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# Cyclisations of Tryptophans. II.† Protonated Species Derived from L-Tryptophan Methyl Ester and its $N_b$-Acetyl Derivative

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L-Tryptophan methyl ester has been shown to undergo protonation in the $N_b$ and 3-position in conc. $H_2SO_4$. The absolute configuration and solution structures of the resulting diastereomers have been assigned and are discussed. An assignment of $^1H$ and $^{13}C$ NMR signals is presented. After two days in $H_2SO_4$ the ester underwent sulfonation giving 5- or 6-monosulfonates and later 5,7-, 4,6-, 2,5-, and 2,6- disulfonates. $N_b$-Acetyl-L-tryptophan methyl ester was studied analogously in conc. $H_2SO_4$ and afforded the derivative diprotonated at the 3-position and the amide oxygen. However, sulfonation proceeded analogously to L-tryptophan methyl ester.

Protonation of $N_b$-acetyl-L-tryptophan methyl ester (**4**) in 85% $H_3PO_4$, $CF_3COOH$, or 70–85% $H_2SO_4$ occurs at the 3-position forming diastereomeric **5a** and **5b** which subsequently cyclise to pyrroloindoles **7a** and **7b** (Scheme 1).[1,2] Similar cyclisation reactions with $N_b$-methoxycarbonyl-L-tryptophan methyl ester have been investigated in previous papers in this series.[3,4] The cyclisation reaction requires a nucleophilic $N_b$-nitrogen. Accordingly, cyclisation is observed for neither the protonated forms **2** and **3** nor for **4** in conc. sulfuric acid, where the diprotonated species **6a** and **6b** are expected to predominate. However, attempts to characterize **6a** and **6b** by $^1H$ NMR spectroscopy have been unsuccessful.[2] UV spectroscopy does not distinguish between sites of protonation but may at best verify that it has occurred. Furthermore, in sulfuric acid sulfonation may mask the changes induced on protonation even in cases where the latter is reported to be reversible (cf. the NMR revision[5] of UV-results for gramine[6,7]). The postulated formation of the species **6a** and **6b** in conc. sulfuric acid is thus not experimentally supported. The aim of this paper is to present complete $^1H$ and $^{13}C$ NMR data for L-tryptophan methyl ester (**1**) and the $N_b$-acetyl derivative (**4**) as well as the corresponding mono- and di-protonated species. These results allow definite structural and conformational assignments and may serve as reference data for future investigations of acid-catalyzed reactions of indoles.

Monoprotonation of **1** to give **2** results in the expected shifts in the $^1H$ and $^{13}C$ NMR frequencies (Tables 1 and 3) towards lower and higher[8] fields, respectively. It is noteworthy that the shifts of H1 (0.32 ppm) and H2 (0.15 ppm) are considerably larger than those of H4–H7 (0.03–0.05 ppm). Obviously the positive center created on protonation in the side chain exerts a notable effect on the shielding of the proton of the pyrrole ring. Since the coupling constants of the α and β protons correspond to the usual average values for staggered conformations (5–8 Hz), the decreased shielding of H1 and H2 is compatible with essentially free rotation of the side chain. $^1H$ and $^{13}C$ NMR shifts for **4** are intermediate between **1** and **2** reflecting the influence of the resonance structure $NH_2^+ = C–O^-$ of the amide group.[9]

By analogy to theoretical,[10] synthetic,[11] and NMR spectroscopic[12,13] evidence from related indole derivatives diprotonisation of **1** is expected to give exclusively the diastereomeric 3-protonated derivatives **3a** and **3b**. The changes in chemical shift of C2 (124 to 176 ppm) and C3 (110 to 48 ppm) observed in **3a/b** (Table 3) confirm this expectation. Studies of cyclic tryptamines such as β-carbolines[14] and *Rauwolfia*-alkaloids[15] in strong sulfuric acid indicate that protonation of a fixed exocyclic nitrogen exerts a strong electrostatic destabilizing effect on indole ring protonation. Accordingly, only the extended conformations of **3a/b** were expected, i.e., with the side chain $NH_3^+$ and indolic $–CH = NH^+–$ as far apart as

† Part I, see Ref. 3
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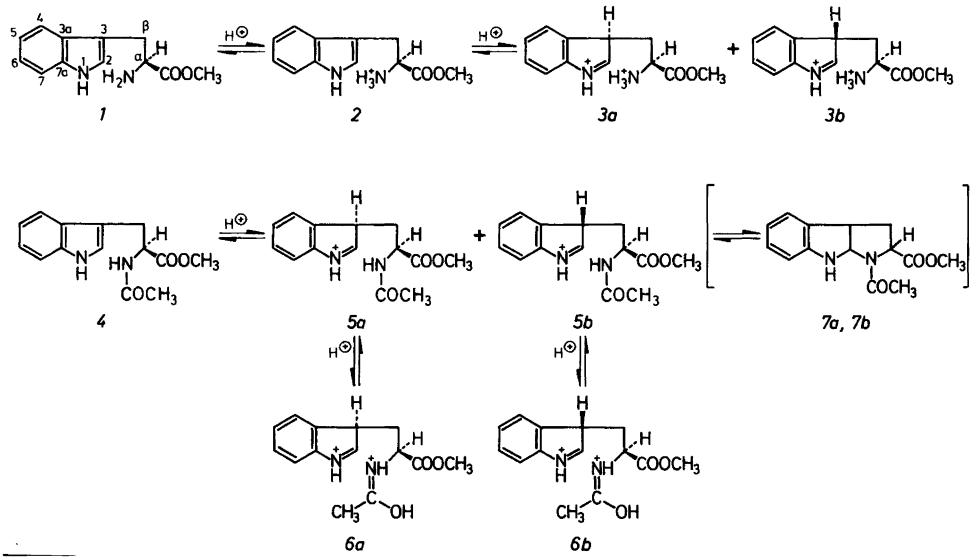

*Scheme 1.*

*Table 1.* $^1$H NMR spectra of L-tryptophan methyl ester 1, hydrochloride **2**, and $N_b$-acetyl derivative **4** in DMSO-$d_6$.

| Position | 1 | 2 | 4 |
|---|---|---|---|
| 1 | 10.84 s, br | 11.17 s, br | 10.95 s, br |
| 2 | 7.12 d (2) | 7.27 d (2) | 7.14 d (2) |
| 4 | 7.48 d (8) | 7.52 d (8) | 7.48 d (8) |
| 5 | 6.97 td (8, 1) | 7.01 td (8, 1) | 6.95 td (8, 1) |
| 6 | 7.06 td (8, 1) | 7.09 td (8, 1) | 7.06 td (8, 1) |
| 7 | 7.33 d (8) | 7.38 d (8) | 7.34 d (8) |
| α | 3.63 t (6.4) | 4.19 dd (7.0, 5.5) | 4.5 ddd (8.2, 7.5, 5.7) |
| β | 3.02 dd (14.2, 6.4) | 3.38 dd (14.7, 5.5) | 3.14 dd (14.7, 5.7) |
| | 2.94 dd (14.2, 6.4) | 3.30 dd (14.7, 7.0) | 3.03 dd (14.7, 8.2) |
| $COOCH_3$ | 3.57 s | 3.63 s | 3.58 s |
| $COCH_3$ | | | 1.82 s |
| $N_bH$ | 3.33 s, br | 8.73 s, br | 8.32 d (7.5) |

*Table 2.* $^1$H NMR spectra in conc. $H_2SO_4$ of diprotonated L-tryptophan methyl ester (**3a**, **3b**) and acetyl derivatives (**6a**, **6b**).

| Position | **3a** (55%) | **3b** (45%) | **6a** (58,3%) | **6b** (41.7%) |
|---|---|---|---|---|
| 1 | 11.91 | 12.05[a] | 11.90[a] | 12.00[a] |
| 2 | 8.37[a] | 8.37[a] | 8.35 d (6) | 8.35 d (6) |
| 3 | 3.80[a] | 3.80[a] | 3.76 dd (5, 5) | 3.68 dd (8, 8) |
| 4 | 6.84 d (7) | 6.86 d (7) | 6.85 d (7) | 6.87 d (7) |
| 5 | 6.77 t (7) | 6.77 t (7) | 6.78 t (7) | 6.78 t (7) |
| 6 | 6.80 t (7) | 6.80 t (7) | 6.82 t (7) | 6.82 t (7) |
| 7 | 6.90 d (7) | 6.92 d (7) | 6.93 d (7) | 6.95 d (7) |
| α | 3.23 qdd (4.6, 10, 2) | 3.63 qdd (4, 9, 5) | 3.83 ddd (8, 7, 7) | 4.10 ddd (8, 8, 8) |
| β | 2.20 ddd (12, 10, 2–4) | 1.92 ddd(13, 9, 4) | 2.20 ddd (15, 7, 5) | 1.94 ddd (15, 7, 5) |
| | 1.80 ddd (12, 2, 9) | 1.72 ddd (13, 5, 5) | 1.92 ddd (15,8, 8) | 1.87 ddd (15, 8, 8) |
| $NH_3^+$ | 5.97 d (4.6) | 6.05 d (4) | | |
| $COOCH_3$ | 3.00 s | 2.90 s | 3.00 s | 2.90 s |
| $CONH^+$ | | | 8.20 d (8) | 8.31 d (8) |
| $COCH_3$ | | | 1.58 s | 1.70 s |

[a] Broad signals or unresolved multiplets.

possible. The average structure of **3a/b** in conc. $D_2SO_4$ was studied by NOE difference measurements for three different concentrations (0.10–0.26 M). Irradiation of the (overlapping **3a/b**) H2 proton signals at 8.37 ppm gave rise to identical NOE enhancements of both $NH_3^+$ signals at 5.97 ppm (**3a**) and 6.05 ppm (**3b**) increasing with concentration from 4% (0.10 M) to 15% (0.26 M). Smaller enhancements were observed of all signals from Hα and Hβ protons increasing from almost zero (0.10 M) to 6–8% (0.26 M). Although the results are

*Table 3.* $^{13}C$ NMR spectra of L-tryptophan methyl ester (**1**) and derivatives (**2–6**).

| Position | 1 | 2 | 3a | 3b | 4 | 6a | 6b |
|---|---|---|---|---|---|---|---|
| 2 | 123.7 | 124.8 | 176.0 | 175.8 | 123.7 | 176.7 | 177.3 |
| 3 | 110.0 | 106.2 | 48.2 | 47.9 | 109.6 | 49.4 | 48.9 |
| 3a | 127.5 | 126.8 | 130.4 | 131.5 | 127.2 | 131.8 | 132.4 |
| 4 | 118.3 | 117.8 | 115.9 | 115.9 | 117.9 | 116.7 | 116.7 |
| 5 | 118.4 | 118.4 | 128.8[a] | 128.8[a] | 118.5 | 129.6[a] | 129.6[a] |
| 6 | 120.9 | 121.0 | 129.6[a] | 129.6[a] | 121.0 | 130.4[a] | 130.4[a] |
| 7 | 111.4 | 111.4 | 122.4 | 122.6 | 111.5 | 123.4 | 123.4 |
| 7a | 136.2 | 136.1 | 138.0 | 138.0 | 136.2 | 139.0 | 138 |
| α | 55.2 | 52.6 | 49.2 | 50.5 | 53.3 | 51.9 | 52.6 |
| β | 30.8 | 26.0 | 25.0 | 25.3 | 27.2 | 27.0 | 27.2 |
| $COOCH_3$ | 175.6 | 169.5 | 167.2 | 167.5 | 172.6 | 169.5 | 169.4 |
| $COOCH_3$ | 51.4 | 52.4 | 53.8 | 53.8 | 51.8 | 54.5 | 54.5 |
| $COCH_3$ | | | | | 22.4 | 18.4 | 18.5 |
| $COCH_3$ | | | | | 169.4 | 178.1 | 178.6 |

[a] May be interchanged.

concentration dependent, they indicate similar side chain conformations in **3a** and **3b** with H2 close to the $NH_3^+$ group.

These conformations of **3a/b** with spatially close positive N atoms must be due to solvent properties. Conc. sulfuric acid is much more highly organized than water both in the solid[16–18] and the liquid state.[19] It is strongly hydrophilic and lipophobic and is markedly able to decrease electrostatic repulsion between like ions.[20–22] Studies of micelle formation of cations connected to a paraffinic chain indicate that salts may be accommodated without major disturbance of the sulfuric acid structure provided they are present as hydrogen sulfates.[20–22] Therefore, **3a/b** are probably stabilized in conc. sulfuric acid as tight ion-pairs with two chelating hydrogen sulfate ions. One of these connects the $NH_3^+$ and indolic $C=NH^+$ while the other may connect $NH_3^+$ with the $COOCH_3$ moiety.

Based on NOE results and coupling constant analysis of the H3 –Hα–Hβ's spin system (which was almost independent of concentration), **3a/b** were assigned the structures shown in Fig. 1. First, the diastereomers differ in the position of the COOMe group, in one case situated close to the plane of the indole ring and far removed in the other. Since irradiation of signals from the ester Me at 3.00 (**3a**) and 2.90 ppm (**3b**) gave rise to an NOE enhancement of only the H2 signal in the former case (3%), **3a** must be assigned the stereochemistry (*S*)-Cα, (*R*)-C3 and **3b** (*S*)-Cα, (*S*)-C3 as shown.

Second, the coupling constants between H3 and the hydrogens of the β-$CH_2$ group of **3b** indicate H–H angles of ca. 150° ($J=4$ Hz) and 30° ($J=5$ Hz) compatible with a partial *gauche* side conformation. Hα is situated *trans* to one Hβ ($J=9$ Hz) and *gauche* to the other ($J=5$ Hz). This conformation minimizes the repulsion between the positively charged nitrogen atoms which are held together by the hydrogen sulfate ion. The side chain in **3a** is attached to the indole ring with angles of 60° ($J=2$ Hz) and 180° ($J=9$ Hz) corresponding closely to a *gauche* conformation, while Hα is situated between the two Hβ atoms with angles of 30° ($J=5$ Hz) and 150° ($J=4$ Hz). The increased rotation of the side chain in **3a** relative to **3b** allows the COOMe group to be located between H2 and H3 orienting the C=O dipole towards the positively charged C2.

Interpretation of the NMR spectra of **3a/b** in conc. sulfuric acid was possible only by taking into account the progression of two slow reactions. First, in deuteriated sulfuric acid, H/D exchange in specific positions of the tryptophan ring[23] occurs with different rates reaching equilibrium in 2–3 days. Second, in conc. sulfuric acid tryptophan and its derivatives may undergo sulfonation to give mixtures of sulfonic acids. Previously, sulfonation of tryptophan with the 1:1 pyridine–$SO_3$ adducts[24] and chlorosulfonic acid[25] has been described and it is concluded[25] that only traces of sulfonated products are formed when a 10% solution of sulfuric acid in trifluoroacetic acid is left overnight. However, in pure conc. sulfuric acid slow changes in the aromatic region were ob-

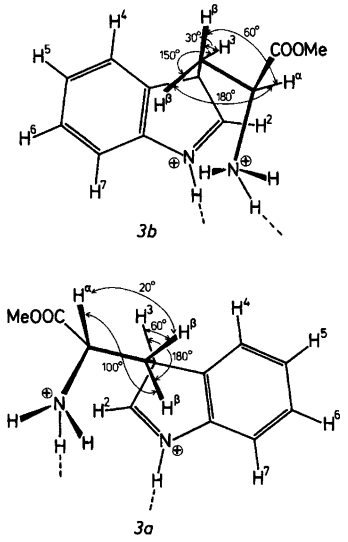


*Fig. 1.* Conformation of diastereomeric **3a** and **3b** in conc. sulfuric acid solution.

served and, in order to interpret this result, the sulfonated products were characterized. In the case of tryptophan, 5- and 6-monosulfonation is succeeded by 5,7- and 4,6-disulfonation and eventually the 2,5,7- and 2,4,6-trisulfonic acids are formed. Sulfonation of the methyl ester **1** proceeded at a slower rate, and even at day 5 trisulfonates were not observed. However, after two days a 5- or 6-monosulfonate was present, and later 5,7-, 4,6-, 2,5-, and 2,6-disulfonates were formed. The position of sulfonation in the benzene ring seems to be identical with that reported for gramine in conc. sulfuric acid[5] as expected if the 3-protonated species are involved in both cases. However, the distribution of isomers and rate of sulfonation are clearly dependent on the 3-substituent.

The $^1$H NMR spectra of **6a/b** and **3a/b** are similar except that the coupling constants of the side chain suggest that both diastereomeric forms have the same conformation. The integrated intensity of the signal from the $NH^+$ proton and the observed coupling to Hα verifies that the amide group in **6** (as usual[26]) is *O*-protonated. One of the hydrogen sulfate ions may thus be chelated to N and OH of the amide group giving rise to a conformer stability different from **3a/b**. The positive charge acquired by the amide group in conc. sulfuric acid explains why cyclisation is not observed.

## Experimental

*General methods.* The $^1$H and $^{13}$C NMR spectra were recorded on a Bruker 250 AM or on a Varian XL-400 spectrometer, operating at 250 or 400 MHz for protons, and at 62.9 or 100.6 MHz for carbon, respectively. Tetramethylsilane (TMS) was used as an internal standard for spectra recorded in DMSO-$d_6$. Spectra in conc. sulfuric acid were recorded with decoupling of the OH signal (11.3 ppm) and with benzene as an external standard. The spectra listed in the tables were assigned completely using standard tables and methods (deuteriation with $D_2SO_4$, spin decoupling, COSY, HETCOR). Coupling constants are given in Hz. Assignment of the aromatic protons (H4–H7 was, moreover, aided by recording the spectra of 5-methyltryptophan, where signals arising from H4, H6, and H7 could be unambiguously identified). The coupling constants given in the tables are the best values obtained from these experiments, but are not necessarily observed in all spectra. Owing to the increased line broadening in spectra recorded of solutions in conc. sulfuric acid, most spin–spin coupling constants observed in this medium are given to the nearest integral values. The solutions used for NMR experiments were **1**: 0.11 M in $H_2SO_4$ (for the tables) and 0.10 M, 0.14 M, and 0.26 M in $D_2SO_4$ (for NOE experiments), and **4**: 0.03 g $N_b$-acetyl-L-tryptophan methyl ester dissolved in 1.08 g $H_2SO_4$. When comparing spectra of the sulfonated compounds in $D_2O$, the OH signal was used as internal reference, and accordingly only the relative values are precise.

*Materials.* L-Tryptophan methyl ester hydrochloride (**2**) was from Fluka (art. 93730). DL-5-Methyltryptophan was from Aldrich (art. M8,672-3) 98% pure. $D_2SO_4$ was from Fluka (art. 36780) 96–99% pure.

*$N_b$-Acetyl-L-tryptophan methyl ester (**4**).* was prepared and purified according to the directions given by Huang *et al.*[27] M.p. 149.5–151°C (lit.[27] m.p. 152.5°C). Anal: $C_{14}H_{16}O_3N_2$: C, H, N.

*L-Tryptophan methyl ester (**1**).* L-Tryptophan methyl ester hydrochloride (2 g) was dissolved in 5 ml of $H_2O$, and 40 ml of NaOH were added. The mixture was stirred for 1 h followed by extraction with ether (4 × 50 ml). The organic layer was dried over anhydrous magnesium sulfate for 24 h and concentrated *in vacuo*. Anal. $C_{12}H_{15}O_2N_2$: C, H, Cl, N.

*Sulfonation of tryptophan.* DL-Tryptophan (10 g, 49 mmol) was dissolved in conc. sulfuric acid (35 ml), cooled in ice and left at room temperature for 7 days until all tryptophan had reacted. The mixture was poured onto ice, neutralized (NaOH) and freeze-dried to give 103 g crude product (including inorganic salt). This (5 g in 15 ml $H_2O$) was fractionated by column chromatography (Sephadex G 25, UV detection at 206 and 254 nm) to give two fractions, **F1** (1.5 g) and **F2** (0.7 g) characterized by $^1$H NMR spectroscopy in $D_2O$. The pattern from the side chain was retained in both fractions. **F1** was a mixture of two disulfonates (**A** and **B**) and two trisulfonates (**C** and **D**) identified by differences in intensity, chemical shift, and coupling constants (with decoupling experiments when necessary) for the aromatic protons of the $^1$H NMR spectrum in $D_2O$. **F2** was pure **D**.

Compounds **A** and **B** are *tryptophan-4,6- and -5,7-disulfonates* with singlets from H2 and *meta*-couplings of the remaining protons. **A** [20% of **F1**; δ 7.53 (s, H2), 8.02 (d, $J$ = 1.6, 1 H), 8.05 (d, $J$ = 1.6, 1 H)] was easily recognized by the close spacing (0.03 ppm) of the aromatic proton signals. **B** [35% of **F2**; δ 7.44 (s, H2), 7.93 (d, $J$ = 1.6, 1 H), 8.26 (d, $J$ = 1.6, 1 H)] had a much higher spacing (0.33 ppm) of the aromatic signals. These spacings are very similar to those found (0.04 and 0.22 ppm) in the gramine-4,6- and -5,7-disulfonates.[5] Compounds **C** and **D** without singlets from H2 are *tryptophan-2,4,6- and -2,5,7-trisulfonates*. **C** [12% of **F1**; δ 8.09 (dd, $J$ = 1.6, 2 H)] had almost superimposed aromatic protons and is undoubtedly derived from **A** by further sulfonation. **D** [35% of **F1**; δ 8.05 (d, $J$ = 1.6, 1 H), 8.34 (d, $J$ = 1.6, 1 H)] had a higher spacing corresponding to a trisulfonic acid derived from **B**.

*Sulfonation of tryptophan methyl ester hydrochloride.* Exploratory experiments showed that even after 8 days only 55% tryptophan methyl ester had been sulfonated. L-Tryptophan methyl ester hydrochloride (3.24 g, 12.7 mmol) was dissolved in conc. sulfuric acid (10 ml) cooled in ice and left at room temperature. After 2 days,

0.84 g was poured onto ice, neutralized (NaOH), freeze–dried, extracted with EtOH (separating unchanged tryptophan methyl ester), and fractionated by column chromatography as before to give three fractions with sulfonated compounds, **F1** (21 mg), **F2** (50 mg) and **F3** (34 mg). After 5 days 4.07 g were treated in the same way to give two fractions **F4** (8 mg) and **F5** (390 mg). Each of the five fractions was characterized as described above for the aromatic protons of the $^1$H NMR spectrum in $D_2O$. The pattern from the side chain appeared to be retained in all fractions. The 4,6- and 5,7-sulfonates are designated **A** and **B** as for tryptophan but trisulfonates corresponding to **C** and **D** were not found.

Compounds **A** and **B** are *methyl esters of tryptophan-4,6- and -5 7-disulfonates* with singlets from H2 and *meta*-couplings of the remaining protons. **A** [25% of **F5**; δ 7.45 (s, H2), 7.94 (d, $J$ = 1.6, 1 H), 8.26 (d, $J$ = 1.6, 1 H)]. Compounds **E** and **F** are *methyl esters of tryptophan-2,5-* and *-2,6-disulfonates* where the singlets from H2 are absent. **E** [50% of **F4**; δ 7.30 (d, $J$ = 8.2, 1 H), 7.55 (dd, $J$ = 1.1 and 8.2, 1 H), 7.97 (d, $J$ = 1.1, 1 H)]. **F** [40% of **F5**, 50% of **F3**; δ 7.58 (d, $J$ = 8.5, 1 H), 7.67 (dd, $J$ = 1.6 and 8.5, 1 H), 8.18 (d, $J$ = 1.6, 1 H)]. Compound **G** is the *methyl ester of tryptophan-6-* or *-7-sulfonate* [75% of **F2**; δ 7.44 (s, H2), 7.56 (d, $J$ = 8.5, 1 H), 7.68 (dd, $J$ = 8.5 and partly resolved *meta*-coupling, 1 H), 8.17 (d, $J$ = 1.5, 1 H)] with a pattern corresponding closely to that of **F**.

## References


1. Taniguchi, M. and Hino, T. *Tetrahedron 37* (1981) 1487.
2. Sammes, P. G. and Weedon, A. C. *J. Chem. Soc., Perkin Trans. 1* (1979) 3048.
3. Anthoni, U., Christophersen, C., Nielsen, P. H. and Pedersen, E. J. *Acta Chem. Scand. 48* (1994) 91.
4. Anthoni, U., Christophersen, C., Obel, A. and Nielsen, P. H. *Acta Chem Scand. 48* (1994) 334.
5. Fatum, T. M., Anthoni, U., Christophersen, C. and Nielsen, P. H. *Heterocycles 38* (1994) 1619.
6. Nowotarska, G. In: Marekov, N., Ed., *Symp. paper IUPAC 11th Int. Symp. Chem Nat. Prod.* Vol 2 (1978).
7. Nowotarska, G. and Podkowinska, H. *Rocz. Chem. 54* (1976) 789.
8. Breitmaier, E. and Voelter, W. *Carbon-13 NMR Spectroscopy*, VCH Weinheim Germany 1987, 3rd ed. p. 236.
9. Souhassou, M., Lecomte, C., Blessing, R. H., Aubry, A., Rohmer, M.-M., Wiest, R., Benard, M. and Marraud, M. *Acta Crystallogr., Sect. B 47* (1991) 253.
10. Catalan, J., Perez P. and Yanez, M. *Tetrahedron 58* (1982) 3693.
11. Brown, K. and Katritzky, A. R. *Tetrahedron Lett. 14* (1964) 803.
12. Yudin, L. G., Kost, A. N., Zinchenko, E. Ya. and Zhigulin, A. G. *Russian J. Heterocycl. Chem 8* (1974) 1070.
13. Jackson, A. H. and Smith, A. E. *J. Chem. Soc.* (1964) 5510.
14. Guzman, M. C. C., Almeida, M. B., Toledo, J. H., Perez, M. A. M. and Povead, M. L. *Can. J. Chem. 67* (1989) 720.
15. Balon, M., Carmona-Guzman, C. and Gonzalez, D. *Tetrahedron 41* (1985) 4703.
16. Pascard-Billy, P. C. *Acta Crystallogr. 18* (1965) 829.
17. Yu, P.-Y. and Mak, T. C. W. *J. Cryst. Mol. Struct. 8* (1978) 193.
18. Moodenbaugh, A. R., Hartt, J. E., Hurst, J. J., Youngblood, R. W., Cox, D. E. and Frazer, B. C. *Phys. Rev. B 28* (1983) 3501.
19. Andreani, C., Petrillo, C. and Sacchetti, F. *Mol. Phys. 58* (1986) 299.
20. Steigmann, J. and Shane, N. *J. Phys. Chem. 69* (1965) 968.
21. Menger, F. M. and Jerkunica, J. M. *J. Am. Chem. Soc 101* (1979) 1896.
22. Müller, A. and Miethchen, R. *J. Prakt. Chem. 330* (1988) 993.
23. Bak, A., Dambmann, C. and Nicolaisen, F. *Acta Chem. Scand. 21* (1967) 1674.
24. Baumgarten, P., Marggraff, I. and Dammann, E. *Hoppe-Seyler's Zeitsch. Physiol. Chemie 209* (1932) 145.
25. Previéro, A., Cavadore, J. C., Torreilles, J. and Coletti-Previero, M.-A. *Biochim. Biophys. Acta 581* (1979) 276.
26. Liler, M. *Reaction Mechanisms in Sulphuric Acid*, Academic Press, London 1971, p. 100.
27. Huang, H. T. and Niemann, C. J. *J. Am. Chem. Soc. 73* (1951) 1541.


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