (MeOH) at 267.5 nm points to an extension of the enone chromophore by conjugation with the cyclopropane ring.[6] Considering the fact that three methyl groups, an additional aldehyde group and a quarternary carbon have still to be incorporated into the formula, structures **1a** and **2** are derived for merulidial.





1a, R = H
1b, R = Ac

2

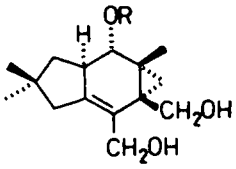
Table 1. ^{1}H NMR spectral data for merulidial (**1a**)
(400 MHz, in $CDCl_3$, δ-values, δ_{CDCl_3} 7.24 ppm)

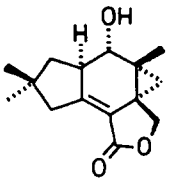
Proton		Proton	
H-1α	2.75 ddd	H-10α	2.05 ddd
H-1β	2.66 dd	H-10β	1.39 dd
H-4	9.58 s	H-12	9.81 s
$H\text{-}5_{en}$	1.17 d	H-13	1.17 s
$H\text{-}5_{ex}$	1.76 dd	H-14	1.06 s
H-8	3.67 br.d	H-15	1.14 s
H-9	2.54 ddddd		

$J_{1\alpha,1\beta}$ = 18.5 Hz; $J_{1\alpha,9}$ = 1.75; $J_{1\beta,9}$ = 3; $J_{1\alpha,10\alpha}$ = 1.5; $J_{5en,5ex}$ = 5.5; $J_{5ex,8}$ = 1; $J_{8,9}$ = 9; $J_{9,10\alpha}$ = 8; $J_{9,10\beta}$ = 11; $J_{10\alpha,10\beta}$ = 12.

Differentiation between these formula in favour of **1a** could be achieved by reduction of merulidial to its tetrahydro derivative **3a**, which on oxidation with MnO_2[7] yielded the γ-lactone **4** (IR: 1755 cm^{-1}). In the ^{1}H NMR spectrum of tetrahydro compound **3a** both of the cyclopropyl doublets are shifted towards higher field (δ 1.17 → 0.52; 1.76 → 1.16), whereas the singlet of the 13-CH_3 group is moved downfield (δ 1.17 → 1.42). The latter effect indicates a shielding of this methyl group

by the adjacent aldehyde function in the case of **1a**. Whereas **3a** is devoid of any antibiotic activity, **4** shows similar inhibition of several bacteria as does merulidial itself.





3a, R = H
3b, R = Ac

4

Formula **1a** is further supported by the ^{13}C NMR data (Table 2). The assignments were confirmed by heteronuclear $^{13}C/^{1}H$ 2D shift correlation experiments.[8]

Table 2. ^{13}C NMR spectrum of merulidial (**1a**) (100.2 MHz, δ-values, in $CDCl_3$)

Carbon	δ	J (Hz)	Carbon	δ	J (Hz)
C-1	44.27 Tm	129	C-9	47.01 Dm	126.5
C-2	164.65 m		C-10	44.54 Tm	129
C-3	130.73 dm	26	C-11	38.35 m	
C-4	197.18 Ddd	182/4/2	C-12	189.01 D	174.5
C-5	19.64 Tm	161	C-13	15.86 Qddd	126/5/2/2
C-6	38.35 m		C-14	28.42 Qm	124
C-7	34.22 m		C-15	29.42 Qm	124
C-8	75.17 Dm	143			

The relative stereochemistry of merulidial was elucidated by NMR experiments. The coupling constant (J = 9 Hz) observed for H-8 indicates a pseudoequatorial orientation of the OH-group. The cis-arrangement of the angular proton at C-9 and the cyclopropane ring was confirmed by nuclear Overhauser experiments. On irradiation at the signal of the endo-cyclopropane proton (δ 1.17) the signal for H-9 at δ 2.54 is considerably enhanced (16 %). The large value of the coupling constant (^{4}J = 3 Hz) between H-1β and H-9 can be explained by the nearly coplanar arrangement of these C-H bonds with the π-orbital of the C=C double bond.[9] The conformation depicted in Figure 1 also explains the W-coupling (^{4}J = 1.5 Hz) between H-1α and

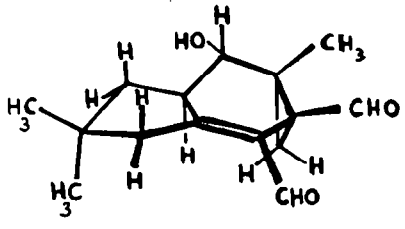


Figure 1

H-10α, which is not observed between the corresponding ß-protons. This stereochemistry is also in accord with the deshielding of H-10α by the pseudoequatorial OH-group and the magnitude of the observed coupling constants between the protons at C-10 and C-9. All interproton couplings have been confirmed by standard two-dimensional (2D) $^1H,^1H$ chemical shift correlation spectroscopy (COSY).[10]

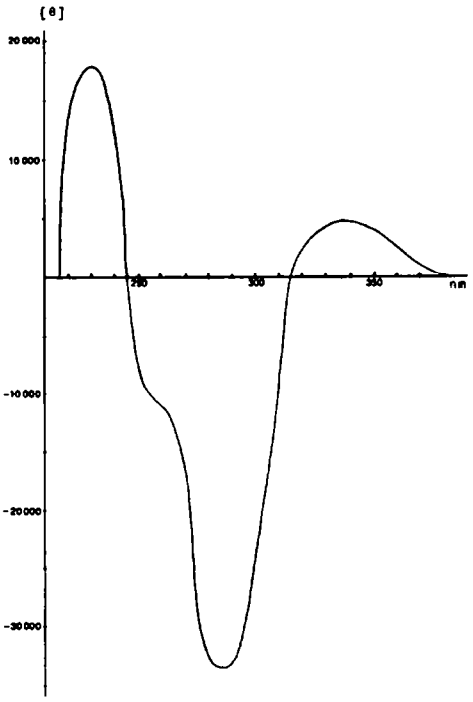
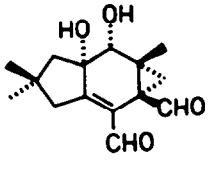


Fig. 2. Circular dichroism spectrum of merulidial (**1a**) in methanol.

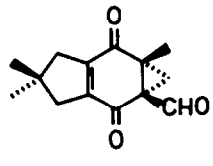
The absolute configuration of merulidial indicated in formula **1** was established by application of the Horeau method.[11,12] On reaction with (±)-2-phenylbutanoic anhydride the corresponding ester was obtained in 72% yield, and the optical yield of the residual 2-phenylbutanoic acid formed was 12.1% in favour of the (-)-form. This indicates the (8S)-configuration for merulidial[13] which is in accord with the absolute configuration determined for other sesquiterpenoids from Basidiomycetes, biosynthetically derived from protoilludane.[14] The CD spectrum of merulidial is depicted in Figure 2.

On acetylation merulidial yields a monoacetate **1b**, which may be reduced by $NaBH_4$ to its tetrahydro derivative **3b**. As expected the ^1H NMR signal of the alcohol methine proton in **1b** is shifted on acetylation from δ 3.67 towards 5.15.

An interesting oxidative degradation is observed on treatment of **1a** with pyridinium chlorochromate (PCC).[15] Besides a small amount of hydroxy compound **5** the enedione **6** is obtained as the main product. Compound **6** exhibits strong inhibitory activity against several microorganisms. In the ^1H NMR spectrum ($CDCl_3$) of **5** the endo-cyclopropane proton experiences considerable deshielding by the α-hydroxy group at C-9 (δ 1.17 → 1.76). That the hydroxylation has occurred with retention of



5

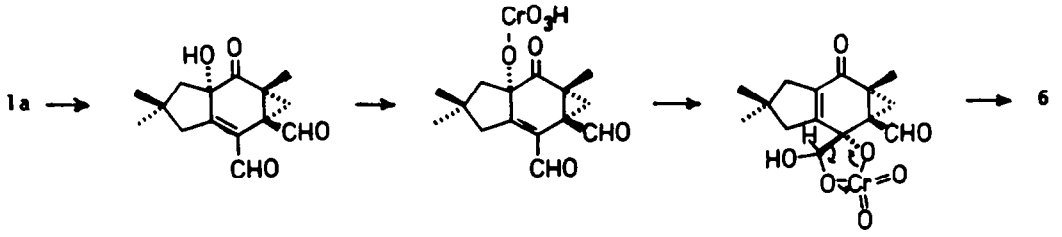


6

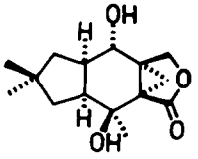
stereochemistry at C-9 is indicated by the unchanged position of the 8-H signal in **5** as compared to **1a**.

In the ^{1}H NMR spectrum of **6** the methylene protons of the cyclopentene ring give rise to multiplets at δ 2.47 and 2.69, and the two doublets of the cyclopropane protons are found at δ 1.95 and 2.18. Methyl singlets at δ 1.14, 1.15 and 1.42 are in accord with structure **6**.

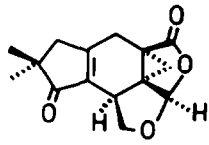
The formation of **6** may be explained by hydroxylation of merulidial at C-9, followed by oxidation of the secondary hydroxy group, allylic rearrangement of the intermediary chromate[16] and oxidative loss of the aldehyde group:



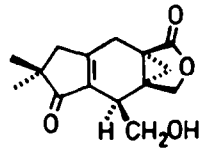
Merulidial belongs to a small group of fungal sesquiterpenoids which contain the isolactarane skeleton. Other members are isolactarorufin (**7**)[17] from Lactarius rufus, and sterepolide (**8**) and its dihydro derivative **9**, which have recently been isolated from cultures of Stereum purpureum.[18] The high biological activity of **1a** may be explained by the presence of the α,β-unsaturated dialdehyde moiety, which has the same spatial arrangement as that in the marasmane derivatives isovelleral (**10**)[19] and marasmic acid (**11**),[20,21] compounds exhibiting similar biological effects.



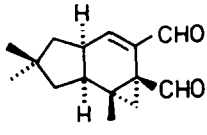
7



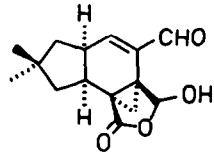
8



9



10



11

EXPERIMENTAL

^{1}H NMR spectra were obtained on Bruker WH 90 and WM 400 spectrometers in deuteriochloroform solutions with tetramethylsilane as internal standard. IR spectra were recorded on a Pye Unicam SP 1100 spectrophotometer. The UV spectra were taken with a Varian Cary 17 spectrometer, and the CD spectra with a Jouan-Roussel III spectropolarimeter. High resolution mass spectra were obtained on an AEI MS 50 instrument. Melting points were determined using a Reichert hot-stage microscope and are uncorrected. Column chromatography was performed on Malinckrodt silica gel (100 mesh).

Merulidial (1a)

1a was obtained from cultures of *Merulius tremellosus* as described before.[2] Colourless needles, m.p. 99° ($CHCl_3$/EtOH 95:5); $[\alpha]_D^{20}$ -154° (c 0.5, MeOH); UV (MeOH): λ_{max} (log ε) = 267.5 nm (4.20); CD (MeOH): $[\theta]_{239}$ = 17980, $[\theta]_{245}$ = 0, $[\theta]_{262}$ = -11465, $[\theta]_{285}$ = -33560, $[\theta]_{315}$ = 0, $[\theta]_{357.5}$ = 4690, $[\theta]_{351}$ = 3960, $[\theta]_{367}$ = 1565; IR (KBr): 3375 (s), 3290 (s), 2950 (s), 2920 (m), 2890 (m), 2860 (s), 1699 (s), 1693 (s), 1656 (s), 1648 (m), 1633 (w), 1628 (m), 1461 (w), 1438 (w), 1420 (w), 1398 (m), 1363 (w), 1334 (w), 1309 (w), 1288 (w), 1234 (w), 1200 (m), 1157 (w), 1135 (w), 1120 (w), 1069 (m), 1040 (s), 1030 (s), 992 (w), 965 (m), 900 (w), 885 (w), 860 (w), 821 (m), 785 (w), 786 (w), 728 (w), 680 cm^{-1} (w); IR ($CDCl_3$): 1690 (s), 1650 cm^{-1} (s); ^{1}H NMR see Table 1; ^{13}C NMR see Table 2; MS (70 eV): *m/z* 248.1399 (M^+, 8.5%, calc. for $C_{15}H_{20}O_3$ 248.1412), 230 (75, $C_{15}H_{18}O_2$), 228 (30), 219 (39), 217 (32), 215 (100, $C_{14}H_{15}O_2$), 203 (44), 201 (54, $C_{14}H_{17}O$), 197 (27), 191 (25), 189 (39), 187 (47, $C_{13}H_{15}O$), 185 (30), 173 (32, $C_{13}H_{17}$), 171 (20), 161 (21), 159 (34, $C_{12}H_{15}$), 157 (28, $C_{12}H_{13}$), 149 (18), 145 (45), 143 (35, $C_{11}H_{11}$), 141 (30), 131 (37, $C_{10}H_{11}$), 129 (40), 128 (45), 117 (38, C_9H_9), 115 (49, C_9H_7), 105 (65); (Found: C, 72.11; H, 8.17; $C_{15}H_{20}O_3$ requires: C, 72.55, H, 8.12%).

O-Acetylmerulidial (1b)

A solution of **1a** (20 mg) and Ac_2O (1 ml) in pyridine (1 ml) was stirred at room temperature for 30 min. The solvent was removed under reduced pressure and the residue dried for several h *in vacuo*. Yield 20.6 mg (84%), colourless oil; IR ($CHCl_3$): 3050 (m), 2980 (s), 2890 (m), 1740 (s), 1710 (s), 1670 (s), 1370 (m), 1245 (s), 1125 (m), 1035 cm^{-1} (m); ^{1}H NMR (90 MHz): δ 1.18, 1.21, 1.27, 2.20 (each *s*, 4 CH_3), 5.15 (*d*, *J* = 9 Hz, 1H), 9.64 (*s*, 1H), 9.86 (*s*, 1H), other signals not resolved; MS: *m/z* 290.1503 (M^+, 3%, calc. for $C_{17}H_{22}O_4$ 290.1518), 262 (7), 260 (9), 258 (5), 247 (8), 234 (10), 233 (12), 229 (28), 228 (30, $C_{15}H_{16}O_2$), 227 (7), 220 (7), 219 (22), 215 (49), 214 (8), 213 (27), 203 (30), 202 (35), 201 (52), 199 (17), 191 (14), 190 (22), 189 (43), 185 (23), 174 (24), 171 (14), 162 (11), 159 (31), 157 (15), 145 (10), 143 (12), 131 (13), 129 (11), 128 (12), 115 (13), 105 (17), 91 (22).

Tetrahydromerulidial (3a)

$NaBH_4$ (100 mg) was added in small portions to a stirred soln of **1a** (30 mg) in dioxane/H_2O (4:1, 4 ml) at 0°. The stirring was continued for 1 h at 0°C and 4 h at 20°. The excess of $NaBH_4$ was destroyed by addition of dilute aqueous oxalic acid. The dioxane was removed under reduced pressure, and after addition of water the solution was extracted six-times with EtOAc. The organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*. The residue yielded **3a** after crystallization from benzene (15.1 mg, 50%), mp 210-212°C (decomp.); IR ($CHCl_3$): 3640 (m), 3500 (m, br.), 2980 (s), 2940 (s), 1430 (m, br.), 1330 (m, br.), 1380 (m), 1020 cm^{-1} (s); ^{1}H NMR (90 MHz): δ 0.52, 1.16 (AB-system, *J* = 5 Hz, 2H), 1.00 (*s*, 3H), 1.07 (*s*, 3H), 1.42 (*s*, 3H), 3.44, 4.29 (AB-system, *J* = 12.5 Hz, 2H), 3.53 (br. *d*, *J* = 9 Hz, 1H), 4.29 (*s*, 2H), other signals not resolved; MS: *m/z* 252 (M^+, 2%), 234 (4), 221 (6), 216 (20), 203 (30), 201 (28), 187 (60), 175 (40), 173 (70), 159 (35), 145 (39), 131 (40), 119 (90), 105 (70), 91 (70), 59 (68), 43 (100).

Lactone 4

A soln of **3a** (15 mg) in diethyl ether (100 ml) was stirred at room temp overnight with MnO_2 (1 g). The solution was filtered through a celite pad, which was subsequently carefully washed with

ether. The combined filtrate was concentrated to give **4** as a colourless oil (10.2 mg, 68% yield); IR ($CHCl_3$): 3660 (w), 3520 (w, br.), 2980 (s), 1755 (s), 1465 (w), 1355 (w), 1140 (s), 1030 cm^{-1} (s); ^1H NMR (90 MHz): δ 0.63 (d, J = 5.5 Hz, 1H), 1.03, 1.09, 1.27 (each s, 3 CH_3), 1.53 (d, J = 5.5 Hz, 1H), 1.70 (s, OH), 3.51 (d, J = 9 Hz, 1H), 4.23, 4.40 (AB-system, J = 9 Hz, 14-CH_2), other signals unresolved; ^{13}C NMR ($CDCl_3$): δ 17.22 (C-13), 21.65 (C-5), 28.22 (C-14 or C-15), 29.07 (C-14 or C-15), 29.71 (C-6 or C-7), 30.46 (C-6 or C-7), 38.91 (C-11), 44.80 (C-1 or C-10), 45.19 (C-1 or C-10), 46.97 (C-9), 69.75 (C-4), 77.26 (C-8), 120.18 (C-3), 152.29 (C-2), 168.96 (C-12); MS: m/z 248.1417 (M^+, 50%, calc. for $C_{15}H_{20}O_3$ 248.1412), 233 (63), 230 (30), 215 (52), 203 (31), 191 (28), 187 (31), 175 (45), 163 (100), 159 (35), 145 (36), 131 (25), 119 (63), 105 (40), 91 (60).

O-Acetyltetrahydromerulidial (**3b**)

Acetate **3b** was obtained from **1b** (20 mg) in the same manner as described for the conversion of **1a** into **3a**. Colourless oil which solidified on standing (16.8 mg, 85%); ^1H NMR (90 MHz): δ 0.56 (d, J = 5.5 Hz, 1H), 0.96, 1.05, 1.25, 2.13 (each s, 4 CH_3), 3.42, 4.28 (AX-system, J = 12.5 Hz, 2H), 4.29 (s, 2H), 5.08 (d, J = 9.5 Hz, 1H), other signals not resolved; MS: m/z 294.1828 (M^+, 0.2%, calc. for $C_{17}H_{26}O_4$ 294.1831), 248 (3), 236 (4), 234 (6, $C_{15}H_{22}O_2$), 230 (7), 216 (29, $C_{15}H_{20}O$), 203 (56, $C_{14}H_{19}O$), 201 (28, $C_{14}H_{17}O$), 186 (100, $C_{14}H_{18}$), 185 (81, $C_{14}H_{17}$), 175 (21), 173 (70), 171 (27), 159 (23), 158 (12), 157 (24), 143 (30), 131 (20), 119 (33), 105 (25).

Oxidation of **1a** with pyridinium chlorochromate

1a (100 mg) was added to an ice-cold stirred suspension of pyridinium chlorochromate[15] (150 mg) and NaOAc (150 mg) in dichloromethane (3 ml). The mixture was allowed to warm up to 25°, and the CO_2 evolution was followed by means of a tube filled with aqu. $Ba(OH)_2$. When CO_2 ceased to be evolved, ether (10 ml) was added and the precipitate was filtered off. After careful washing with ether the filtrates were evaporated in vacuo. Chromatography of the residue over silica gel (eluent: CCl_4/EtOAc 1:1) yielded **6** (25 mg, 28%) and **5** (3 mg).

5: Oil; ^1H NMR (90 MHz): δ 1.08, 1.20, 1.31 (each s, 3 CH_3), 1.53 (s, OH), 1.62, 1.76 (AB-system, J = 5.5 Hz, 2H), 1.87, 1.89 (AB-system, J = 12 Hz, 2H), 2.46 (s, OH), 2.83, 2.93 (AB-system, J = 18 Hz, 2H), 3.73 (s, 1H), 9.57 (s, 1H), 9.97 (s, 1H); MS: m/z 264 (0.5%), 237 (7), 207 (6), 179 (7), 161 (7), 127 (35), 111 (25), 99 (100), 82 (25), 81 (45), 69 (38).

6: Oil, $[\alpha]_D^{20}$ -35.5° (c = 0.04, $CHCl_3$); IR (CCl_4): 2980 (m), 2960 (m), 2900 (w), 1723 (s), 1677 (ss), 1630 (w), 1465 (w), 1430 (w), 1380 (w), 1365 (w), 1330 (m), 1300 (m), 1080 (m), 990 cm^{-1} (m); ^1H NMR (90 MHz): δ 1.14, 1.15, 1.42 (each s, 3 CH_3), 1.95, 2.18 (AB-system, J = 5.5 Hz, 2H), 2.47, 2.69 (each m, 4H), 10.20 (s, 1H); MS: m/z 232.1099 (M^+, 12.7%, calc. for $C_{14}H_{16}O_3$ 232.1099), 205 (13), 204 (100, $C_{13}H_{16}O_2$), 203 (19, $C_{13}H_{15}O_2$), 190 (6), 189 (38, $C_{12}H_{13}O_2$), 176 (16, $C_{12}H_{16}O$), 162 (8), 161 (52, $C_{11}H_{13}O$), 148 (13, $C_9H_8O_2$), 147 (5, $C_{10}H_{11}O$), 143 (6, $C_{11}H_{11}$), 133 (14, $C_{10}H_{13}$), 128 (6, $C_{10}H_8$), 121 (7, C_8H_9O), 119 (5), 115 (7), 107 (11, C_7H_7O), 105 (10), 93 (6), 91 (22).

Determination of the absolute configuration of **1a** (Horeau method)[12]

A soln of **1a** (38 mg) and (±)-2-phenylbutanoic anhydride (209 mg) in anhydrous pyridine (2 ml) was stirred at 20°C for 24 h, after which time several drops of water were added, and the stirring was continued for an additional h. After addition of some benzene and water the organic acid formed was titrated against 0.1 N NaOH with phenolphthalein as indicator (12.38 ml of base were required which corresponds to an esterification yield of 71.9%). After separation of the benzene layer the aqueous phase was first washed with $CHCl_3$ and then acidified with N HCl. Extraction of the 2-phenylbutanoic acid with benzene (4 x 5 ml) and concentration of the dried extracts (Na_2SO_4) to 3 ml yielded a solution which exhibited an optical rotation of -0.070° at the sodium D line corresponding to an optical yield of 12.1%.[12]

Acknowledgements - We are pleased to acknowledge financial support by the Deutsche Forschungsgemeinschaft. Our thanks go to Dr. G. Eckhardt, Bonn, for MS spectra, to Mr. C. Schmidt, Bonn, for NMR measurements and to Mrs. A. Hovenbitzer for technical assistance.

REFERENCES AND NOTES

1. For Part 22, see S. Hilbig, T. Andries, W. Steglich and T. Anke, Angew. Chem. **97**, 1063 (1985); Angew. Chem. Int. Ed. Engl. **24**, 1063 (1985).
2. W. Quack, T. Anke, F. Oberwinkler, B.M. Giannetti and W. Steglich, J. Antibiot. **31**, 737 (1978).
3. O. Sterner, R. Carter, T. Liljefors and L. Nilsson, Mutation Research, submitted.
4. B.M. Giannetti, W. Steglich, W. Quack, T. Anke and F. Oberwinkler, Z. Naturforsch. **33c**, 807 (1978).
5. This work has been in part presented at the 12th IUPAC Symposium on the Chemistry of Natural Products, Puerto de la Cruz, Tenerife 1980; W. Steglich, Pure Appl. Chem. **53**, 1233 (1981).
6. Compare e.g. M.J. Jorgenson and T. Leung, J. Am. Chem. Soc. **90**, 3769 (1968) and references therein.
7. Review: A.J. Fatiadi, Synthesis **1976**, 65, 133.
8. A.A. Mandsley, L. Müller and R.R. Ernst, J. Magn. Reson. **28**, 463 (1977); G. Bodenhausen and R. Freeman, Ibid. **28**, 471 (1977); A. Bax and G.A. Morris, Ibid. **42**, 501 (1981).
9. L. Jackman and S. Sternhell, Applications of Nuclear Magnetic Resonance Spectrocopy in Organic Chemistry, p. 338, 2nd. ed., Pergamon Press, Oxford 1969.
10. A. Bax, R. Freeman and G. Morris, J. Magn. Reson. **42**, 164 (1981); A. Bax and R. Freeman, Ibid. **44**, 542 (1981).
11. A. Horeau, Tetrahedron Lett. **1961**, 506; A. Horeau, Ibid. **1962**, 965; A. Horeau and H.B. Kagan, Tetrahedron **20**, 2431 (1964).
12. A. Horeau in Stereochemistry, Fundamentals and Methods, H.B. Kagan, Ed., Vol. 3, p. 78, G. Thieme, Stuttgart 1977.
13. For related examples compare e.g. W. Herz and H.B. Kagan, J. Org. Chem. **32**, 216 (1967).
14. Review: W.A. Ayer and L.M. Browne, Tetrahedron **37**, 2199 (1981).
15. E.J. Corey and J.W. Suggs, Tetrahedron Lett. **1975**, 2847.
16. W.G. Dauben and D.M. Michno, J. Org. Chem. **42**, 682 (1977).
17. W.M. Daniewski, M. Kocór and S. Thorén, Pol. J. Chem. **52**, 561 (1978).
18. W.A. Ayer and M.H. Saeedi-Ghomi, Tetrahedron Lett. **22**, 2071 (1981).
19. G. Magnusson, S. Thorén and B. Wickberg, Tetrahedron Lett. **1972**, 1105; G. Magnusson, S. Thorén and T. Drakenberg, Tetrahedron **29**, 1621 (1973). Reversal of absolute configuration of isovelleral (**10**) and marasmic acid (**11**): R. Bergman, L. Nilsson, O. Sterner and B. Wickberg, J. Am. Chem. Soc., submitted.
20. J.J. Dugan, P. de Mayo, M. Nisbet and M. Anchel, J. Am. Chem. Soc. **87**, 2768 (1965).
21. J. Kupka, T. Anke, K. Mizomoto, B. Giannetti and W. Steglich, J. Antibiot. **36**, 155 (1983).