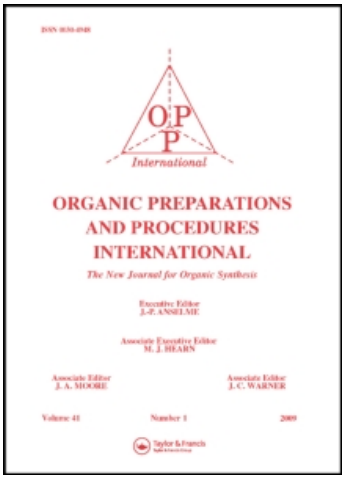

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A CONVENIENT ONE-POT SYNTHESIS OF 2-METHYL-2-BENZYLTHIOPROPANAL

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A CONVENIENT ONE-POT SYNTHESIS OF 2-METHYL-2-BENZYLTHIOPROPANAL

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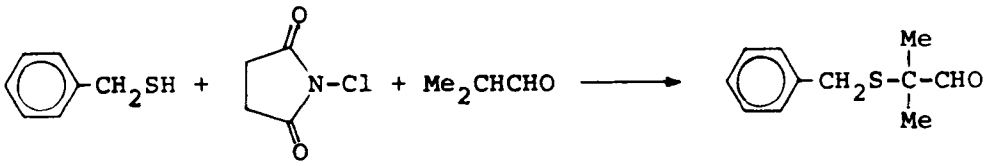
During a synthetic effort aimed at the development of novel chelating bis(aminoethanethiol) ligands, it became necessary to prepare 2-methyl-2-(benzylthio)propanal. The most recent of the four literature references,[1-4] a Russian patent,[1] describes the controlled addition of sulfuryl chloride to a mixture of benzyl mercaptan and isobutyraldehyde at two time points during the reaction. In a Japanese patent, the synthesis of the title compound was reported in roughly 75% yield via hydrolysis of the corresponding dimethyl acetal.[2] Retrosynthetically, 2-methyl-2-benzylthiopropanal dimethyl acetal could have been prepared from the corresponding α-halo analog which was obtained from isobutyraldehyde dimethyl acetal. A similar route has been described which afforded 2-methyl- 2-bromopropanal diethyl acetal in an overall yield of about 25% from isobutyraldehyde.[5] There are two essentially identical reports of the synthesis of the title compound in virtually quantitative yield by the reaction of 2-methyl-2-bromopropanal (derived from the diethyl acetal) with sodium benzylthiolate.[3,4] However, the overall yield of the α-sulfenylated aldehyde by this method was probably closer to 25% when the preparation of the requisite precursor is taken into account. Improved methods for the preparation of 2-methyl-2-bromopropanal have been reported;[6,7] however, each method requires two or more steps or the purchase of rather expensive brominating agents.

We now report an efficient, one-step synthesis of 2-methyl-2-benzylthiopropanal from equimolar amounts of benzyl mercaptan, isobutyraldehyde and N-chlorosuccinimide. This route obviates the controlled addition and multi-step methods employed previously and affords the product in 40-50% yield.



EXPERIMENTAL SECTION

2-Methyl-2-benzylthiopropanal.- Benzyl mercaptan (11.7 mL, d 1.058, 0.1 mol) in 75 mL

benzene was added dropwise to a suspension of N-chlorosuccinimide (13.35 g, 0.1 mol)[8] in 300 mL benzene containing isobutyraldehyde (7.21 g, 0.1 mol) stirred at 40°. After 12 hrs, the reaction mixture was filtered and the filtrate was concentrated to about 50 mL, then refiltered. In this manner, a nearly quantitative yield of succinimide was obtained. Concentration of the filtrate afforded a golden liquid which was distilled in vacuo to give 9.27 g (48%) of a colorless liquid, bp. 115-130°/2 mm, lit.[2] bp. 90-115°/7 mm, lit.[3,4] bp. 144-147°/14 mm; n_D^{20} 1.5460, lit.[3,4] n_D^{21} 1.5450; mp. of 2,4-dinitrophenylhydrazone 120-121° (EtOH), lit.[4] mp. 122°; ^{1}H NMR (60 MHz; CCl_4): δ 1.34 (s, 6H, CH_3), 3.49 (s, 2H, $CH_2C_6H_5$), 7.23 (s, 5H, C_6H_5), 9.24 (s, 1H, CHO).

REFERENCES

1. N. K. Bliznyuk, V. A. Efimenko and L. D. Protasova, USSR SU 1,214,661 (1986); Chem. Abstr., 105, P225779x (1986).
2. S. Tatsuoka and A. Morimoto, Japan 180,987 (1949); Chem Abstr., 46, P7585g (1952).
3. H. M. Crooks, Jr., "The Chemistry of Penicillin", pp. 455-472, Princeton University Press, Princeton, NJ, 1949.
4. I. M. Heilbron, A. H. Cook and J. R. Catch, Brit. 607,539 (1948); Chem. Abstr., 43, P4688d (1949).
5. F. M. Hamer and R. J. Rathbone, J. Chem. Soc., 595 (1945).
6. G. Grundke, W. Keese, M. Rimpler, Chem. Ber., 118, 4288 (1985).
7. R. Bloch, Synthesis, 140 (1978).
8. Benzylsulfenyl chloride has been prepared by the action of N-chlorosuccinimide on benzyl mercaptan as described by H. Emde, Ger. Offen. 804,572 (1951); Chem. Abstr., 46, 529 (1952).

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IMPROVED SYNTHESIS OF NITRO DERIVATIVES OF N-PHENYLGLYCINE

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Nitro derivatives of N-phenylglycine which are structurally similar to stable explosives TNT (2,4,6-trinitrotoluene) and tetryl (N-methyl-N,2,4,6-tetranitroaniline) are used in different explosive formulations. Methods of synthesis and properties of three nitro derivatives of