

Carboxylation of Sydnone

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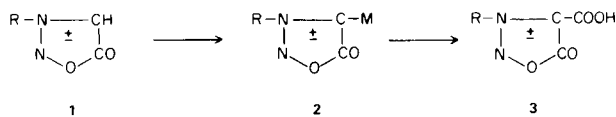
Received August 6, 1971

A previous report (2) described the direct lithiation and subsequent carboxylation of 3-phenylsydnone (1, R = Ph). It has been stated that 3-phenylsydnonylmagnesium bromide (2, R = Ph, M = MgBr) failed to react with carbon dioxide although it otherwise reacted normally. We now describe our results which are inconsistent with that finding (3).

The carboxylation of 3-phenylsydnone (4) occurred readily when after direct treatment with ethylmagnesium bromide the resultant 3-phenylsydnonylmagnesium bromide was treated with carbon dioxide. Similarly, the aralkylsydnone, benzylsydnone (5) (1, R = PhCH₂) with ethylmagnesium bromide probably yielded only 3-benzylsydnonylmagnesium bromide (2, R = PhCH₂, M = MgBr) since on carbonation only 3-benzylsydnone-4-carboxylic acid (3, R = PhCH₂) was obtained (39%). There appeared to be no involvement of the benzylic hydrogens in this reaction.

To dispel any doubts concerning the scope of the direct metalation procedures (2,6) we also wish to describe here the lithiation of an alkylsydnone, 3-methylsydnone (7), (1, R = Me) and its subsequent carbonation to 3-methylsydnone-4-carboxylic acid (3, R = Me). Again, no reaction involving the methyl group was observed.

The yields of the pure acids indicate the electronic effects of the substituents at position three of the sydnone ring to not radically influence the reactivity of the 4-methine proton in the formation of organometallic derivatives.



EXPERIMENTAL (8)

3-Phenylsydnone-4-carboxylic Acid.

To a solution of 3-phenylsydnone (3.24 g., 0.02 mole) in 70 ml. of tetrahydrofuran (THF) was added 25 ml. of ethylmagnesium bromide (0.05 mole) at 3° and stirred one hour. The slurry was poured over 100 g. of dry ice and stirred one hour. Water (200 ml.) was added and the reaction mixture washed with 3 x 100 ml. of benzene. The aqueous layer was acidified with 6 ml. of concentrated hydrochloric acid (0.075 mole) to afford 1.94 g. (47%) of the title acid, m.p. 190-191°. Two recrystallizations from

ethyl acetate yielded pure acid (0.68 g., 16%), m.p. 191-192°; ir 3.3-3.9 μ (broad OH), 5.55 (COOH), and 5.95 (sydnone carbonyl); uv λ max 220 (log ϵ 3.43) and 311 nm (3.22); nmr (deuterioacetone-trile) δ 7.63 (s, 5H, phenyl), 5.81 (broad s, 1H, COOH).

Anal. Calcd. for C₉H₆N₂O₄: C, 52.43; H, 2.93; N, 13.59. Found: C, 52.57; H, 3.03; N, 13.58.

3-Benzylsydnone-4-carboxylic Acid.

As described above, 3-benzylsydnone (3.52 g., 0.02 mole) and ethylmagnesium bromide (0.04 mole) were reacted at 5° and after the treatment with dry ice, 200 ml. of water was added. The entire reaction mixture was acidified with hydrochloric acid (4 ml., 0.05 mole) and then extracted with 3 x 50 ml. of ethyl acetate. Evaporation of the ethyl acetate extract yielded the title carboxylic acid (1.70 g., 38.7%), m.p. 142-147°. One crystallization from ethanol afforded pure acid (1.10 g., 25%), m.p. 152-154°; ir 3.3-4.0 μ (broad OH), 5.6 (COOH) and 5.95 (sydnone carbonyl); uv λ max 210 nm (log ϵ 3.84), 305 (3.74); nmr (Me₂SO-d₆) 7.41 δ (s, 5H, phenyl), 6.62 (broad s, 1H, COOH) and 6.01 (s, 2H, -CH₂-).

Anal. Calcd. for C₁₀H₈N₂O₄: C, 54.55; H, 3.66; N, 12.72. Found: C, 54.22; H, 3.65; N, 12.95.

3-Methylsydnone-4-carboxylic Acid.

To a solution of 3-methylsydnone (1.0 g., 0.01 mole) in 45 ml. of THF was added *n*-butyllithium (7.6 ml., 0.011 mole) at -20° and, after 1 hour stirring, 20 g. of dry ice was added and stirring continued an additional hour. The slurry was treated with 50 ml. of water followed by acidification with concentrated hydrochloric acid (2 ml., 0.025 mole). The reaction mixture was extracted with ethyl acetate (4 x 50 ml.) and the extract evaporated. Crystallization of the residue from ethyl acetate afforded the title compound (0.73 g., 51%), m.p. 160-165°. Three recrystallizations from ethyl acetate gave 0.28 g. (20%) of pure acid, m.p. 165-166°; ir 2.9-3.4 μ (broad OH); 5.73 (COOH); and 5.88 (sydnone carbonyl); uv λ max 221 (log ϵ 4.95) and 300 nm (4.93); nmr (Me₂SO-d₆) 6.86 δ (broad s, 1H, COOH) and 4.28 (s, 3H, CH₃).

Anal. Calcd. for C₄H₄N₂O₄: C, 33.34; H, 2.80; N, 19.44. Found: C, 33.23; H, 3.15; N, 19.52.

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(8) The ir spectra were measured by the potassium bromide pellet technique, the uv spectra were measured in absolute methanol

and the nmr spectra performed on a Varian A60A, chemical shifts in ppm (δ) with TMS as internal standard. All reactions were performed under a nitrogen atmosphere. The ethylmagnesium bromide was purchased from Matheson, Coleman and Bell and the *n*-butyllithium from Foote Mineral Co., Pa. All microanalyses were performed by Childers Laboratories, Milford, N. J.