the addition of solid ammonium chloride, and the subsequent work-up procedure was the same as above.

**Glc Analysis.** Analysis of the chloroform solutions of toluene (prepared in 25-ml volumetric flasks) was conducted on a Varian 1420 instrument with a 0.125 in. × 10 ft column of 10% Dow Corning 710 on Chromosorb W, helium flow rate of 30 ml/min, and column temperature of 100°. The following retention times (in minutes) were observed: 1-methylcyclohexene, 3.7; toluene, 4.6; 1-methyl-1,4-cyclohexadiene, 5.2; benzyl alcohol, 37. Each product solution was analyzed in triplicate using a fixed-volume injection and the average peak height was related to millimoles of toluene by a least-squares computer plot of peak heights *vs.* known concentrations of toluene. The precision of this method was ±1%. Each reduction was carried out at least twice and the data in Table I are average values (±2%).

A control experiment in which a solution of toluene (10 mmol) and *tert*-butyl alcohol (10 mmol) in THF was added to a solution of lithium (3 mg-atoms) in liquid ammonia and the reaction solution was subjected to the standard work-up and glc analysis established that 90% of the toluene was recovered.

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**Registry No.**—**3,** 140-11-4; **4,** 120-51-4; **5,** 621-84-1; **6,** 104-57-4; **7,** 351-70-2; **8,** 32362-99-5; lithium, 7439-93-2.

## References and Notes

(1) (a) Presented at the 5th Northeast Regional Meeting of the American Chemical Society, Rochester, N. Y., Oct 1973; (b) based on the Honors Thesis of L. I. Shoer, Williams College, 1973.
(2) J. H. Markgraf, S. J. Basta, and P. M. Wege, *J. Org. Chem.*, **37**, 2361 (1972).
(3) A. S. Hallsworth, H. B. Henbest, and T. I. Wrigley, *J. Chem. Soc.*, 1969 (1957).
(4) W. H. Hartung and R. Simonoff, *Org. React.*, **7**, 263 (1953).
(5) L. E. Khoo and H. H. Lee, *Tetrahedron Lett.*, 4351 (1968).
(6) J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 2, Wiley, New York, N. Y., 1961, pp 1239–1243.
(7) H. Smith, "Organic Reactions in Liquid Ammonia, Chemistry in Anhydrous Liquid Ammonia," Vol. 1, Wiley, New York, N. Y., 1963, Part 2, pp 160–161, 173–181.
(8) We thank a referee for assistance with the mechanistic interpretations.
(9) (a) S. S. Hall, S. D. Lipsky, and G. H. Small, *Tetrahedron Lett.*, 1853 (1971); (b) S. S. Hall, S. D. Lipsky, F. J. McEnroe, and A. P. Bartels, *J. Org. Chem.*, **36**, 2588 (1971).
(10) V. T. Oliverio and E. Sawicki, *J. Org. Chem.*, **20**, 363 (1955).
(11) A. C. Pierce and M. M. Joullie, *J. Org. Chem.*, **27**, 3968 (1962).
(12) A. A. Chilingaryan, Y. Y. Usaevich, and A. Y. Nazarov, *Tr. Leningrad. Khim.-Farm. Inst.*, 5 (1962); *Chem. Abstr.*, **60**, 10541*i* (1964).
(13) B. Wladislaw, H. Viertler, and E. B. Demant, *J. Chem. Soc. B*, 565 (1971).

## Thiophenyl Malonate. A New Synthesis

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We wish to report a convenient procedure for synthesizing thiophenyl malonate, the active ester of choice for forming malonyl coenzyme A, based upon the reaction of malonic acid monochloride with thiophenol. We were led to develop this synthesis when we discovered that scaling up the normal procedure of Trams and Brady,[1,2] which involves coupling malonic acid with thiophenol using dicyclohexylcarbodiimide, produced no thiophenyl malonate but only a bright orange crystalline side product. In addition we had observed that some preparations of malonyl coenzyme A obtained from thiophenyl malonate synthesized by the Trams and Brady procedure were inexplicably one-half to one-third as active as others when used as substrate in enzymatic synthesis of fatty acids, indicative of the possible presence of inhibitory by-products.

The thiol ester obtained in low (13%) yield from the reaction of acid chloride with thiophenol is a colorless, stable solid. Using this material, a 10-mg sample of coenzyme A (approximately 10 μmol) yields about 8 μmol of malonyl coenzyme A.[1] The malonyl coenzyme A produced is fully active in reactions catalyzed by pigeon liver and rabbit mammary fatty acid synthetases as assayed spectrophotometrically in the presence of acetyl coenzyme A and NADPH.

**Malonic Acid Monochloride.** Malonic acid (15.6 g, 0.15 mol) and thionyl chloride (18 g, 0.15 mol) in 60 ml of ether were heated under reflux for 6 hr with stirring in a flask surmounted with a condenser and drying tube. During the reflux period, evolution of hydrogen chloride was observed. The solvent was then removed on a rotary evaporator under vacuum, and the remaining solid was triturated at 40° with ten 30-ml portions of a 1:2 mixture of chloroform–hexane. The combined extract was cooled to −15° and allowed to crystallize. The yellow crystals (5.27 g, 28.7%) of malonic acid monochloride were washed with hexane and dried overnight under vacuum, mp 58–61° (lit.[3] mp 63–65°).

**Thiophenyl Malonate (Shirley's Ester).** Thiophenol (1.9 g, 0.017 mol) was added dropwise to a stirred solution of 2.1 g (0.015 mol) of malonic acid monochloride in 25 ml of ether under an atmosphere of dry argon. The reaction was allowed to continue for 3 hr, after which time the solvent was removed on a rotary evaporator, leaving a moist solid which was placed under a vacuum of 0.1 mm until no more yellowish oil (thiophenol) could be observed. The majority of the solid was then dissolved in a minimum amount of chloroform and filtered to provide a clear yellow solution. Addition of hexane to the cloud point and subsequent cooling resulted in crystallization, providing a yellow solid, mp 57–68°. Dissolution in chloroform, decolorization with carbon, addition of hexane, and cooling in a Dry Ice–acetone bath provided 0.37 g (13%) of colorless crystals of thiophenyl malonate, mp 69–71° (lit.[2] mp 72–73°), which were collected and dried under vacuum: nmr ($CDCl_3$) δ 3.70 (s, 2 H), 7.42 (s, 5 H), 10.73 (s, 1 H); mass spectrum (80 eV) *m/e* (rel intensity) 196 (0.1, $M^+$), 152 (1.4, $M^+ - CO_2$), 110 (100, $PhSH^+$); ir (KBr) 1690 (O=CS), 1718 $cm^{-1}$ (O=CO).

*Anal.* Calcd for $C_9H_8O_3S$: C, 55.09; H, 4.11; S, 16.34. Found: C, 54.79; H, 4.30; S, 16.61.

**Registry No.**—Malonic acid monochloride, 51932-41-3; malonic acid, 141-82-2; thionyl chloride, 7719-09-7; thiophenyl malonate, 4279-77-0; thiophenol, 108-98-5.

## References and Notes

(1) E. G. Trams and R. O. Brady, *J. Amer. Chem. Soc.*, **82**, 2972 (1960).
(2) J. C. Howard, M. C. Lin, P. Matthews, and S. A. Singal, *J. Med. Chem.*, **8**, 888 (1965).
(3) H. Eggerer and F. Lynen, *Biochem. Z.*, **335**, 519 (1962).