This article was downloaded by: [University of Illinois Chicago] On: 09 June 2012, At: 23:55 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

EFFICIENT SYNTHESIS OF SELENOUREAS FROM THE CORRESPONDING CARBODIIMIDES

Mamoru Koketsu^a, Naotaka Takakura^a & Hideharu Ishihara^b

^a Department of Chemistry, Faculty of Engineering, Gifu University, Gifu, 501-1193, Japan

^b Department of Chemistry, Faculty of Engineering, Gifu University, Gifu, 501-1193, Japan

Available online: 16 Aug 2006

To cite this article: Mamoru Koketsu, Naotaka Takakura & Hideharu Ishihara (2002): EFFICIENT SYNTHESIS OF SELENOUREAS FROM THE CORRESPONDING CARBODIIMIDES, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:19, 3075-3079

To link to this article: <u>http://dx.doi.org/10.1081/SCC-120013001</u>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <u>http://www.tandfonline.com/page/terms-and-conditions</u>

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.



©2002 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

SYNTHETIC COMMUNICATIONS Vol. 32, No. 19, pp. 3075–3079, 2002

EFFICIENT SYNTHESIS OF SELENOUREAS FROM THE CORRESPONDING CARBODIIMIDES

Mamoru Koketsu,* Naotaka Takakura, and Hideharu Ishihara*

Department of Chemistry, Faculty of Engineering, Gifu University, Gifu 501-1193, Japan

ABSTRACT

Selenoureas were synthesized by the reaction of carbodiimides with LiAlHSeH in the presence of hydrogen chloride.

Key Words: Selenourea; Carbodiimide; Hydrogen chloride

New synthetic methods for the preparation of selenocarbonyl compounds have been extensively developed.^[1] Selenoureas, generally prepared from the reaction of isoselenocyanate with amine,^[2] are useful precursors for the synthesis of selenium–nitrogen heterocyclic compounds.^[3] However, a facile method for the preparation of selenoureas, in which formation of unstable isoselenocyanate intermediate is not required, has been desired. In the present study, we investigated the preparation of various selenoureas from the corresponding carbodiimides using LiAlHSeH **2**. Herein, we report a new method for preparation of selenoureas by the reaction of carbodiimides with LiAlHSeH **2** in the presence of hydrogen chloride (Scheme 1).

3075

DOI: 10.1081/SCC-120013001 Copyright © 2002 by Marcel Dekker, Inc. 0039-7911 (Print); 1532-2432 (Online) www.dekker.com

^{*}Corresponding authors. E-mail: koketsu@cc.gifu-u.ac.jp

©2002 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

3076

KOKETSU, TAKAKURA, AND ISHIHARA



Sch	ieme	1.

Entry	Carbodiimide (1)		Viald $(0/)^a$
	R	R'	(3)
1	$4-CH_3C_6H_4$	4-CH ₃ C ₆ H ₄	93 (3a)
2	$2-CH_3C_6H_4$	$2-CH_3C_6H_4$	89 (3b)
3	C_6H_5	C_6H_5	88 (3c)
4	$(CH_3)_2CH$	$(CH_3)_2CH$	90 (3d)
5	$(CH_3)_3C$	$(CH_3)_3C$	85 (3e)
6	$(CH_3)_3C$	C_2H_5	59 (3f)
7	C_6H_{11}	C ₆ H ₁₁	56 (3g)

Table 1. Synthesis of Selenoureas

^aIsolated yield.

1N Hydrogen chloride in diethyl ether was added to N,N'-di-p-tolylcarbodiimide **1a** in THF at room temperature. The reaction mixture was stirred at room temperature for 4h under an argon atmosphere. To the mixture, an anhydrous THF solution of LiAlHSeH **2**^[4] was added at 0°C. The mixture was stirred at 0°C for 1h under an argon atmosphere. After standard workup, N,N'-di-p-tolylselenourea **3a** was obtained in 93% yield. Several selenoureas were obtained from the corresponding carbodiimides **1**.^[5] Both *N*-aryl- and *N*-alkyl-selenoureas and also both symmetric and unsymmetric selenoureas were obtained in moderate to high yields (Table 1).

In the present reaction, chlorination of carbodiimide^[6] was important for obtaining higher yield of **3**. Various reaction conditions were tested to determine the optimal conditions. When the reaction of carbodiimide **1d** with LiAlHSeH **2** was carried out without hydrogen chloride, the yield of **3d** was 45%. A **BF**₃-promoted reaction of **1d** with LiAlHSeH gave **3d** in only 28% yield. When the reaction mixture of **1d** and hydrogen chloride was stirred for only 1h under similar conditions shown in Sch. 1, the yield of **3d** was 53%. When HCl was added to the mixture of **1d** and **2**, the yield of **3d** was 62%. Finally, the conditions shown in Sch. 1 gave the highest yield of **3d** (Entry **4**, Table 1). These results would indicate that increasing

©2002 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

SYNTHESIS OF SELENOUREAS





electrophilicity of carbon atom of carbodiimide by chlorination of carbodiimide using hydrogen chloride might provide higher yield of selenourea (Scheme 2).

In previously, 1,3-disubstituted selenoureas have been synthesized by the reaction with carbodiimides and H_2Se ,^[7] which is highly toxic and air sensible. In present method, selenoureas **3** were readily synthesized by reacting carbodiimides **1** with LiAlHSeH **2** in the presence of hydrogen chloride.

EXPERIMENTAL

Melting points were determined by use of Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were measured on Perkin-Elmer 1600 spectrometer. ¹H, ¹³C and ⁷⁷Se NMR spectra were recorded on a JEOL-JNM- α 400 (400 MHz) spectrometer. Mass spectra were obtained on Shimadzu 9020-DF mass spectrometer. Tetrahydrofuran was distilled from benzophenone immediately prior to use.

General Procedure: To a solution of carbodiimide (2 mmol) in 10 mL anhydrous THF at room temperature under argon was added 1 N dry hydrogen chloride in diethyl ether (2 mL, 2 mmol). The reaction mixture was stirred at the same temperature for 4h. To the mixture was added an anhydrous THF solution (10 mL) of LiAlHSeH $2^{[4]}$ (1 mmol) at 0°C. The resulting mixture was stirred at 0°C for 1 h under argon. The mixture was extracted with diethyl ether (50 mL) and washed with saturated NaCl aqueous solution. The organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography on silica gel with diethyl ether : dichloromethane (50 : 1) to give selenourea **3**.

N,*N*'-**Di**-*p*-tolylselenourea 3a: M.p. 180.2–181.2°C (lit.^[2b] 176°C); IR (KBr) 1554, 3173 cm⁻¹; ¹H NMR (CDCl₃) δ 2.33 (6H, s, CH₃), 7.17 (4H, d, *J* = 8.0 Hz, Ar), 7.23 (4H, d, *J* = 8.0 Hz, Ar), 8.54 (2H, br, NH); ¹³C NMR

 $\mathcal{H}\mathcal{H}$

3078

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

©2002 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

KOKETSU, TAKAKURA, AND ISHIHARA

(CDCl₃) δ 20.9, 125.6, 130.0, 134.7, 137.3, 178.3; ⁷⁷Se NMR (CDCl₃) δ 241.3; MS (CI) m/z = 305 [M⁺+1]; Anal. Calcd. for C₁₅H₁₆N₂Se: C, 59.41; H, 5.32; N, 9.24. Found: C, 59.24; H, 5.25; N, 8.94.

N,*N*'-**Di**-*o*-tolylselenourea 3b: M.p. 159.8–161.1°C (lit. ^[2b] 174°C); IR (KBr) 1529, 3117, 3319 cm⁻¹; ¹H NMR (CDCl₃) δ 2.31 (6H, s, CH₃), 7.26–7.42 (8H, m, Ar), 8.5 (2H, br, NH); ¹³C NMR (CDCl₃) δ 18.0, 127.0, 128.0, 128.6, 131.2, 135.5, 179.4; ⁷⁷Se NMR (CDCl₃) δ 228.1; MS (Cl) m/z = 305 [M⁺+1].

N,N'-Diphenylselenourea 3c: M.p. 195.2–197.2°C (lit. 186^[2b], 192–194°C^[8]); IR (KBr) 1560, 3257 cm⁻¹; ¹H NMR (CDCl₃) δ 7.26–7.36 (10H, m, Ar), 8.2 (2H, br s, NH); ¹³C NMR (CDCl₃) δ 120.6, 125.7, 127.7, 129.2, 179.0; ⁷⁷Se NMR (CDCl₃) δ 140.1; MS (EI) *m*/*z* = 276 [M⁺].

N,*N*[']-Diisopropylselenourea 3d: M.p. 142.6–148.2°C (lit.^[9]); IR (KBr) 1570, 3195, 3245 cm⁻¹; ¹H NMR (CDCl₃) δ 1.19 (12H, d, CH₃), 4.21 (2H, br s, CH), 6.1 (2H, br, NH); ¹³C NMR (CDCl₃) δ 22.4, 47.9, 176.2; ⁷⁷Se NMR (CDCl₃) δ 140.3, MS (EI) *m*/*z* = 208 [M⁺]; HRMS Calcd. for C₇H₁₆N₂Se 208.0478, Found 208.0503; Anal. Calcd. for C₇H₁₆N₂Se: C, 40.58; H, 7.78; N, 13.52. Found: C, 40.59; H, 7.78; N, 13.51%.

N,*N*'-**Di**-*tert*-**butylselenourea 3e:** M.p. 144.8–147.6°C IR (KBr) 1542, 3062, 3258 cm⁻¹; ¹H NMR (CDCl₃) δ 1.51 (18H, s, CH₃), 6.2 (2H, br, NH); ¹³C NMR (CDCl₃) δ 29.2, 29.4, 54.1, 175.2; ⁷⁷Se NMR (CDCl₃) δ 262.3; MS (EI) m/z = 236 [M⁺]; HRMS (EI) Calcd. for C₉H₂₀N₂Se 236.0791, Found 236.0788;

N-tert-Butyl-*N'*-ethylselenourea 3f: M.p. 114.8–116.0°C; IR (KBr) 1549, 3009, 3238 cm⁻¹; ¹H NMR (CDCl₃) δ 1.08 (3H, t, CH₃), 1.27 (9H, s, CH₃), 3.05 (2H, br s, CH₂), 5.94 (1H, br, NH), 6.33 (1H, br, NH); ¹³C NMR (CDCl₃) δ 14.4, 29.3, 43.2, 53.8, 177.4; ⁷⁷Se NMR (CDCl₃) δ 209.6; MS (CI) m/z = 209 [M⁺+1]; HRMS (EI) Calcd. for C₇H₁₆N₂Se 208.0478, Found 208.0492; Anal. Calcd. for C₇H₁₆N₂Se: C, 40.58; H, 7.78; N, 13.52. Found: C, 40.68; H, 7.90; N, 13.47%.

N,*N*'-**Dicyclohexylselenourea 3g:** M.p. 134.6–137.2°C; IR (KBr) 1560, 3257 cm⁻¹; ¹H NMR (CDCl₃) δ 1.15–1.29 (12H, m, C₆H₁₁), 1.52–1.83 (8H, m, C₆H₁₁), 4.27 (2H, br, CH), 7.46 (2H, br, NH); ¹³C NMR (CDCl₃) δ 24.6, 25.3, 32.6, 34.9, 53.6, 175.8; ⁷⁷Se NMR (CDCl₃) δ 141.5; MS (EI) *m*/*z* = 288 [M⁺]; HRMS Calcd. for C₁₃H₂₄N₂Se 288.1103, Found 288.1097.

REFERENCES

 (a) Dell, C.P. Thioamides and Their Selenium and Tellurium Analogues. In *Comprehensive Organic Functional Group Transformations*, Katritzky, A.R., Meth-Cohn, O., Rees, C.W. Eds. Pergamon: Oxford, 1995; Vol. 5,

©2002 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

SYNTHESIS OF SELENOUREAS

3079

pp. 565–628; (b) Organoselenium Chemistry: A Practical Approach, Back, T.G., Ed.; Oxford University Press: U.K., 1999; (c) Murai, T.; Kato, S. Selenocarbonyls. In Organoselenium Chemistry. Modern Developments in Organic Synthesis, Wirth, T., Ed. Springer Verlag: 2000; pp. 177–199.

- (a) Sheehan, J.C.; Hlavka, J.J. J. Org. Chem. 1956, 21, 439. (b) Bulka, E.; Ahlers, K.-D.; Tucek, E. Chem. Ber. 1967, 100, 1459. (c) Sonoda, N.; Yamamoto, G.; Tsutsumi, S. Bull. Chem. Soc. Jpn. 1972, 45, 2937; (d) Boccanfuso, A.M.; Griffin, D.W.; Dunlap, R.B.; Odom, J.D. Bioorg. Chem. 1989, 17, 231; (e) Koketsu, M.; Suzuki, N.; Ishihara, H. J. Org. Chem. 1999, 64, 6473.
- (a) Maslankiewicz, A.; Skrzypek, L.; Niedbala, A. Pol. J. Chem. 1996, 70, 54; (b) Keil, D.; Hartmann, H. Phosphorus, Sulfur Silicon Relat. Elem. 1999, 152, 169; (c) Shafiee, A.; Ebrahimzadeh, M.A.; Maleki, A. J. Heterocycl. Chem. 1999, 36, 901; (d) Zhou, Y.; Linden, A.; Heimgartner, H. Helv. Chim. Acta 2000, 83, 1576.
- Ishihara, H.; Koketsu, M.; Fukuta, Y.; Nada, F. J. Am. Chem. Soc. 2001, 123, 8408.
- 5. Carbodiimides 1 and LiAlHSeH 2 were prepared according to previously reported methods. See: for 1; Fell, J.B.; Coppola, G.M. Synth. Commun. 1995, 25, 43 and for 2; ref. 4. Biriefly, to a solution of selenium powder (0.80 g, 10.0 mmol) in dry THF (100 mL) was added lithium aluminium hydride (0.38 g, 10.0 mmol) at 0°C under an argon atmosphere. The mixture was stirred at 0°C for 30 min. The formed LiAlHSeH 2 is then ready for use in further reaction without concentration.
- 6. Jung, F.; Olivier, A.; Boucherot, D. Tetrahedron Lett. 1989, 30, 2379.
- (a) Zetzche, F.; Pinske, H. Ber. 1941, 74B, 1022; (b) Zingaro, R.A.; Bennett, F.C.; Hammr, G.W. J. Org. Chem. 1953, 18, 292; (c) Giudicelli, J.F.; Menin, J.; Najer, H. Bull. Soc. Chim. Fr. 1968, 1099.
- 8. Warner, J.S. J. Org. Chem. 1963, 28, 1642.
- (a) Rosenbaum, A.; Kirchberg, H.; Liebnitz, E. J. Prakt. Chem. 1962, 19, 1; (b) Rosenbaum, A. J. Prakt. Chem. 1968, 37, 200.

Received in Japan July 2, 2001



©2002 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.