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Facile Synthesis of *N*,*N*-Dialkylselenoamides from Amides

Mamoru Koketsu, Yoshihiro Okayama, Hiroshi Aoki, and Hideharu Ishihara

Department of Chemistry, Faculty of Engineering, Gifu University, Yanagido 1-1, Gifu 501-1193, Japan

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ABSTRACT: *N,N-Dialkylamides were chlorinated with oxalyl chloride and then allowed to react with LiAlHSeH to afford the corresponding N,N-dialkyselenoamides in moderate to good yields. The N,N-dialkylamides bearing bulky substituent groups were not converted into the corresponding selenoamides because of their steric hindrance.* © 2002 Wiley Periodicals, Inc. Heteroatom Chem 13:195–198, 2002; Published online in Wiley Interscience (www.interscience.wiley.com). DOI 10.1002/hc.10016

INTRODUCTION

The syntheses of many selenocarbonyl compounds have been reported and a recent review details these studies [1]. Selenoamides have been used as the useful precursors for the synthesis of selenium containing heterocyclic compounds [2] and their reactivity has also become of great interest in recent years [3]. Several methods for their preparation have been reported [4]. Generally, the preparation of primary selenoamides has been achieved by the reactions of nitriles with appropriate selenating reagents [5], whereas N-substituted selenoamides have been synthesized by more complicated reactions, including the preliminary formation of selenoketene intermediates from allylic alkylnyl selenides or the reactions of *Se*-alkynyl selenocarboxylates with amines [6]. Previously, bis(dimethylaluminium)selenide has been found to be an excellent reagent for the conversion of N-substituted formamides to the corresponding selenoformamides [4c–4e]. Herein, we describe a new, efficient method for the syntheses of N,N-disubstituted selenoamides from the corresponding amides by treatment with oxalyl chloride and then LiAlHSeH.

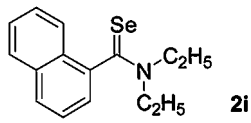
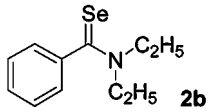
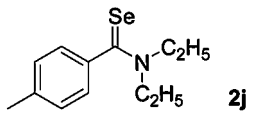
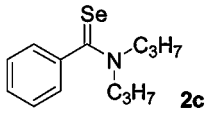
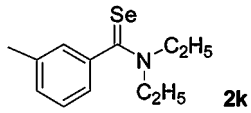
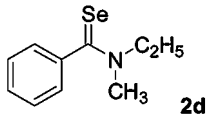
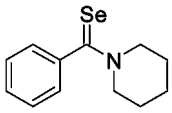
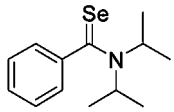
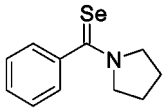
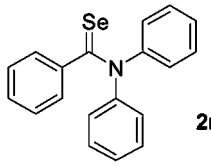
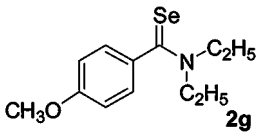
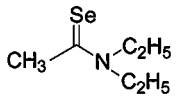
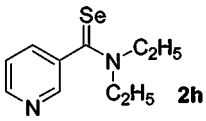
Correspondence to: Mamoru Koketsu; e-mail: koketsu@cc.gifu-u.ac.jp.

RESULTS AND DISCUSSION

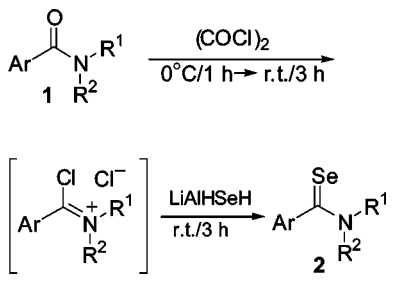
Optimal conditions for the preparation of N,N-disubstituted selenoarylamides from the corresponding amides were best determined by trial and error. Direct reaction of amides with LiAlHSeH failed to produce the corresponding selenoamides at all. Therefore, we tried the preparation of selenoamides from amides by combination of chlorinating agents, such as oxalyl chloride, hydrogen chloride, thionyl chloride, dichlorotriphenylphosphorane, or phosphorus pentachloride, with LiAlHSeH. Finally, the use of oxalyl chloride and LiAlHSeH was found to be the optimal procedure for the syntheses of selenoamides from amides as shown in Scheme 1.

A typical procedure in the preparation of an N,N-disubstituted selenoamide **2** is as follows. Oxalyl chloride was added to an anhydrous ether solution of *N*,*N*-dimethylbenzamide (**1a**). The reaction mixture was stirred at 0°C for 1 h under an argon atmosphere and then further stirred at room temperature for 3 h. LiAlHSeH [7] was added to the mixture. After the usual workup, *N*,*N*-dimethylselenobenzamide (**2a**) was obtained as

TABLE 1 Synthesis of Selenoamide

Entry	*Product*	*Yield (%)*[a]	*Entry*	*Product*	*Yield (%)*
1	 **2a**	75	9	 **2i**	54
2	 **2b**	68	10	 **2j**	61
3	 **2c**	61	11	 **2k**	50
4	 **2d**	72	12	 **2l**	0
5	 **2e**	75	13	 **2m**	0
6	 **2f**	74	14	 **2n**	0
7	 **2g**	65	15		20
8	 **2h**	36	16	 **2p**	Trace

[a]Isolated yield.



SCHEME 1

yellow crystals in 75% yield. The same reaction conditions with NaHSe [8] did not afford the desired selenoamide **2**. Various kinds of N,N-disubstituted arylamides **1** were converted into the corresponding N,N-disubstituted selenoarylamides **2** in moderate to good yields under the present reaction conditions (Table 1). However, 2-methylselenobenzamide was not obtained by the present reaction (entry 12). Also, neither *N*,*N*-diisopropyl nor *N*,*N*-diphenylselenoamide was obtained because of steric hindrance (entries 13 and 14). Aliphatic selenoamides could be obtained only in low yields because of the

instability of the products (entries 15 and 16). Also, the synthesis of N-monosubstituted and N,N-unsubstituted selenoamides failed under the present conditions because of their instability [5h,9].

The present reaction does offer a new, facile method for the preparation of many, various N,N-disubstituted selenoamides from easily available amides using LiAlHSeH.

EXPERIMENTAL

General

LiAlHSeH was prepared in accordance with a previously described procedure [7]. The ^{77}Se chemical shifts were expressed in ppm deshielded with respect to neat Me_2Se in $CDCl_3$.

*N,N-Dimethylselenobenzamide (***2a***). Typical Procedure for* **2a–2o**. Oxalyl chloride (0.09 ml, 1.0 mmol) was added to stirred solution of *N,N*-dimethylbenzamide (0.177 g, 1.0 mmol) in anhydrous diethyl ether (5 ml) and allowed to react at 0°C for 1 h under an argon atmosphere. The mixture was further stirred for 3 h at room temperature An anhydrous THF solution (25 ml) of LiAlHSeH (1.2 mmol) was added to the mixture at room temperature and allowed to react for 3 h. The mixture was extracted with diethyl ether (100 ml) and washed with water (100 ml). The organic layer was dried over sodium sulfate, filtered and evaporated to dryness. The residue was purified by flash chromatography on silica gel with dichloromethane to yield 0.16 g (75%) **2a** that was obtained by flash chromatography on silica gel as yellow crystals. IR (KBr) 1535 cm^{-1}, mp 80.0–81.4°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.10 (s, 3H, CH_3), 3.70 (s, 3H, CH_3), 7.28–7.34 (m, 5H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.7, 47.3, 124.6, 128.1, 128.4, 146.1, 205.3, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 727.7, MS (CI) $m/z = 214$ [$M^+ + 1$], Anal. Calcd for $C_9H_{11}NSe$: C, 37.13; H, 3. 81; N, 4.81. Found: C, 37.02; H, 3.66; N, 4.82%.

*N,N-Diethylselenobenzamide (***2b***)*. Yield: 68%. Yellow crystals, IR (KBr) 1508 cm^{-1}, mp 55.2–56.1°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (t, $J = 7.2$ Hz, 3H, CH_3), 1.44 (t, $J = 7.2$ Hz, 3H, CH_3), 3.44 (q, $J = 7.2$ Hz, 2H, CH_2), 4.25 (q, $J = 7.2$ Hz, 2H, CH_2), 7.19–7.35 (m, 5H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.2, 13.2, 48.2, 49.7, 123.7, 127.7, 127.9, 146.3, 203.9, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 705.3, MS (CI) $m/z = 242$ [$M^+ + 1$], HRMS: $m/z = 241.0369$, calcd. for $C_{11}H_{15}NSe$, found 241.0368.

*N,N-Dipropylselenobenzamide (***2c***)*. Yield: 61%. Yellow crystals, IR (KBr) 1508 cm^{-1}, mp 40.9–42.3°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.71 (t, $J = 7.6$ Hz, 3H, CH_3), 1.02 (t, $J = 7.6$ Hz, 3H, CH_3), 1.59 (sixtet, $J = 7.6$ Hz, 2H, CH_2), 1.95 (sixtet, $J = 7.6$ Hz, 2H, CH_2), 3.34 (t, $J = 7.6$ Hz, 2H, CH_2), 4.14 (t, $J = 7.6$ Hz, 2H, CH_2), 7.18–7.33 (m, 5H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.7, 11.0, 19.1, 21.1, 55.5, 56.6, 123.8, 127.6, 127.7, 146.4, 204.5, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 717.3, MS (CI) $m/z = 270$ [$M^+ + 1$].

*N-Ethyl-N-methylselenobenzamide (***2d***)*. Yield: 72%. Yellow crystals, IR (KBr) 1514 cm^{-1}, mp 61.0–62.6°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.18 (t, $J = 7.2$ Hz, 3H, CH_3), 1.42 (t, $J = 7.2$ Hz, 3H, CH_3), 3.00 (s, 3H, CH_3), 3.48 (q, $J = 7.2$ Hz, 2H, CH_2), 3.62 (s, 3H, CH_3), 4.27 (q, $J = 7.2$ Hz, 2H, CH_2), 7.22–7.35 (m, 5H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.5, 12.9, 41.5, 44.0, 51.3, 53.1, 123.8, 124.0, 127.8, 127.9, 145.9, 146.1, 203.7, 204.5, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 688.9, 731.4, MS (CI) $m/z = 228$ [$M^+ + 1$].

*N-(Phenylselenocarbonyl)piperidine (***2e***)*. Yield: 75%. Yellow crystals, IR (KBr) 1509 cm^{-1}, mp 64.3–66.4°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.58 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 1.88 (m, 2H, CH_2), 3.50 (t, $J = 6.0$ Hz, 2H, CH_2), 4.49 (t, $J = 5.6$ Hz, 2H, CH_2), 7.23–7.35 (m, 5H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.8, 25.4, 26.7, 53.9, 55.0, 124.3, 128.1, 128.2, 146.0, 203.3, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 679.6, MS (CI) $m/z = 254$ [$M^+ + 1$].

*N-(Phenylselenocarbonyl)pyrrolidine (***2f***)*. Yield: 74%. Yellow crystals, IR (KBr) 1508 cm^{-1}, mp 79.7–81.0°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.02 (quint, $J = 6.8$ Hz, 2H, CH_2), 2.12 (quint, $J = 6.8$ Hz, 2H, CH_2), 3.34 (t, $J = 6.8$ Hz, 2H, CH_2), 3.97 (t, $J = 6.8$ Hz, 2H, CH_2), 7.32–7.36 (m, 5H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.6, 26.5, 54.5, 57.1, 124.6, 128.1, 128.5, 146.6, 200.1, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 717.6, MS (CI) $m/z = 240$ [$M^+ + 1$].

*N,N-Diethyl-4-methoxyselenobenzamide (***2g***)*. Yield: 65%. Yellow crystals, IR (KBr) 1515 cm^{-1}, mp 64.3–65.8°C, ^{1}H NMR($CDCl_3$, 400 MHz) δ 1.09 (t, $J = 7.2$ Hz, 3H, CH_3), 1.36 (t, $J = 7.2$ Hz, 3H, CH_3), 3.40 (q, $J = 7.2$ Hz, 2H, CH_2), 3.72 (s, 3H, CH_3), 4.16 (q, $J = 7.2$ Hz, 2H, CH_2), 6.76 (d, $J = 8.8$ Hz, 2H, Ar), 7.11 (d, $J = 8.8$ Hz, 2H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.1, 13.2, 48.1, 49.8, 55.1, 113.1, 125.4, 139.1, 159.1, 203.9, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 704.1, MS (CI) $m/z = 272$ [$M^+ + 1$].

*N,N-Diethylselenonicotinamide (***2h***)*. Yield: 36%. Yellow oil, IR(neat) 1506 cm^{-1}, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (t, $J = 7.2$ Hz, 3H, CH_3), 1.39 (t, $J = 7.2$ Hz, 3H, CH_3), 3.38 (q, $J = 7.2$ Hz,

2H, CH_2), 4.17 (q, $J = 7.2$ Hz, 2H, CH_2), 7.21 (dd, $J = 4.8$, 7.8 Hz, 1H, Ar), 7.52 (dt, $J = 1.4$, 7.8 Hz, 1H, Ar), 8.42 (d, $J = 1.4$ Hz, 1H, Ar), 8.46 (dd, $J = 1.4$, 4.8 Hz, 1H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.1, 13.3, 48.5, 50.0, 122.7, 131.4, 142.2, 143.8, 148.7, 200.0, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 769.0, MS (CI) $m/z = 243$ [$M^+ + 1$].

*N,N-Diethyl-2-selenonaphthylamide (***2i***)*. Yield: 54%. Yellow crystals, IR (KBr) 1509 cm^{-1}, mp 97.1–97.8°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 (t, $J = 7.2$ Hz, 3H, CH_3), 1.47 (t, $J = 7.2$ Hz, 3H, CH_3), 3.44 (q, $J = 7.2$ Hz, 2H, CH_2), 4.27 (q, $J = 7.2$ Hz, 2H, CH_2), 7.34 (dd, $J = 1.6$, 8.4 Hz, 1H, Ar), 7.44–7.49 (m, 2H, Ar), 7.65 (s, 1H, Ar), 7.77–7.81 (m, 3H, Ar),^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.2, 13.3, 48.3, 49.7, 122.0, 122.3, 126.3, 126.5, 127.5, 127.8, 128.0, 132.3, 132.4, 143.5, 203.8, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 716.5, MS (CI) $m/z = 292$ [$M^+ + 1$].

*N,N-Diethyl-4-methylselenobenzamide (***2j***)*. Yield: 61%. Yellow crystals, IR (KBr) 1509 cm^{-1}, mp 89.8–91.0°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (t, $J = 7.2$ Hz, 3H, CH_3), 1.45 (t, $J = 7.2$ Hz, 3H, CH_3), 2.34 (s, 3H,CH_3), 3.46 (q, $J = 7.2$ Hz, 2H, CH_2), 4.25 (q, $J = 7.2$ Hz, 2H, CH_2), 7.13 (s, 4H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.3, 13.4, 21.4, 48.3, 49.9, 123.9, 128.7, 137.9, 143.9, 204.6, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 704.5, MS (CI) $m/z = 257$ [$M^+ + 1$].

*N,N-Diethyl-3-methylselenobenzamide (***2k***)*. Yield: 50%. Yellow crystals, IR (KBr) 1508 cm^{-1}, mp 79.8–81.9°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (t, $J = 7.2$ Hz, 3H, CH_3), 1.45 (t, $J = 7.2$ Hz, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.44 (q, $J = 7.2$ Hz, 2H, CH_2), 4.25 (q, $J = 7.2$ Hz, 2H, CH_2), 7.01 (d, $J = 7.6$ Hz, 1H, Ar), 7.04 (s, 1H, Ar), 7.09 (d, $J = 7.6$ Hz, 1H, Ar), 7.22 (t, $J = 7.6$ Hz, 1H, Ar), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.4, 13.4, 21.4, 48.3, 49.8, 120.9, 124.5, 128.0, 128.7, 137.9, 146.5, 204.5, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 698.0, MS (CI) $m/z = 257$ [$M^+ + 1$], Anal. Calcd for $C_{12}H_{17}NSe$: C, 56.69; H, 6.74; N, 5.51. Found: C, 56.49; H, 6.74; N, 5.51%.

*N,N-Diethylselenoacetoamide (***2o***)*. Yield: 16%. Brown oil, IR (neat) 1519 cm^{-1}, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26–1.38 (m, 6H, CH_3), 2.71 (s, 3H, CH_3), 3.61 (q, $J = 7.2$ Hz, 2H, CH_2), 4.13 (q, $J = 7.2$ Hz, 2H, CH_2), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.2, 12.5, 36.4, 46.9, 52.0, 201.1, ^{77}Se NMR ($CDCl_3$, 76 MHz) δ 589.6, MS (CI) $m/z = 180$ [$M^+ + 1$].

REFERENCES

[1] (a) Ogawa, A.; Sonoda, N. In Comprehensive Organic Synthesis; Trost, B. M.; Fleming, I. (Eds.); Pergamon Press: Oxford, 1991; Vol. 6, p. 461; (b) Ogawa, A.; Sonoda, N. Rev Heteroat Chem 1994, 10, 43. (c) Dell, C. P. In Comprehensive Organic Functional Group Transformations; Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W. (Eds.); Pergamon Press: Oxford, 1995; Vol. 5, p. 565; (d) Back, T. G., Ed. Organoselenium Chemistry: A Practical Approach; Oxford University Press: U.K., 1999; (e) Murai, T.; Kato, S. Organoselenium Chemistry: Modern Developments in Organic Synthesis; Springer-Verlag: Berlin, 2000; p. 177.

[2] (a) Koketsu, M.; Takenaka, Y.; Ishihara, H. Synthesis 2001, 731; (b) Koketsu, M.; Senda, T.; Yoshimura, K.; Ishihara, H. J Chem Soc, Perkin Trans 1 1999, 453; (c) Koketsu, M.; Hiramatsu, S.; Ishihara, H. Chem Lett 1999, 485; (d) Zhang, P.-F.; Chen, Z.-C. Synthesis 2000, 1219; (e) Petrov, M. L.; Abramov, M. A. Phosphorus Sulfur Silicon Relat Elem 1998, 134/135, 331; (f) Heuze, K.; Purseigle, F.; Dubreuil, D.; Pradere, J. P. Synth Commun 1998, 28, 301; (g) Shimada, K.; Jin, N.; Kawaguchi, M.; Dobashi, K.; Nagano, Y.; Fujimura, M.; Kudoh, E.; Kai, T.; Saito, N.; Masuda, J.; Iwaya, M.; Fujisawa, H.; Aoyagi, S.; Takikawa, Y. Bull Chem Soc Jpn 1997, 70, 197.

[3] (a) Murai, T.; Suzuki, A.; Ezaka, T.; Kato, S. Org Lett 2000, 2, 311; (b) Murai, T.; Mori, T.; Kato, S. Synlett 1998, 619; (c) Murai, T.; Ezaka, T.; Kato, S. Tetrahedron Lett 1998, 39, 4329.

[4] (a) Koketsu, M.; Suzuki, N.; Ishihara, H. J Org Chem 1999, 64, 6473; (b) Murai, T.; Ezaka, T.; Kato, S. Bull Chem Soc Jpn 1998, 71, 1193; (c) Li, G. M.; Zingaro, R. A. J Chem Soc Perkin Trans 1 1998, 647; (d) Segi, M.; Kojima, A.; Nakajima, T.; Suga, S. Synlett 1991, 105; (e) Li, G. M.; Zingaro, R. A.; Segi, M.; Reibenspies, J. H.; Nakajima, T. Organometallics 1997, 16, 756; (f) Murai, T.; Ezaka, T.; Kanda, T.; Kato, S. Chem Commun 1996, 1809; (g) Murai, T.; Ezaka, Tatsuya; Ichimiya, T.; Kato, S. Synlett 1997, 775.

[5] (a) Ruan, M.-D.; Zhang, P.-F.; Tao, Y.; Fan, W.-Q. Synth Commun 1996, 26, 2617; (b) Cohen, V. I. Synthesis 1978, 668; (c) Shimada, K.; Hikage, S.; Takeishi, Y.; Takikawa, Y. Chem Lett 1990, 1403; (d) Ogawa, A.; Miyake, J.; Karasaki, Y.; Murai, S.; Sonoda, N. J Org Chem 1985, 50, 384; (e) Zhao, X.-R.; Ruan M.-D.; Fan, W.-Q.; Zhao, X.-R. Synth Commun 1994, 24, 1761; (f) Lai, L.-L.; Reid, D. H. Synthesis 1993, 870; (g) Shimada, K.; Matsuda, Y.; Hikage, S.; Takeishi, Y.; Takikawa, Y. Bull Chem Soc Jpn 1991, 64, 1037; (h) Ishihara, H.; Yoshimura, K.; Koketsu, M. Chem Lett 1998, 1287.

[6] (a) Ishihara, H.; Yoshimi, M.; Hara, N.; Ando, H.; Kato, S. Bull Chem Soc Jpn 1990, 63, 835; (b) Murai, T.; Ezaka, T.; Kanda, T.; Kato, S. Chem Commun 1996, 1809; (c) Murai, T.; Ezaka, T.; Niwa, N.; Kanda, T.; Kato, S. Synlett 1996, 865.

[7] Ishihara, H.; Koketsu, M.; Fukuta, Y.; Nada, F. J Am Chem Soc 2001, 123, 8408.

[8] (a) Klayman, D. L.; Griffin, T. S. J Am Chem Soc 1973, 95, 197; (b) Copeland, C. M.; Ghosh, J.; McAdam, D. P.; Skelton, B. W.; Stick, R. V.; White, A. H. Aust J Chem 1988, 41, 549.

[9] (a) Paulmier, C. Selenium Reagents and Intermediates in Organic Synthesis; Pergamon Press: Oxford, 1986; Ch. 3; (b) Ogawa, A.; Miyake, J.; Karasaki, Y.; Murai, S.; Sonoda, N. J Org Chem 1985, 50, 384.