BISCARBAMOYL DISELENIDES AS NEW CARBAMOYLATING REAGENTS. LEWIS ACID PROMOTED CARBAMOYLATION OF AROMATIC COMPOUNDS

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Summary: The reaction of biscarbamoyl diselenides with aromatic compounds in the presence of Lewis acids resulted in Friedel-Crafts type carbamoylation (Gatterman amide synthesis) to give corresponding aromatic amides in good yields. This methodology was successfully applied to aroylation and benzylation by use of dibenzoyl diselenide and dibenzyl diselenide, respectively.

Although biscarbamoyl diselenides 1 are easily prepared from corresponding secondary amines, selenium, and carbon monoxide,1) their synthetic uses have not been well developed so far. Since selenium atom exhibits a high affinity for soft metal atoms,²⁾ it can be expected that cationic carbamoyl species may be generated by the combination of 1 with Lewis acids containing soft metal atom. We examined the reaction of 1 with several aromatic compounds in the presence of the Lewis acids, and have found that electron-rich aromatic compounds 2 undergo Friedel-Crafts type carbamoylation (Gatterman amide synthesis) to give corresponding aromatic amides 3. Among several Lewis acids examined, HgBr2 and SnCl4 exhibited notable activities.³⁾ Typical Friedel-Crafts catalysts such as AICI3 were ineffective, and copper(I) triflate-benzene complex [(CuOTf)2PhH] was less effective for this carbamovlation.4)



Results of the HgBro promoted carbamovlation of several aromatic compounds are summarized in Table 1.5) When the reaction was conducted in toluene as the solvent, which was inert under the conditions employed, the yield of amide 3a was well improved (run 1).⁶⁾ Characteristic features of this reaction are as follows: i) Both carbamoyl groups of 1 could be efficiently transferred into aromatic compounds by using two equivalents of HgBro over 1. ii) Aromatic heterocyclic compounds such as thiophene and furan were easily carbamoylated to give 2-carbamoylated derivatives under mild conditions (runs 3 and 4).7) iii) High regioselectivity was attained, especially in the cases of anisole, thiophene, and furan.

A typical experimental procedure is as follows. To a solution of bis(N,N-diethylcarbamoyl)

run	diselenide	substrate	method ^{a)}	product ^{b)}	yield,	ξc)
1	$\begin{array}{ccc} 0 & 0 \\ II & II \\ Et_2 NCSeSeCNEt_2 \end{array}$	мео-	A	MeO-CNEt ₂	76	
	1a	2a		3a	69 ^{d)}	
					51 ^{e)}	
					3 ^{f)}	
			В		53 ^{g)}	
			С		24	
			D		0	
2	la	Me	В	Me CNEt ₂	46 ^{h)}	
3	1a		E	S S CNEt ₂ II O	76	
4	1a	$\langle \rangle$	F		56	
5	NCSesec N 1b	2a	A	Meo- CN	73	
6		2a	A	мео- () -СN	63	

Table 1. HgBr₂ Promoted Carbamoylation of Aromatic Compounds

Conditions: diselenide(1 mmol), HgBr₂(2 mmol), substrate(10 mmol), solvent(8 mL), reflux, 12 h, unless otherwise stated. a) Method: A, toluene, 111°C; B, tetrachloroethane, 147°C; C, chlorobenzene, 138°C; D, DMF, 153°C; E, benzene, 80°C; F, pentane, 35°C. b) All products gave satisfactory 1H-NMR, ¹³C-NMR, IR, and mass spectra. c) Isolated yields based on carbamoyl groups of diselenide. d) HgBr₂(4 mmol) was used. e) HgBr₂(1.5 mmol) was used. f) HgBr₂(1 mmol) was used. g) In addition, *o*-isomer (7 %) was also detected by GLC. h) In addition, 2,6-dimethyl isomer (3 %) was also detected by GLC.

diselenide (1a) (1 mmol, 0.36 g) and anisole (2a) (10 mmol, 1.1 mL) in toluene (8 mL) was added HgBr₂ (2 mmol, 0.72 g), and the mixture was heated under reflux for 12 h. After filtration of precipitates, the filtrate was diluted with CH_2CI_2 (50 mL), washed with saturated aqueous NaHCO₃, saturated aqueous NH₄Cl, and dried (MgSO₄). The crude product was purified by column chromatography (silica gel, ether) to afford 0.31 g of N,N-diethyl-*p*-methoxybenzamide (3a) (1.52 mmol, 76 %).

At present, details on the reaction mechanism have not been clarified yet, but we can postulate the following reaction path (Scheme 1).⁸) Cationic carbamoyl species 4 may be generated by the interaction of selenium atom of 1 with the soft metal atom of Lewis acid, and then 4 undergoes electrophilic aromatic substitution to afford amide 3 and diselenide 5. Resulting diselenide 5 may react likewise with another Lewis acid, and then with aromatic compound to give amide 3. Thus, the transfer of both carbamoyl groups of 1 may be attained.

Scheme 1



In a similar manner, aroylation and alkylation were also successfully performed. Anisole was smoothly aroylated by use of dibenzoyl diselenide (6) to give *p*-methoxybenzophenone (7) in 82 % yield together with 6 % of its *ortho* isomer (eq. 2). The reaction of dibenzyl diselenide (8) with toluene resulted in the formation of a mixture of *o*- and *p*-benzyl toluenes 9 (79 %; *ortho/para* ratio = 45/55) (eq. 3).

$$\begin{array}{c} 0 & 0 \\ - \overset{\circ}{\mathsf{C}}\mathsf{SeSe}\overset{\circ}{\mathsf{E}}\overset{\circ}{-$$

9

In conclusion, biscarbamoyl diselenides 1 have shown to act as convenient carbamoylating reagents of aromatic compounds in the presence of Lewis acids containing soft metal atom such as HgBr₂ and SnCl₄. A high affinity of selenium atom for soft metal atoms may be the key for this reaction. A similar procedure employing dibenzoyl and dibenzyl diselenides led to successful aroylation and benzylation of aromatic compounds.

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References and notes

(1) Bis(N,N-disubstituted carbamoyl) diselenides 1 can be readily obtained by the air oxidation of carbamoselenoate ammonium salts 10 arising from corresponding secondary amines, carbon monoxide, and selenium: Kondo, K.; Sonoda, N.; Yoshida, K.; Koishi, M.; Tsutsumi, S. *Chem. Lett.* **1972**, 401.



(2) For example, potassium selenobenzoate reacts with trimethylsilyl chloride at the oxygen center to afford O-trimethylsilyl ester, whereas corresponding reactions with trimethyltin chloride and trimethylgermanium chloride afford Se-metallated derivatives: Ishihara, H.; Kato, S. Terahedron Lett. 1972, 3751.

(3) The following Lewis acids were ineffective in this carbamoylation (AlBr3, FeCl₃, CuCl, BF₃·OEt₂, CoCl₂, Hg₂Cl₂, and Hg(OAc)₂).

(4) Copper(I) triflate-benzene complex [(CuOTf)₂PhH] is known to assist Friedel-Crafts type acylation of aromatic compounds with selenol esters, see: a) Kozikowski, A. P.; Ames, A. J. Am. Chem. Soc. **1980**, *102*, 860. b) Kozikowski, A. P.; Ames, A. Tetrahedron **1985**, *41*, 4821.

(5) Similar results were obtained by use of SnCl₄.

(6) On heating 1a and HgBr₂ in anisole (2a), 3a was obtained in only 39 % yield together with several uncharacterizable by-products.

(7) Some other alkylsubstituted benzene derivatives examined (*o*- and *p*-xylene, *p*-cymene, and ^tbutylbenzene) gave only a small amount of desired amides under reflux conditions of toluene or tetrachloroethane.

(8) An alternative mechanism, where carbamoyl halide 11 acts as a key intermediate, may also be possible.

