A Convenient Method for the Synthesis of Thiobenzamide Derivatives and O-Thiobenzoates by Use of 2-Benzothiazolyl Dithiobenzoate as Effective Thiobenzoylation Reagent

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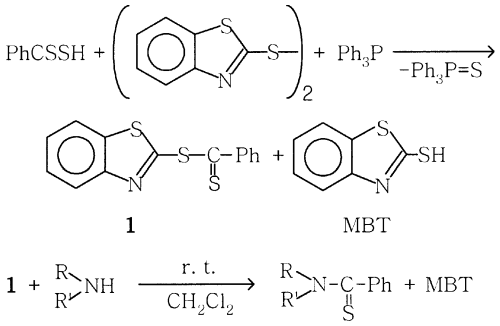
In previous papers,[1-4] many useful syntheses of thioamides and thioesters have been extensively exploited. In connection with our research[5] directed toward synthetic utility of active S-thioester containing benzothiazole-2-thiol moiety, the so-called 2-mercaptobenzothiazole (MBT) in the rubber industry, we wish to report additional studies of improved thiobenzoylation reagent, S-thiobenzoyl derivative of MBT for the synthesis of thiobenzamide derivatives and O-thioesters.

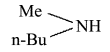
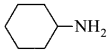
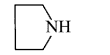
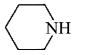
S-Thiobenzoyl derivative of MBT was easily prepared by heating equimolar amounts of dithiobenzoic acid,[6] 2,2'-dithiobis[benzothiazole], and triphenyl phosphine in benzene in good yield.



The reaction of 2-benzothiazolyl dithiobenzoate (**1**) with several amines was carried out. The thioester (**1**) easily reacted with pri-amines and sec-amines to give quantitative yields of the corresponding thioamides in dichloromethane at room temperature. The original reddish color of **1** disappeared immediately. On the other hand, thiobenzoylation of aniline and tertiary butylamine was carried out in benzene under reflux. The thiolate moiety of MBT having the excellent leaving property was easily removed by washing the reaction mixture with dil. alkaline aqueous solution, and the solvent was evaporated off *in vacuo* to afford only desirable thiobenzamide derivatives without further purification in quantitative yields (Table 1). MBT could be also easily recovered as precipitate by acidifying the aqueous filtrate with hydrochloric acid.

In particular, aminoalcohols, for example, 2-aminoethanol and 2-amino-1-buthanol containing amino group together with hydroxyl group in one molecule were selectively converted into the desired thiobenzamide derivatives in high yields without protection of hydroxyl group.

Table 1. Thiobenzoylation of Several Amines with 2-Benzothiazolyl dithiobenzoate (**1**)

Amine	Time	Thioamide (% yield)[b]	mp (°C)[7]
$PhNH_2$	5 hr[a]	93	99-100[1a, 2c]
$PhCH_2NH_2$	1 min	92	77-78
n-$BuNH_2$	1 min	93	oil
sec-$BuNH_2$	1 min	93	37-38
tert-$BuNH_2$	10 hr[a]	85	72-73
Et_2NH	1 min	87	oil[2a,2c]
	1 min	82	oil
	1 min	85	80-82
	1 min	94	oil
	1 min	85	oil[2c]
$HOCH_2CH_2NH_2$	1 min	90	88-89
$HOCH_2CH(NH_2)CH_2CH_3$	10 min	85	115-117

[a]Heating under reflux in benzene. [b]Yields by isolation.

Otherwise, the reaction of **1** with alcohols by heating under reflux in benzene for several hours, until the original reddish color of **1** disappeared, afforded also excellent yields of the corresponding O-thiobenzoates except phenol and benzyl alcohol. Especially phenol and benzyl alcohol treated with sodium hydride in diethyl ether reacted with **1** at room temperature immediately (Table 2).

It is advantageous that the compound (**1**) is crystalline red solid having excellent hydrolytic, thermal, and oxidative stability and, therefore, is handled more easily than thiobenzoyl chloride,[6] which was unstable above 78 °C (bp 88 °C/3.75 Torr) and very susceptible of oxygen. The present method provides an experimentally simple and convenient procedure for the preparation of thiobenzamide derivatives and the corresponding O-thiobenzoates from this thiobenzoylation reagent with amines and alcohols, respectively.

This commercially available compound **1** is expected to application for the synthesis of thioamides and O-thioesters.

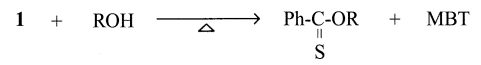


Table 2. Reaction of **1** with Several Alcohols

Alcohol	Time	Thioester[7] (% Isolated yield)[c]
MeOH	4 hr[a]	99[1b]
EtOH	4 hr[a]	99[1b]
n-PrOH	4 hr[a]	95
i-PrOH	20 hr[a]	99
n-BuOH	5 hr[a]	96[1b]
t-BuOH	70 hr[a]	92
PhO^-	1 min[b]	99
$PhCH_2O^-$	1 min[b]	98[1b]

[a]Heating under reflux. [b]Treatment with sodium hydride. [c]All thioesters are yellowish oil.

Experimental Section

Preparation of 2-Benzothiazolyl dithiobenzoate (1). A mixture of 2,2'-dithiobis[benzothiazole] (3.32 g, 10 mmol) and triphenylphophine (2.63 g, 10 mmol) in benzene (30 mL) was stirred at room temperature and ethereal solution of dithiobenzoic acid[6] (10 mL, approximately 12 mmol) was added dropwise. After being heated at reflux for 2 hr under Argon atmosphere. The reaction mixture was washed with dil. HCl solution and water, and then the solvent was evaporated under reduced pressure. Recrystallization of the residue from n-hexane gave 1.75 g (61%) of 1 as reddish solid, mp 99 °C; IR (KBr) 3060, 1441, 1405, 1246, 1055, 751, 684 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.12-7.93 (m, 4H), 7.60-7.41 (m, 5H); MS (EI) m/z 287 (M^+, 71), 167 (71), 121 (100), 108 (58), 77 (80).

The Typical Procedure for Aminolysis of Benzylamine. To a solution of **1** (1.44 g, 5.0 mmol) in dichloromethane (10 mL), a solution of benzylamine (0.64 g, 6.0 mmol) in dichloromethane (5 mL) was added dropwise at room temperature for 1 min. The original reddish color of **1** disappeared immediately. The reaction mixture was washed with dil. hydrochloric acid, dil. sodium hydroxide solution, and finally water, dried, and evaporated *in vacuo* to give a yellowish solid[7] 1.04 g (92%) which was recrystallized from *n*-hexane.

The Typical Precedure for Preparation of O-Methyl thiobenzoate. A solution of **1** (86 mg, 0.3 mmol) in methanol (20 mL) was heated under reflux for 4 hr, until the particular reddish color of **1** disappeared. The alcohol was removed *in vacuo*. The residue was dissolved in diethyl ether (20 mL), the ethereal solution was washed with dil. sodium hydoxide solution and water, dried, and evaporated *in vacuo* to give yellowish liquid[7] 45 mg (99%).

The Typical Procedure for Preparation of O-Phenyl thiobenzoate. To a solution of phenol (329 mg, 3.5 mmol) in diethyl ether, sodium hydride (160 mg, 4 mmol) was added. After being stirred at room temperature for 10 min, a solution of **1** (861 mg, 3 mmol) in diethyl ether (5 mL) was added dropwise at room temperature. The particular reddish color of **1** disappeared immediately. The reaction mixture was washed with dil. sodium hydroxide solution and water, dried, and evaporated *in vacuo* to give yellowish liquid[7] 637 mg (99%).

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7. Products identity was established by comparison with authentic samples prepared by the treatment of the corresponding amides and benzoic ester with Lawesson's reagent[1], respectively. Products purity was checked by IR and TLC analysis.