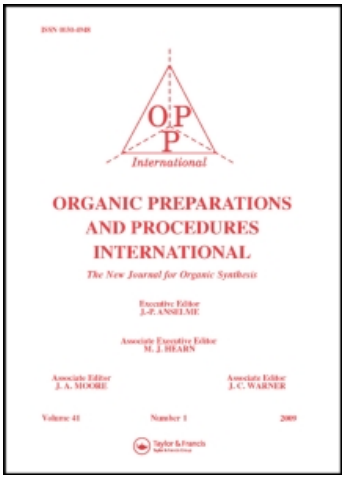

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N-CARBOXYMETHYL-1,2-BENZISOTHIAZOLIN-3-ONE-1,1-DIOXIDE

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N-CARBOXYMETHYL-1,2-BENZISOTHIAZOLIN-3-ONE-1,1-DIOXIDE

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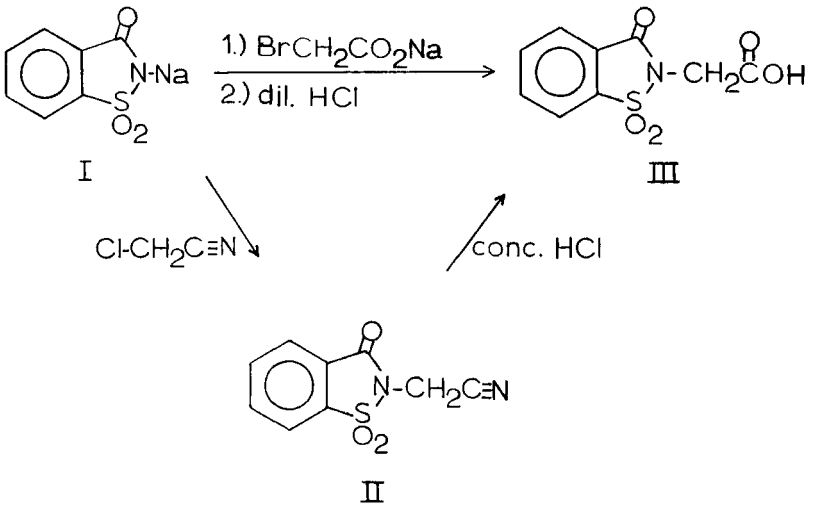
N-Carboxymethyl-1,2-benzisothiazolin-3-one-1,1-dioxide (III) is needed in our studies as a precursor in preparing a series of compounds for screening for central nervous system activity. It has been obtained in 20% yield by hydrolysis of its ethyl ester with hydrochloric acid.[2] Abe and co-workers[3] hydrolyzed the ester with silver acetate solution to give III in 7.6% yield. The above methods require up to 5.5 hours total reaction time. The following two novel syntheses require shorter reaction time and give notably higher yields of III.



The sodium salt of 1,2-benzisothiazolin-3-one-1,1-dioxide (sodium saccharin) was treated with sodium bromoacetate in N,N-dimethylformamide (DMF), followed by acidification with dilute hydrochloric acid to give III in 79% yield. Sodium saccharin was also treated with chloroacetonitrile in DMF to give N-cyanomethyl-1,2-benzisothiazolin-3-one-1,1-dioxide (II), which was then hydrolyzed with concentrated hydrochloric acid to give III in 65% overall yield.

EXPERIMENTAL

N-Carboxymethyl-1,2-benzisothiazolin-3-one-1,1-dioxide (III). To a stirred solution of sodium saccharin (4.1 g, 0.02 mole) dissolved in 20 ml DMF was added sodium bromoacetate (3.22 g, 0.02 mole). The solution was heated under reflux for 30 minutes (white solid precipitated) and filtered while hot. The solvent was removed by distillation under reduced pressure leaving a solid residue which was taken up in 30 ml water. On acidification with dil. hydrochloric acid to pH 1, a solid precipitated. The solid was recrystallized from water to give 3.8 g (0.158 mole, 79% yield) of III, mp. 215-216° (lit.[2] 212-215°); nmr (acetone) δ4.5 (s, 2, $-CH_2-$), 5.5 (s, 1, OH[4]), and 7.5-7.9 (m, 4, benzo); ir (KBr) 1720 (C=O) and 3470 cm^{-1} (OH).

N-Cyanomethyl-1,2-benzisothiazolin-3-one-1,1-dioxide (II). To a stirred solution of sodium saccharin (11.8 g, 0.058 mole) dissolved in 30 ml DMF was added chloroacetonitrile (5.0 g, 0.071 mole). After being heated under reflux for 30 minutes with constant stirring (white solid precipitated), the reaction mixture was cooled to room temperature and treated with 60 ml water. The product precipitated as a solid and was recrystallized from aqueous ethanol to give 11.2 g (0.05 mole, 88% yield) of II, mp. 142-143°; nmr (acetone) δ4.93 (s, 2, $-CH_2-$) and 8.0-8.4 (m, 4,

benzo); ir (KBr) 1740 cm^{-1} (C=O).

Anal. Calcd for $C_9H_6N_2O_3S$: C, 48.64; H, 2.72; N, 12.61. Found: C, 48.60; H, 2.72; N, 12.75.

Hydrolysis of II to III. A stirred mixture of conc. hydrochloric acid (75 ml) and of N-cyanomethyl-1,2-benzisothiazolin-3-one-1,1-dioxide (16.7 g, 0.75 mole) was heated under reflux for 15 minutes. Upon cooling, a white solid precipitated which was filtered and recrystallized from water giving 13.4 g (0.056 mole, 74% yield) of III, mp. 215-216°.

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