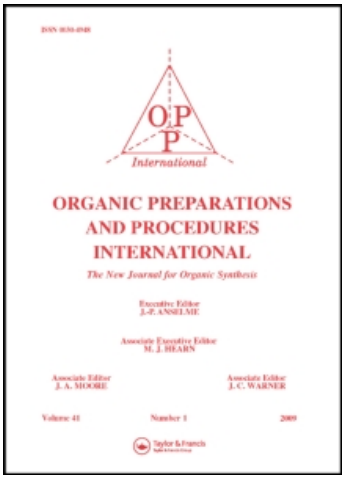

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AN IMPROVED SYNTHESIS OF 3,4-DIHYDRO-1H-2,1-BENZOTHIAZIN-4-ONE 2,2-DIOXIDE

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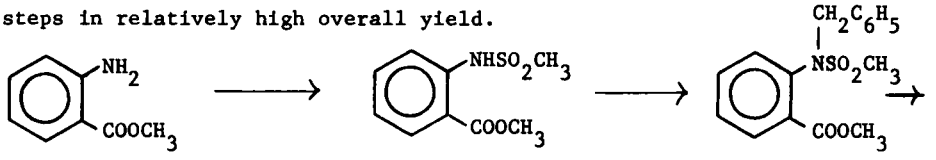
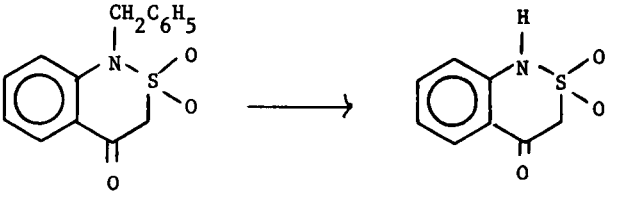
The title compound, 3,4-dihydro-1H-2,1-benzothiazin-4-one 2,2-dioxide (IV) is a valuable intermediate to "sulfostyryl"[1] and has also been functionalized to a variety of 2,1-benzothiazines.[2] Previously reported[1,3] syntheses of IV employed highly reactive intermediates, often difficult to prepare, and some of the steps in the multi-step procedures were of unspecified yield. Now, IV may be made in four short, convenient steps in relatively high overall yield.



(I) (II)



(III) (IV)

This new procedure now offers a much more facile general approach to the 2,1-benzothiazine 2,2-dioxide ring system.

EXPERIMENTAL

N-Methylsulfonylanthranilic acid methyl ester (I). To a stirred solution of 30.2 g (0.20 mole) of methyl anthranilate in 30 ml of ether was slowly added a solution of 11.4 g (0.10 mole) of methanesulfonyl chloride in 10 ml of ether. After stirring 19 hours at room temperature, another 5.7 g (0.05 mole) of methanesulfonyl chloride was added and the reaction mixture warmed 1 hr. at 40°, cooled and washed several times with water. After drying (calcium sulfate) and concentration, there was obtained a yellow oil which was crystallized from isopropanol to give 14.3 g (62%) of I as a white solid. An analytical sample prepared by recrystallization from isopropanol had mp 92-93° (corr.)

Anal. Calcd. for $C_9H_{11}NO_4S$: C, 47.15; H, 4.84; N, 6.11. Found: C, 47.15; H, 4.84; N, 6.14.

Methyl N-benzyl-N-methylsulfonylanthranilate (II). To a stirred suspension of 1.3 g (0.026 mole) of hexane-washed sodium hydride (50% in oil) in 50 ml of dry N,N-dimethylformamide, was slowly added a solution of 5 g (0.022 mole) of N-methylsulfonylanthranilic acid methyl ester (I). When gas evolution ceased, a solution of 11.2 g (0.06 mole) of benzyl bromide in 50 ml of ether was slowly added and the reaction stirred at room temperature for 1 hr. The reaction was then cooled and poured slowly into 500 ml of cold 3N hydrochloric acid to produce an oil which was extracted with ether. After drying (calcium sulfate) and concentration, there was obtained 6.9 g (99%) of II as a yellow, viscous oil. Ir: (KBr film) 13.23 and 14.35 μ (phenyl), no NH absorption near 3.0 μ. This liquid was used immediately in the next step.

1-Benzyl-4-oxo-3,4-dihydro-1H-2,1-benzothiazine 2,2-dioxide (III). To a stirred suspension of 1.2 g (0.0259 mole) of hexane-washed sodium hydride (50% in oil) in 35 ml of dry N,N-dimethylformamide, was slowly added a solution of 6.9 g (0.0216 mole) of ester II in 45 ml of dry N,N-dimethylformamide and the reaction stirred at room temperature for 4.5 hrs. The reaction was then poured into 500 ml of cold 3N hydrochloric acid and the soft, yellow precipitate was extracted with ether. The extracts were dried (calcium sulfate) and concentrated and the residue triturated with hexane to give a yellow solid (4.2 g, 68%) which was recrystallized from ethanol, mp 95-96°. Ir (KBr): 5.90 (C=O), 7.38 and 8.57 (SO_2), 13.05 and 14.75 μ (phenyl). NMR (in deuterodimethylsulfoxide): τ 1.87-2.88 (m, 9, aromatic protons), 4.78 (s, 2, $CO\underset{\sim}{CH_2}SO_2$), 4.94 (s, 2, $\underset{\sim}{CH_2}C_6H_5$).

Anal. Calcd. for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.88. Found: C, 62.88; H, 4.75; N, 4.74.

3,4-dihydro-1H-2,1-benzothiazin-4-one 2,2-dioxide (IV). A solution of 0.5 g (0.0017 mole) of III in 35 ml absolute ethanol was reduced with hydrogen within 1.5 hr at atmospheric pressure using 0.15 g of 10% palladium on carbon as catalyst. Filtration and concentration resulted in a yellow semi-solid which was triturated with hexane to give 0.23 g (68%) of IV. Recrystallization from ether-hexane gave mp 191-192° (corr.), lit.[1] mp 192°. An infrared spectrum was consistent with the reported[1] spectrum. Nmr: (in deuterodimethylsulfoxide) τ 2.02-2.95 (m, 5, aromatic protons), 5.25 (s, 2, $\underset{\sim}{CH_2}$, exchanges with D_2O).

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