Title	Mild Acetylation of Amides, Thioamides, Ureas, and Thioureas Using Methyl Bis(1-naphthyl)bismuthinate in Acetic Acid
Author(s)	Ogawa, Takuji; Miyazaki, Kikuko; Suzuki, Hitomi
Citation	CHEMISTRY LETTERS. 19(9) p.1651-p.1654
Issue Date	1990-09
oaire:version	VoR
URL	https://hdl.handle.net/11094/3188
rights	
Note	

Osaka University Knowledge Archive : OUKA

<https://ir.library.osaka-u.ac.jp/>

Osaka University

Mild Acetylation of Amides, Thioamides, Ureas, and Thioureas
Using Methyl Bis(1-naphthyl)bismuthinate in Acetic Acid

Takuji OGAWA,* Kikuko MIYAZAKI, and Hitomi SUZUKI*†

Department of Chemistry, Faculty of Science,
Ehime University, Matsuyama, Ehime 790

† Department of Chemistry, Faculty of Science,
Kyoto University, Kitashirakawa, Kyoto 606

Amides, thioamides, ureas, and thioureas were N-acetylated in good yield with acetic acid in the presence of methyl bis(1-naphthyl)bismuthinate at room temperature.

Alkyl diarylbismuthinates ($\text{Ar}_2\text{Bi}(=\text{O})\text{OR}$) are a new class of pentavalent organobismuth compounds, easily prepared from triaryl bismuthine and chloramine-T.¹⁾ Uniqueness of this type of compounds is well exhibited by the lability of the alkoxy group attached to bismuth atom; ester exchange reaction with alcohols occurs with unusual ease.¹⁾ We wish to report herein that such unique property can be successfully applied for the mild acetylation of amides, thioamides, ureas, and thioureas with acetic acid; simple stirring of these compounds in acetic acid in the presence of methyl diarylbismuthinate at room temperature afforded the corresponding N-acetyl derivatives in good yields (Table 1).

Non-symmetrical imides, thioimides, and acylated ureas and thioureas have attracted considerable interests as physiologically²⁾ and bactericidally active compounds.³⁾ Direct acylations of amides, thioamides, ureas, and thioureas require strong acylating reagents and/or vigorous reaction conditions because of the low basicity of these amide compounds. Thus indirect approaches are often employed to prepare N-acylated derivatives of amidic compounds.⁵⁻¹⁰⁾ To our knowledge, the reaction described here is the first example in which amidic compounds are N-acetylated in acetic acid at room temperature.

Of many alkyl diarylbismuthinates so far obtained, methyl bis(1-naphthyl)bismuthinate is the best choice as an activator because of its high stability and easy accessibility. Less sterically crowded bismuthinates such as methyl diphenylbismuthinate tend to decompose into triphenylbismuthine and other polymeric bismuth compounds during the course of reaction. When catalytic amount of methyl bis(1-naphthyl)bismuthinate was used, the rate of conversion diminished significantly, and the decomposition of the catalyst became predominant. To make sure high yields of N-acetylated product, stoichiometric use of the bismuthinate was necessary.

A typical example is as follows: Benzamide (1.0 mmol, 121 mg) and methyl bis(1-naphthyl)bismuthinate (1.0 mmol, 510 mg) were stirred in a mixture of acetic acid (5 cm³) and dichloromethane (20 cm³) at room temperature (around 15 °C). When the starting amide was consumed completely, the mixture was evaporated to dryness in vacuo and the residue was passed through a silica-gel column using hexane - dichloromethane (with gradient from 100% hexane to 100% dichloromethane) as an eluent. N-Acetylbenzamide was obtained in 89% isolated yield.

We propose a tentative mechanism for our reaction as shown in Scheme 1. The key step is formation of a mixed anhydride (**3**) from methyl bismuthinate with acetic acid. This anhydride then reacts with amide nitrogen to give N-acetylated product (**2**) via a proposed intermediate (**4**). Bismuth(III) triacetate was earlier reported to acetylate formamides, amines, and alcohols at high temperature (ca. 200 °C).¹¹⁾ However, we can easily exclude the possible participation of the salt, because it lacks the ability to acetylate amidic nitrogens under our conditions.

The present results demonstrate that some bismuthinates may be used as an efficient reagent for coupling of amides with carboxylic acids. Studies are now undertaken to define the scope and limitations.

Table 1. Acetylation of amides, thioamides, ureas, and thioureas in acetic acid and CH_2Cl_2 .^{a)}

		$\text{R}^1\text{C}(=\text{X})\text{NHR}^2$		$\xrightarrow[\text{AcOH, CH}_2\text{Cl}_2, \text{rt}]{\text{Np}_2\text{Bi}(=\text{O})\text{OMe}}$		$\text{R}^1\text{C}(=\text{X})\text{N}(\text{Ac})\text{R}^2$	
		<u>1</u>				<u>2</u>	
R^1	R^2	X	Time ^{b)} h	Yield ^{b)} /%		Mp of <u>2</u> /°C (lit. mp /°C or bp)	¹ H NMR (CDCl_3) δ /ppm
				<u>2</u>	<u>1</u>		
Ph	H	O	12	89	0	114–115 (120) ⁷⁾	2.40 (s, 3H), 7.2–7.9 (m, 5H)
Ph	H	S	24	76	0	103–105 (103–105) ⁸⁾	6.28 (bs, 1H) 2.54 (s, 3H), 7.1–7.9 (m, 5H), 9.78 (bs, 1H)
c-hexyl-NH	c-hexyl	O	24	76	0	123–126 (125) ⁹⁾	1.15–2.05 (m, 22H), 2.38 (s, 3H), 5.03 (bs, 1H)
c-hexyl-NH	c-hexyl	S	24	68	21	168–170 ¹²⁾	0.9–2.44 (m, 22H), 2.13 (s, 3H), 5.03 (bs, 1H)
Ph-NH	Ph	O	24	84	0	102–104 (106) ¹³⁾	2.05 (s, 3H), 7.0–7.5 (m, 10H), 9.0 (bs, 1H)
Ph-NH	Ph	S	24	48	44	155–160 (169–170) ⁷⁾	1.94 (s, 3H), 7.0–7.3 (m, 10H), 8.7 (bs, 1H)
Me	H	O	24	84	0	75–77 (79)	2.40 (s, 6H), 9.50 (bs, 1H)
$\text{CH}_2(\text{CH}_2)_2\text{CH}_2$		O	24	86	0	oil (74–75/0.5 Torr) ⁴⁾	2.0–2.7 (m, 9H), 3.4–3.8 (m, 2H)

a) Substrates 1, 1 mmol; methyl bis(1-naphthyl)bismuthinate, 1 mmol; acetic acid, 5 cm^3 ; CH_2Cl_2 , 20 cm^3 ; room temperature (ca. 15 °C).

b) Yields refer to the isolated compounds. Reaction times and yields are not optimized.

References

- 1) T. Ogawa, T. Murafuji, K. Iwata, and H. Suzuki, *Chem. Lett.*, **1988**, 2021.
- 2) E. Wertheim, *J. Am. Chem. Soc.*, **57**, 545 (1935); J. Gieldanowski, B. Bobranski, J. Deckert, B. Szaga, and J. Teodorczyk, *Arc. Immunol. Ther. Exp.*, **21**, 517 (1973); *Chem. Abstr.*, **79**, 132939d; E. C. Beuvery, G. J. A. Speijers, B. I. G. Lutz, D. Freudenthal, and H. J. G. M. Derks, *Pathog. Neisseriae. Proc. Int. Symp.* **1985**, 622; *Chem. Abstr.*, **104**, 205061h; L. M. Manoiliva, E. N. Kirilliva, V. G. Beilin, R. N. Zozulya, and L. B. Dashkevich, *Khim. -Farm. Zh.*, **11**, 89 (1977); *Chem. Abstr.*, **88**, 68939k.
- 3) J. Mollin, K. Polaskova, Z. Odlerova, and V. Bekarek, *Collect. Czech. Chem. Commun.*, **52**, 2087 (1987); *Chem. Abstr.*, **108**, 167082p.
- 4) A. K. Bose, J. L. Fahey, and M. S. Manhas, *Tetrahedron*, **30**, 3 (1974).
- 5) T. N. Sumarokova, R. A. Slavinskaya, A. T. Vladul, and T. A. Tember, *Zh. Obshch. Khim.* **42**, 1789 (1972).
- 6) E. C. Beuvery, C. J. A. Speijers, B. I. G. Lutz, D. Freudenthal, V. Kanhai, B. Haagmans, and H. J. G. M. Derks, *Develop. Biol. Standard.*, **63**, 117 (1986).
- 7) G. N. Dorofeenko, V. D. Karpenko, Yu. I. Ryabukhin, and S. A. Kitaigorodskaya, *Zh. Obshch. Khim.*, **48**, 2254 (1978).
- 8) Y. Lin, M. N. Jennings, D. R. Sliskovic, T. L. Fields, and S. A. Lang, Jr., *Synthesis*, **1984**, 946.
- 9) N. A. Smart, G. T. Young, and M. W. Williams, *J. Chem. Soc.*, **1960**, 3902.
- 10) J.-C. Gramain, R. Remuson, and Y. Troin, *Tetrahedron*, **35**, 759 (1979); J. C. Sheehan and R. W. Tulis, *J. Org. Chem.*, **39**, 2264 (1974).
- 11) A. L. Reese, K. McMartin, D. Miller, and P. P. Wickham, *J. Org. Chem.*, **38**, 764 (1973).
- 12) K. Hartke, *Arch. Pharm. Ber. Dtsch. Pharm. Ges.*, **300**, 766 (1967); *Chem. Abstr.*, **68**, 21904s.
- 13) H. G. Schweim, *Arch. Pharm.*, **322**, 125 (1989); *Chem. Abstr.*, **111**, 38978y.

(Received June 7, 1990)