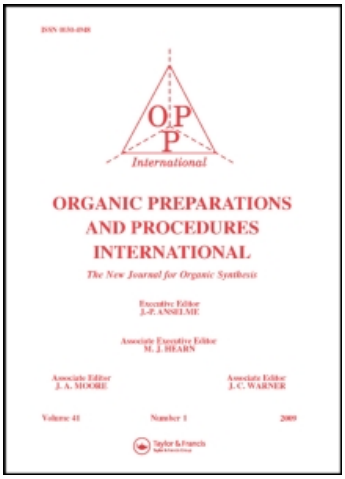

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L-DOPA-3-0-SULFATE BY THE PERSULFATE OXIDATION OF L-TYROSINE

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7.19-7.21 (m, 4H, Ar-H); 4.01 (t, 2H, OCH_2); 3.85 (s, 2H, $ArCH_2$-); 3.01 (t, 2H, $ArCH_2$); 2.56-2.70 (m, 6H, $CH_2N[CH_2]_2$); 0.85-2.16 (m, 13H, CH_2 and CH_3). ^{13}C NMR ($CDCl_3$): 156.5, 156.0, 154.1, 139.7, 139.5, 129.1, 123.5, 122.4, 119.0, 111.7, 110.9 (Ar carbons); 90.9 (= C-I); 71.2 (-OCH_2-); 52.1 (CH_2N); 47.8 ($N[CH_2]_2$); 30.5, 28.0, 26.3, 22.5 (-CH_2-); 13.9, 12.1 (CH_3). hydrochloride, mp. 119-121°.

Anal. Calcd for $C_{25}H_{31}NO_2I_2$: C, 47.56; H, 5.06; N, 2.22 Found: C, 47.54; H, 4.94; N, 2.52

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L-DOPA-3-O-SULFATE BY THE PERSULFATE OXIDATION OF L-TYROSINE

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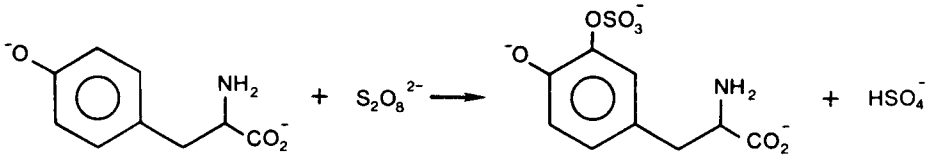
The Elbs persulfate oxidation of p-substituted phenols proceeds with poor yields of the catechol sulfates for unknown reasons;[1] the oxidation of L-tyrosine is no exception. A dark, polymeric melanin-like material is the major product.[2] Oxidation of the amino group does not appear to be responsible for the poor yields of the sulfate ester as this reaction is slow.[3] We have studied various factors which might influence the yield of the sulfate ester.[3] The best yields, as measured by the Folin-Denis phosphotungstic acid reagent,[4] were around 25% with a persulfate-tyrosine ratio between two and three;[3,5] the yield decreased with increasing concentration of alkali. Despite these relatively poor yields, we have carried out the isolation and

characterization of the title compound because of considerable interest in the related dopamine sulfates[6] and because persulfate oxidation yields the 3-O-sulfate without the ambiguity which



might attend procedures involving sulfonation of a dihydric phenol. Syntheses of L-DOPA sulfates have not been previously reported. There are many unidentified metabolites of L-DOPA.[7]

EXPERIMENTAL SECTION

L-DOPA-3-O-sulfate.- L-Tyrosine (9.05 g, 0.05 mol) was dissolved in a mixture of 100 ml of 28% aqueous NH_4OH and 3.3 g of 85.5% KOH (0.05 mol). The solution was cooled to room temperature and then a solution of 22.8 g (0.1 mol) $(NH_4)_2S_2O_8$ in 100 ml water was added slowly with stirring during 5 hrs. After three days, analysis[4] for L-DOPA following acid-catalyzed hydrolysis of the sulfate ester showed a yield of about 20%. The isolation was based on a procedure for tyrosine-O-sulfate.[8] The solution was evaporated to dryness in vacuo at 40°, taken up in 50 ml of water, and filtered. The insoluble material was largely tyrosine. The filtrate was treated with 0.2 mol of barium hydroxide and barium sulfate removed by gravity filtration. The filtrate was again evaporated to dryness in vacuo, taken up in 20 ml of water, and the additional tyrosine which had precipitated after standing overnight was centrifuged. The supernatant material was brought to pH 2 by batchwise treatment with Dowex-50, H^+. The resin was removed on a Buchner filter. Potassium hydroxide was carefully added to the filtrate to bring the pH to 5. The slow addition of ethanol and cooling gave crystals of the potassium salt of the sulfate ester as the monohydrate. Further crops of crystals may be obtained from the mother liquor if some of the colored material is removed by the following procedure. Both L-DOPA sulfate and the colored material are bound to DEAE cellulose, but L-DOPA sulfate is easily eluted with 2M NH_4OH while most of the colored material remains bound. Further crops of crystalline material may be obtained from these fractions by the addition of ethanol. No detectable racemization occurred during this synthesis as expected[9] as established by the rotation of the L-DOPA formed by acid-catalyzed hydrolysis of the sulfate ester: $[\alpha]_D^{25} = -11.4 \pm 1°$, lit.[10], -12.3°.

Anal. Calcd for $C_9H_{10}NO_7SK.H_2O$: C, 32.42; H, 3.63; N, 4.20; S, 9.62

Found : C, 32.88; H, 3.59; N, 4.27; S, 9.70

UV in water: λ_{max} 222,276.5 nm, ε 7630, 2070 $M^{-1}cm^{-1}$; in 0.09M KOH: λ_{max} 241,297

nm, ε 11,500, 3650 $M^{-1}cm^{-1}$.

Fluorescence in water, excitation at 276 nm: λ_{max} 317 nm; in base, excitation at 297 nm: λ_{max} 410 nm.

$[\alpha]D^{24}$ -27.3° (c, 2.78, D_2O), $[\alpha]_{578}^{24}$ -28.6° (c, 2.78, D_2O); $[\alpha]_{546}^{24}$ -32.5°(c, 2.78, D_2O).

The IR spectrum taken as a mull in fluorolube (4000-2000 cm^{-1}) and in nujol (2000-650 cm^{-1}) showed strong bands at 3600, 3480, 3130(br.), 1625, 1600, 1520, 1240, 1060, 980, 890, 805, & 710 cm^{-1}. The nmr spectrum (in D_2O, HDO at 4.63 ppm, 500 MHz) cleanly resolved all six non-exchangeable protons: Hβ 2.931 (dd, Jββ' 14.77, Jαβ 8.63); Hβ' 3.170 (dd, Jββ' 14.82, Jαβ' 4.83); Hα 3.870 (dd, Jαβ 8.66, Jαβ' 4.80); H_5 6.927 (d, J_{ortho} 8.33); H_6 7.009 (dd, J_{ortho} 8.34, J_{meta} 2.11); H_2 7.194 (d, J_{meta} 2.15) The positive ion FAB spectrum (glycerol matrix) showed prominent peaks at m/e 316 (MH+), 354 (MK+), and 392 MK_2+, -H).

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