Thermal Elimination of Carbonyl Sulfide from *O*-Aryl Thionocarbonates of Pyrrolidine-, Piperidine-, and Tetrahydrothiophene-2-ethanol

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Pyrolysis of *O*-2-(1-benzyl-2-pyrrolidinyl and 2-piperidyl)ethyl *O*-phenyl thionocarbonates (4 and 25) in acetonitrile gave 1-benzyl-4-phenoxyhexahydro-1*H*-azepine (7) and 1-benzyl-4-phenoxyoctahydroazocine (26) with liberation of COS in 55% and 32% yields, accompanied with 2-(2-phenoxyethyl)pyrrolidine and piperidine (8 and 27), *via* the azetidinium intermediate (6). On the other hand, *O*-phenyl *O*-2-(2-tetrahydrothienyl)ethyl thionocarbonate (32) resulted in the predominant formation of the *O,S*-rearrangement product (35) in 53% yield.

Keywords thionocarbonate; pyrolysis; carbonyl sulfide; ring enlargement; azetidinium salt; hexahydro-1*H*-azepine; octahydroazocine; thiepane; dithionocarbonate; thiolcarbonate

Recently, we have reported a novel transformation of an azabicyclothionocarbonate (**1**) by treatment with α,α′-azobisisobutyronitrile (AIBN) in refluxing benzene to give the azaspirolactone (**2**) *via* a tertiary radical intermediate.[1] As part of our continuing investigation of radical cyclization involving the thionocarbonate, we now report the application of this reaction to acyclic systems, such as *O*-aryl thionocarbonates of *N*-benzylpyrrolidine-, *N*-benzylpiperidine-, and tetrahydrothiophene-2-ethanol.

The phenyl thionocarbonate (**4**) was prepared in 62% yield by treatment of 1-benzyl-2-(2-hydroxyethyl)pyrrolidine (**3**)[2] with phenyl chlorothionoformate (PCTF) in the presence of triethylamine and 4-dimethylaminopyridine (4-DMAP) in acetonitrile at 0 °C. After refluxing of **4** in toluene in the presence of AIBN (cat.) for 3.5 h, two new spots were seen on thin layer chromatography (TLC) (SiO_2–EtOAc) at $Rf=0.46$ and 0.6. Without addition of AIBN, similar results were obtained. This result indicates that AIBN does not play any role in this reaction. When acetonitrile was used as the solvent, the reaction proceeded under milder conditions to give the two components (**7** in 55% yield and **8** in 16% yield), which were separated by SiO_2 column chromatography. The spectral data for **7** and **8** excluded the azaspirolactone structure (**5**) which was expected to be obtained *via* radical cyclization.[1] The structure of the more polar component (**8**) was determined as 1-benzyl-2-(2-phenoxyethyl)pyrrolidine based on the mass spectrum (MS), which exhibited a parent peak at *m/z* 281, and a comparison of the proton nuclear magnetic resonance (^{1}H-NMR) spectrum with that of **3**. Assignment of the structure of the less polar product (**7**), 1-benzyl-4-phenoxyhexahydro-1*H*-azepine, was made on the basis of MS data [281 (M^+), 188 (M^+-OPh)] and carbon-13 nu-

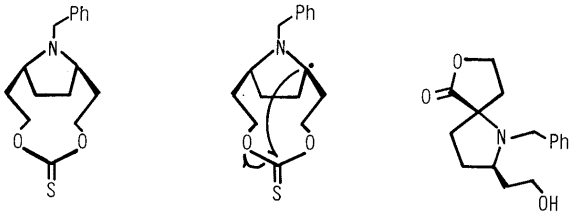

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Chart 1

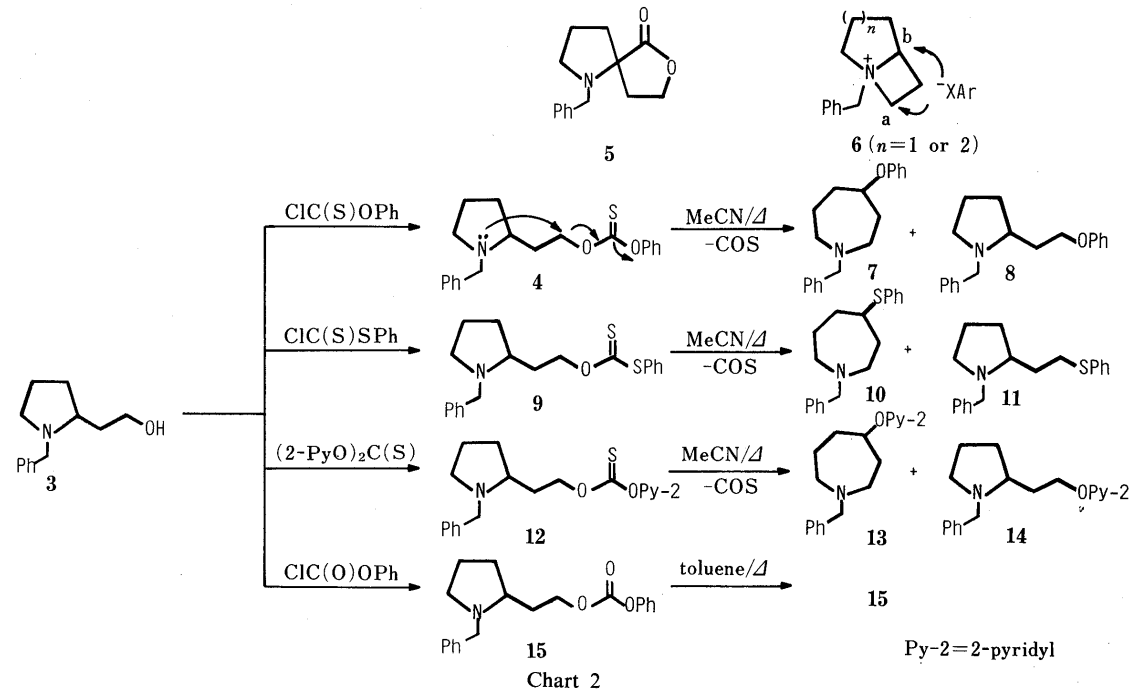

Chart 2

clear magnetic resonance (^{13}C-NMR) spectroscopy, which showed the presence of a secondary carbon atom adjacent to the phenoxy group at δ 78.5. The structure (**7**) was further corroborated by the following chemical transformations. Chlorination [triphenyl phosphine (Ph_3P)–carbon tetrachloride (CCl_4)] of 1-benzyl-4-azepinol (**17**), readily available from the azepinone (**16**)[3] by reduction with lithium aluminum hydride ($LiAlH_4$), gave only a chloropyrrolidine (**19**), with ring contraction occurring *via* a azetidinium salt (**18**). Thus, the *N*-benzyl group of **16** was replaced with a vinyloxycarbonyl (VOC) group[4] in order to avoid ring contraction. Refluxing of **16** with vinyl chloroformate (VOCCl)[4] in dichloromethane (CH_2Cl_2) gave *N*-VOC-4-azepinone (**20**) in 30% yield, which was then subjected to reduction [sodium borohydride ($NaBH_4$)] followed by chlorination [*N*-chlorosuccinimide (NCS)–Ph_3P] to give *N*-VOC-4-chloroazepine (**22**) in 55.5% overall yield. Conversion of the chloro group into a phenoxy group was achieved by treatment of **22** with phenol in the presence of potassium carbonate (K_2CO_3) to give *N*-VOC-4-phenoxyazepine (**23**), which was identical with the product (**23**) prepared from **7** and VOCCl. Therefore, the structure (**7**) was confirmed, as described above. The formation of the products (**7** and **8**) can be considered to proceed *via* the azetidinium phenoxide (**6**) derived by attack of the nitrogen atom at α-position of the thionocarbonate (**4**) with liberation of carbonyl sulfide (COS), followed by attack of the phenoxy anion at position a or b as depicted in Chart 2. Although numerous studies[5] on the liberation of COS in organic synthesis have been reported, little is known about the liberation of COS from *O*-phenyl thionocarbonate of heterocycles containing a nitrogen or sulfur atom. It is interesting to note that the corresponding carbonate (**15**) was quite stable even on refluxing for 18 h in toluene, indicating the greater facility of the COS liberation from *O*-phenyl thionocarbonate. Thus, our attention was next turned to pyrolysis of the phenyl dithionocarbonate (**9**) and 2-pyridyl thionocarbonate (**12**). The required substrates (**9** and **12**) were prepared by reaction of **3** with phenyl chlorodithioformate and di-2-pyridyl thionocarbonate,[6] respectively. On refluxing in acetonitrile, decomposition of **9** to form phenylthioazepine (**10**) and phenylthiopyrrolidine (**11**) in the ratio of 1:2 in 89% yield was completed in about 1 h. Analogously, **12** afforded a mixture of the 2-pyridyloxyazepine (**13**) and 2-pyridyloxypyrrolidine (**14**) in the ratio of 2:3 in 56% yield. Although the present experimental results did not indicate a distinct superiority in substrate range, the *O*-phenyl thionocarbonate (**4**) appeared to be preferable for the predominant formation of the ring-enlargement product.

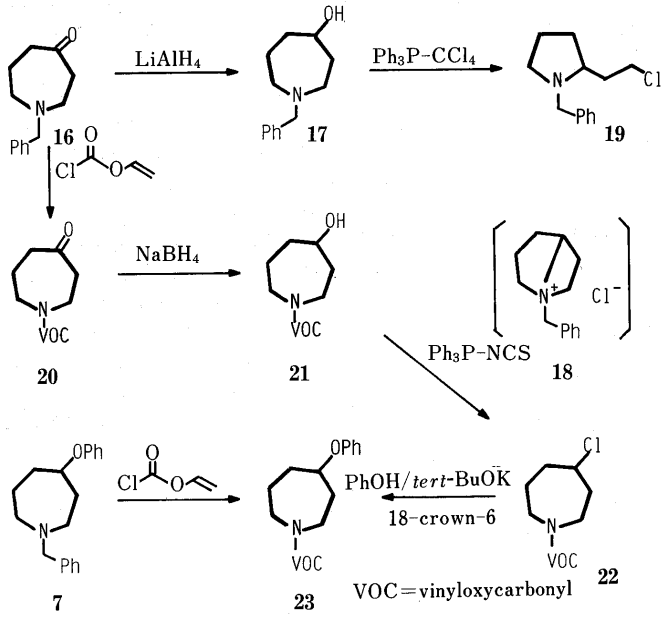

Chart 3

Thermal reactions of the phenyl thionocarbonate (**25**) and phenyl dithionocarbonate (**28**) of the piperidine-2-ethanol (**24**)[7] proceeded similarly in acetonitrile, but the 4-phenoxy- and 4-phenylthioazocines (**26** and **29**) were obtained in only 14% and 3% yields as minor products, accompanied with the preferential formation of the phenoxy- and phenylthiopiperidines (**27** and **30**).

Next, pyrolysis of thionocarbonate or dithionocarbonate having an *S*-heterocycle instead of an *N*-heterocycle was investigated. Pyrolysis of the phenyl thionocarbonate (**32**), prepared from tetrahydrothiophene-2-ethanol (**31**) and PCTF in 74% yield, was carried out in refluxing *o*-dichlorobenzene to give a mixture of 4-phenoxythiepane (**33**), 2-(2-phenoxyethyl)tetrahydrothiophene (**34**) and the thiolcarbonate (**35**), from which only **35** was isolated in 53% yield in a pure form. Since attempts to separate the two compounds (**33** and **34**) failed, compound **34** was

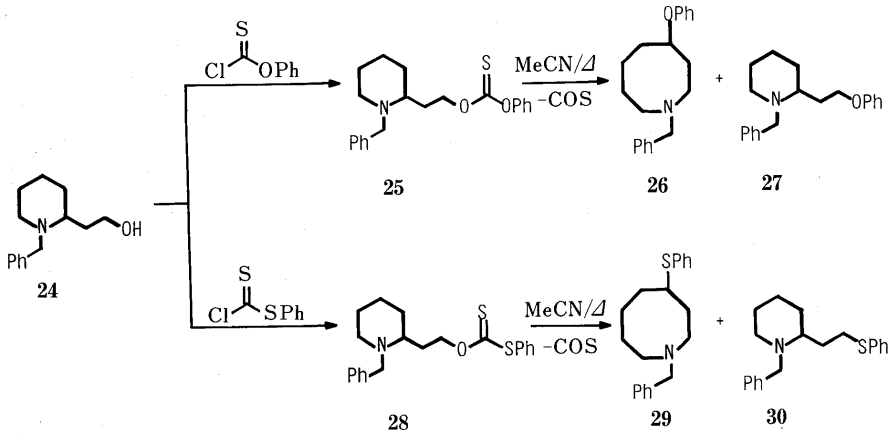

Chart 4

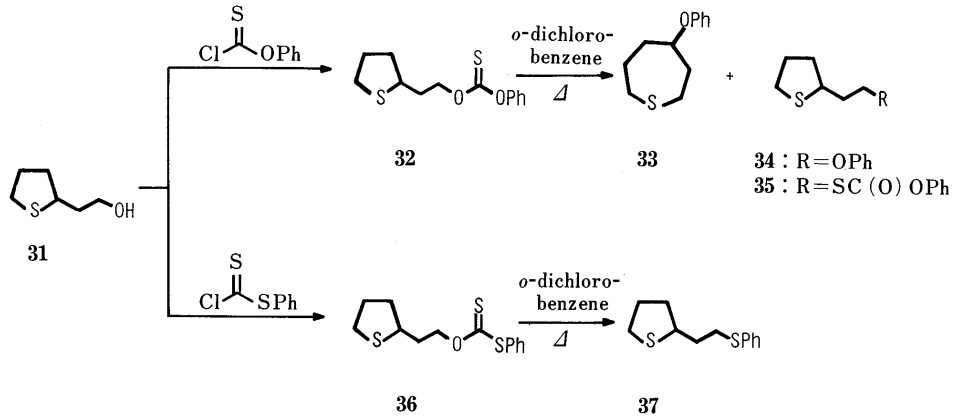

Chart 5

alternatively synthesized from **31** by means of the following reaction sequences: i) *p*-toluenesulfonyl chloride (TsCl)/triethylamine/4-DMAP ii) phenol/K_2CO_3 (see Experimental). By comparison of the ^{1}H-NMR spectrum of **34** [δ 3.56 (1H, m, CHS), 4.01 (2H, q, J=6 Hz, CH_2O)] thus obtained with that of a mixture of the two compounds, it was clearly apparent that a minor component (*ca.* 33%) of the mixture was **34**. Thus, the major component of the mixture was supposed to be the product (**33**) with ring-enlargement on the basis of the ^{1}H-NMR spectral data [δ 4.58 (1H, m, CHOPh)] as well as the mechanistic proposal involving a four membered intermediate as described above. The isolated product (**35**) was readily assigned as the *O,S*-rearrangement product (thiolcarbonate), which may be obtained by Schonberg rearrangement,[8] based on the spectroscopic data [infrared (IR) spectrum: 1710 cm^{-1} (CO), ^{1}H-NMR: 2.60—3.10 (4H, m, C_5-H_2 and CH_2S), and MS *m/z* 268 (M^+)]. On the other hand, pyrolysis of dithionocarbonate (**36**) in *o*-dichlorobenzene provided only the COS elimination product (**37**) in 74% yield. Thus, it was found that thionocarbonate containing *S*-heterocycles are rather stable and require a higher temperature for pyrolysis than thionocarbonate containing *N*-heterocycles, resulting in the predominant formation of the *O,S*-rearrangement product.

Experimental

The IR spectra were taken on a Shimadzu IR-435 spectrophotometer. MS were taken on a Hitachi M-80 spectrometer. ^{1}H- and ^{13}C-NMR spectra were taken with tetramethylsilane as an internal standard on a Varian Gemini-200 spectrometer in $CDCl_3$. Kieselgel 60 (Art 9834; Merck) and Kieselgel 60 F_{254} plates (Art 5715; Merck) were employed for column chromatography and TLC, respectively. In general, reactions were carried out under a nitrogen stream.

***O*-2-(1-Benzyl-2-pyrrolidinyl)ethyl *O*-Phenyl Thionocarbonate (4)** Phenyl chlorothionoformate (0.48 ml, 3.51 mmol) was added to a solution of **3** (0.6 g, 6.93 mmol), 4-DMAP (36 mg, 0.29 mmol) and triethylamine (0.48 ml, 3.51 mmol) in acetonitrile (6 ml) under ice-cooling, and the mixture was stirred for 1.5 h. After removal of the solvent, the residue was dissolved in CH_2Cl_2 (30 ml). The CH_2Cl_2 solution was washed with H_2O and brine, dried over anhydrous Na_2SO_4, and then evaporated under reduced pressure. The residue was purified by column chromatography [eluent: hexane–EtOAc (9 : 1)] to give **4** (614 mg, 62%) as an oil. IR ν max (film) cm^{-1}: 1200 (C=S). ^{1}H-NMR δ: 1.49—2.38 (7H, m, 3 × CH_2 and NCH), 2.61 and 2.95 (each 1H, each m, NCH_2), 3.25 and 4.20 (each 1H, each d, J=16 Hz, NCH_2Ph), 4.51—4.78 (2H, m, CH_2O), and 7.15—7.53 (10H, m, Ar-H). MS *m/z*: 341 (M^+). High-resolution MS (HRMS) Calcd for $C_{20}H_{23}NO_2S$: 341.1448. Found: 341.1463.

Pyrolysis of 4 A solution of **4** (99 mg, 0.29 mmol) in acetonitrile (3 ml) was refluxed for 3 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (9 : 1)] to give 1-benzyl-4-phenoxyhexahydro-1*H*-azepine (**7**) (45 mg, 55%) as an oil from the first fraction. IR ν max (film) cm^{-1}: 1240 (PhOCH). ^{1}H-NMR δ: 1.50—2.20 (6H, m, 3 × CH_2), 2.50—2.85 (4H, m, 2 × CH_2), 3.65 (2H, s, NCH_2), 4.57 (1H, m, OCH), and 6.82—7.0 (10H, m, Ar-H). MS *m/z*: 281 (M^+). HRMS Calcd for $C_{19}H_{23}NO$: 281.1778. Found: 281.1767. The second fraction of the eluate gave 1-benzyl-2-(2-phenoxyethyl)pyrrolidine (**8**) (13 mg, 16%) as an oil. IR ν max (film) cm^{-1}: 1240 ($ArOCH_2$). ^{1}H-NMR δ: 1.50—2.30 (7H, m, C_3- and C_4-H_2, C_5-H, and CH_2CH_2O), 2.65 (1H, m, C_5-H), 2.93 (1H, m, C_2-H), 3.25 and 4.05 (each 1H, each d, J=16 Hz, NCH_2), 3.95—4.18 (2H, m, OCH_2), and 7.12—7.41 (10H, m, Ar-H). ^{13}C-NMR δ: 78.5 (C-4). MS *m/z*: 281 (M^+). HRMS Calcd for $C_{19}H_{23}NO$: 281.1778. Found: 281.1775.

***O*-2-(1-Benzyl-2-pyrrolidinyl)ethyl *S*-Phenyl Dithionocarbonate (9)** Phenyl chlorodithiocarbonate (0.36 ml, 2.4 mmol) was added to a solution of **3** (410 mg, 2.0 mmol), 4-DMAP (24 mg, 0.2 mmol) and triethylamine (0.35 ml, 2.4 mmol) in acetonitrile (10 ml) under ice-cooling, and the mixture was stirred for 4 h. Work-up as described for the preparation of **4** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (20 : 1)] to give **9** (344 mg, 70%) as an oil. IR ν max (film) cm^{-1}: 1230 (C=S). ^{1}H-NMR δ: 1.20—2.45 (8H, m, 4 × CH_2), 2.85 (1H, m, CH), 3.10 and 3.85 (each 1H, each d, J=16 Hz, NCH_2), 4.50—4.72 (2H, m, OCH_2), and 7.15—7.57 (10H, m, Ar-H). MS *m/z*: 357 (M^+). HRMS Calcd for $C_{20}H_{23}NOS_2$: 357.1219. Found: 357.1212.

Pyrolysis of 9 A solution of **9** (97 mg, 0.27 mmol) in acetonitrile (3 ml) was refluxed for 1 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (9 : 1)] to give 1-benzyl-4-phenylthiohexahydro-1*H*-azepine (**10**) (24 mg, 30%) as an oil from the first fraction. ^{1}H-NMR δ: 1.50—2.20 (6H, m, 3 × CH_2), 2.44—2.82 (4H, m, 2 × CH_2), 3.45 (1H, m, CH), 3.62 (2H, s, NCH_2), 7.10—7.50 (10H, m, Ar-H). MS *m/z*: 297 (M^+). HRMS Calcd for $C_{19}H_{23}NS$: 297.1550. Found: 297.1550. The second fraction of the eluate gave 1-benzyl-2-(2-phenylthioethyl)pyrrolidine (**11**) (48 mg, 59%) as an oil. ^{1}H-NMR δ: 1.20—2.20 (7H, C_3- and C_4-H_2, C_5-H, and CH_2CH_2S), 2.55 (1H, m, C_5-H), 2.90 (2H, m, CH_2S), 3.05 (1H, m, CH), 3.20 and 3.95 (each 1H, each d, J=16 Hz, NCH_2), and 7.05—7.10 (10H, m, Ar-H). MS *m/z*: 297 (M^+). HRMS Calcd for $C_{19}H_{23}NS$: 297.1550. Found: 297.1553.

***O*-2-(1-Benzyl-2-pyrrolidinyl)ethyl *O*-2-Pyridyl Thionocarbonate (12)** Di-2-pyridyl thionocarbonate (85 mg, 0.37 mmol) was added to a solution of **3** (50 mg, 0.25 mmol) and 4-DMAP (3 mg, 0.024 mmol) in acetonitrile (4 ml) at room temperature, and the mixture was stirred for 6 h. Work-up as described for the preparation of **4** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (4 : 1)] to give **12** (13 mg, 16%) as an oil. ^{1}H-NMR δ: 1.40—2.30 (7H, m, C_3- and C_4-H_2, C_5-H, and CH_2CH_2O), 2.57 (1H, m, C_5-H), 2.89 (1H, m, C_2-H), 3.20 and 4.0 (each 1H, each d, J=16 Hz, NCH_2), 4.50—4.75 (2H, m, OCH_2), 7.05 (1H, d, J=9 Hz, $C_{3'}$-H), 7.10—7.38 (6H, m, Ar-H and $C_{5'}$-H), 7.80 (1H, td, J=9, 1 Hz, $C_{4'}$-H), and 8.40 (1H, dd, J=6, 1 Hz, $C_{6'}$-H). MS *m/z*: 342 (M^+).

Pyrolysis of 12 A solution of **12** (30 mg, 0.087 mmol) in acetonitrile (3 ml) was refluxed for 2 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (1 : 1)] to give 1-benzyl-4-(2-pyridyloxy)hexahydro-1*H*-azepine (**13**) (8 mg, 32%) as an oil from the first fraction. ^{1}H-NMR δ: 1.50—2.20 (6H, m, 3 × CH_2), 2.50—2.80 (4H, m, 2 × CH_2), 3.65 (2H, s, NCH_2), 5.30 (1H, m, CH), 6.65 (1H, d, J=9 Hz, $C_{3'}$-H), 6.78 (1H, t, J=6 Hz, $C_{5'}$-H), 7.15—7.40 (5H, m,

Ar-H), 7.51 (1H, td, $J=9$, 1 Hz, $C_{4'}$-H), and 8.10 (1H, dd, $J=6$, 1 Hz, $C_{6'}$-H). MS *m/z*: 282 (M^+). HRMS Calcd for $C_{18}H_{22}N_2O$: 282.1731. Found: 282.1738. The second fraction of the eluate gave 1-benzyl-2-(pyridyloxyethyl)pyrrolidine (**14**) (6 mg, 24%) as an oil. ^{1}H-NMR δ: 1.40—2.80 (6H, m, C_3- and C_4-H_2, and C$\underline{H}_2$CH_2O), 2.50—2.80 (2H, m, C_5-H_2), 2.90 (1H, m, C_2-H), 4.22—4.50 (2H, m, OCH_2), 6.60—6.88 (2H, m, $C_{3'}$- and $C_{5'}$-H), 7.15—7.40 (5H, m, Ar-H), 7.50 (1H, td, $J=9$, 1 Hz, $C_{4'}$-H), and 8.15 (1H, dd, $J=6$, 1 Hz, $C_{6'}$-H). MS *m/z*: 282 (M^+). HRMS Calcd for $C_{18}H_{22}N_2O$: 282.1731. Found: 282.1731.

***O*-2-(1-Benzyl-2-pyrrolidinyl)ethyl *O*-Phenyl Carbonate (15)** Phenyl chloroformate (233 mg, 1.48 mmol) was added to a solution of **3** (254 mg, 1.24 mmol), 4-DMAP (15 mg, 0.12 mmol) and triethylamine (0.21 ml, 1.48 mmol) in acetonitrile (10 ml) under ice-cooling, and the mixture was stirred for 30 min. Work-up as described for the preparation of **4** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (9 : 1)] to give **15** (361 mg, 89%) as an oil. IR ν max (film) cm^{-1}: 1760 (C=O). ^{1}H-NMR δ: 1.50—2.25 (7H, m, C_3- and C_4-H_2, C_5-H, and C$\underline{H}_2$CH_2O), 2.58 (1H, m, C_5-H), 2.92 (1H, m, CH), 3.24 and 4.02 (each 1H, each d, $J=16$ Hz, NCH_2), 4.25—4.45 (2H, m, CH_2O), and 7.10—7.45 (10H, m, Ar-H). MS *m/z*: 325 (M^+). HRMS Calcd for $C_{20}H_{23}NO_3$: 325.1677. Found: 325.1683.

1-Benzyl-4-hydroxyhexahydro-1*H*-azepine (17) A solution of 1-benzyl-4-azepinone (**16**) (1.0 g, 4.93 mmol) in dry Et_2O (10 ml) was added dropwise to a suspension of $LiAlH_4$ (562 mg, 14.78 mmol) in dry Et_2O (10 ml) under ice-cooling, and the mixture was stirred for 1 h. The reaction mixture was quenched by the addition of 6 N HCl (8 ml) followed by 6 N NaOH (10 ml), and the product was extracted with Et_2O (100 ml × 4). The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure to give **17** (803 mg, 80%), which was used for the following reaction without purification. IR ν max (film) cm^{-1}: 3450 (OH). ^{1}H-NMR δ: 1.40—3.0 (10H, m, 5 × CH_2), 3.45—3.65 (2H, br s, NCH_2), 4.08 (1H, m, CH), and 7.18—7.40 (5H, m, Ar-H). MS *m/z*: 205 (M^+).

1-Benzyl-2-(2-chloroethyl)pyrrolidine (19) A solution of **17** (100 mg, 0.49 mmol) and Ph_3P (137 mg, 0.52 mmol) in CCl_4 (3 ml) was refluxed for 3 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (7 : 3)] to give **19** (58 mg, 53%) as an oil. ^{1}H-NMR δ: 1.40—2.28 (7H, m, C_3- and C_4-H_2, C_5-H, and C$\underline{H}_2$CH_2Cl), 2.52—2.70 (1H, m, C_5-H), 2.82—2.92 (1H, m, CH), 3.24 and 4.0 (each 1H, each d, $J=16$ Hz, NCH_2), 3.46—3.77 (2H, m, CH_2Cl), and 7.12—7.40 (5H, m, Ar-H). MS *m/z*: 223 (M^+).

1-Vinyloxycarbonylhexahydro-1*H*-azepin-4-one (20) VOCCl (0.33 ml, 3.9 mmol) was added dropwise to a solution of **16** (609 mg, 3 mmol) in CH_2Cl_2 (15 ml), and the mixture was refluxed for 10 min. The reaction mixture was washed with cold saturated $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, and then evaporated. The residue was purified by column chromatography [eluent: hexane–EtOAc (7 : 3)] to give **20** (164 mg, 30%) as an oil. IR ν max (film) cm^{-1}: 1710 (C=O). ^{1}H-NMR δ: 1.70—1.90 (2H, m, C_6-H_2), 2.57—2.73 (4H, m, C_3- and C_5-H_2), 3.54—3.72 (4H, m, C_2- and C_7-H_2), 4.43 (1H, d, $J=8$ Hz, ), 4.75 (1H, d, $J=16$ Hz, ), 7.14 (1H, dd, $J=16$, 8 Hz, OCH=). MS *m/z*: 183 (M^+). HRMS Calcd for $C_9H_{13}NO_3$: 183.0895. Found: 183.0896.

4-Hydroxy-1-vinyloxycarbonylhexahydro-1*H*-azepine (21) $NaBH_4$ (36 mg, 0.97 mmol) was added portionwise to a solution of **20** (148 mg, 0.80 mmol) in MeOH (10 ml) and the mixture was stirred at room temperature for 30 min. After decomposition of excess $NaBH_4$ by the addition of AcOH (5 drops), the solvent was removed by evaporation. The residue was agitated with H_2O (10 ml), and extracted with EtOAc (50 ml). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to give **21** (148 mg), which was used for the following reaction without purification. IR δ max (film) cm^{-1}: 3420 (OH), 1700 (C=O). ^{1}H-NMR ν: 1.50—2.15 (6H, m, C_3-, C_5-, and C_6-H_2), 3.28—3.71 (4H, m, C_2- and C_7-H_2), 3.80—4.0 (1H, m, CH), 4.42 (1H, d, $J=8$ Hz, ), 4.75 (1H, d, $J=16$ Hz, ), 7.19 (1H, dd, $J=16$, 8 Hz, OCH=). MS *m/z*: 185 (M^+). HRMS Calcd for $C_9H_{15}NO_3$: 185.1050. Found: 185.1041.

4-Chloro-1-vinyloxycarbonylhexahydro-1*H*-azepine (22) A solution of Ph_3P (147 mg, 0.56 mmol) in dimethyl formamide (DMF) (2 ml) was added dropwise to a solution of NCS (75 mg, 0.56 mmol) and **21** (52 mg, 0.28 mmol) in DMF (2 ml) under ice-cooling, and the mixture was stirred for 20 min. The reaction mixture was quenched by the addition of H_2O (5 ml), and extracted with benzene–EtOAc (1 : 1) (30 ml). The extract was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The residue was purified by column chromatography [eluent: hexane–EtOAc (3 : 1)] to give **22** (32 mg, 56%) as an oil. IR ν max (film) cm^{-1}: 1710 (C=O). ^{1}H-NMR δ: 1.60—2.30 (6H, m, C_3-, C_5-, and C_6-H_2), 3.31—3.70 (4H, m, C_2- and C_7-H_2), 4.17—4.37 (1H, m, CH), 4.47 (1H, d, $J=8$ Hz, ), 4.77 (1H, d, $J=16$ Hz, ), 7.20 (1H, dd, $J=16$, 8 Hz, OCH=). MS *m/z*: 203 (M^+). HRMS Calcd for $C_9H_{14}ClNO_2$: 203.0711. Found: 203.0709.

4-Phenoxy-1-vinyloxycarbonylhexahydro-1*H*-azepine (23) Method A: VOCCl (0.01 ml, 0.10 mmol) was added dropwise to a solution of **7** (22 mg, 0.08 mmol) in CH_2Cl_2 (5 ml), and the mixture was refluxed for 10 min. Work-up as described for the preparation of **20** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (7 : 3)] to give **23** (17 mg, 84%) as an oil. IR ν max (film) cm^{-1}: 1710 (CO). ^{1}H-NMR δ: 1.57—2.15 (6H, m, C_3-, C_5-, and C_6-H_2), 3.30—3.78 (4H, m, C_2- and C_7-H_2), 4.40—4.56 (2H, m, OCH and ), 4.78 (1H, d, $J=16$ Hz, ), 6.80—7.32 (6H, m, Ar-H and -OCH=). MS *m/z*: 261

Method B: A suspension of **22** (14 mg, 0.07 mmol), phenol (19 mg, 0.21 mmol), and *tert*-BuOK (23 mg, 0.21 mmol) in the presence of 18-crown-6 (4 mg, 0.014 mmol) in acetonitrile (2 ml) was refluxed for 6 h. After removal of the solvent, the residue was extracted with benzene–EtOAc (1 : 1) (30 ml). The extract was washed with 5% NaOH, H_2O, and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (3 : 1)] to give **23** (3 mg, 15.5%), which was identical with the sample obtained by Method A, based on comparison of their ^{1}H-NMR spectra and *Rf* values on TLC.

***O*-2-(1-Benzyl-2-piperidyl)ethyl *O*-Phenyl Thionocarbonate (25)** Phenyl chlorothionoformate (0.08 ml, 0.575 mmol) was added to a solution of **24** (105 mg, 0.48 mmol), 4-DMAP (6 mg, 0.048 mmol), and triethylamine (0.08 ml, 0.575 mmol) in acetonitrile (2 ml) under ice-cooling. Work-up as described for the preparation of **4** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (9 : 1)] to give **25** (108 mg, 64%) as an oil. IR ν max (film) cm^{-1}: 1195 (C=S). ^{1}H-NMR δ: 1.20—1.90 (6H, m, C_3-, C_4-, and C_5-H_2), 1.95—2.35 (3H, m, C_6-H and C$\underline{H}_2$CH_2O), 2.58 (1H, m, C_6-H), 2.79 (1H, m, C_2-H), 3.31 and 4.0 (each 1H, each d, $J=18$ Hz, NCH_2), 4.55—4.85 (2H, m, OCH_2), and 7.05—7.60 (10H, m, Ar-H). MS *m/z*: 355 (M^+). HRMS Calcd for $C_{21}H_{25}NO_2S$: 355.1604. Found: 355.1608.

Pyrolysis of 25 A solution of **25** (108 mg, 0.31 mmol) in acetonitrile (3 ml) was refluxed for 3 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (9 : 1)] to give 1-benzyl-4-phenoxyoctahydroazocine (**26**) (13 mg, 14%) as an oil from the first fraction. IR ν max (film) cm^{-1}: 1240 (ArOCH). ^{1}H-NMR δ: 1.18—2.37 (8H, m, C_3-, C_5-, C_6-, and C_7-H_2), 2.65 (4H, m, C_2- and C_8-H_2), 3.62 (2H, s, NCH_2), 4.52 (1H, m, OCH), and 6.68—7.60 (10H, m, Ar-H). MS *m/z*: 295 (M^+). HRMS Calcd for $C_{20}H_{25}NO$: 295.1935. Found: 295.1942. The second fraction of the eluate gave 1-benzyl-2-(2-phenoxyethyl)piperidine (**27**) (54 mg, 60%) as an oil. IR ν max (film) cm^{-1}: 1240 ($ArOCH_2$). ^{1}H-NMR δ: 1.25—2.35 (9H, m, C_3-, C_4- and C_5-H_2, C_6-H, and C$\underline{H}_2$CH_2O), 2.62 (1H, m, C_6-H), 2.79 (1H, m, C_2-H), 3.38 and 4.0 (each 1H, each d, $J=18$ Hz, NCH_2), 4.18 (2H, m, OCH_2), and 6.83—7.57 (10H, m, Ar-H). MS *m/z*: 295 (M^+). HRMS Calcd for $C_{20}H_{25}NO$: 295.1935. Found: 295.1937.

***O*-2-(1-Benzyl-2-piperidyl)ethyl *S*-Phenyl Dithionocarbonate (28)** Phenyl chlorodithioformate (0.82 ml, 5.48 mmol) was added to a solution of **24** (1.0 g, 4.57 mmol), 4-DMAP (56 mg, 0.46 mmol), and triethylamine (0.76 ml, 5.48 mmol) in acetonitrile (20 ml). Work-up as described for the preparation of **4** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (20 : 1)] to give **28** (1.41 g, 83%) as an oil. ^{1}H-NMR δ: 1.10—2.31 (10H, m, 5 × CH_2), 2.65 (1H, m, SCH), 3.18 and 3.80 (each 1H, each d, $J=16$ Hz, NCH_2), 4.50—4.78 (2H, m, OCH_2), and 7.15—7.53 (10H, m, Ar-H). MS *m/z*: 371 (M^+). HRMS Calcd for $C_{21}H_{25}NOS_2$: 371.1376. Found: 371.1365.

Pyrolysis of 28 A solution of **28** (102 mg, 0.27 mmol) in acetonitrile (3 ml) was refluxed for 1.5 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (20 : 1)] to give 1-benzyl-4-phenylthiooctahydroazocine (**29**) (3 mg, 3%) from the first fraction as an oil. ^{1}H-NMR δ: 1.45—1.95 (8H, m, C_3-, C_5-, C_6-, and C_7-H_2), 2.15—2.57 (4H, m, C_2- and C_7-H_2), 3.55 (3H, m, NCH_2 and SCH), and 7.08—7.55 (10H, m, Ar-H). MS *m/z*: 311 (M^+). HRMS Calcd

for $C_{20}H_{25}NS$: 311.1707. Found: 311.1708. The second fraction of the eluate gave 1-benzyl-2-(2-phenylthioethyl)piperidine (**30**) (86 mg, 97%) as an oil. ^{1}H-NMR δ: 1.20—2.20 (10H, m, C_3-, C_4-, C_5-, C_6-H_2, and $C\underline{H}_2CH_2S$), 2.75 (1H, m, SCH), 2.90—3.19 (2H, m, SCH_2), 3.25 and 3.91 (each 1H, each d, J=16 Hz, NCH_2), and 7.10—7.50 (10H, m, Ar-H). MS m/z: 311 (M^+). HRMS Calcd for $C_{20}H_{25}NS$: 311.1707. Found: 311.1710.

2-(2-Hydroxyethyl)tetrahydrothiophene (31) A suspension of commercialy available 2-(2-hydroxyethyl)thiophene (1.0 g, 7.8 mmol) in the presence of 5% Pd–C (15 g) and concentrated H_2SO_4 (2 ml) in MeOH (50 ml) was vigorously stirred under an H_2 stream (initial pressure 6 kg/cm^2) using a Skita apparatus for 25 h, according to the method of Mozingo *et al.*[9] The catalyst was filtered off and the solvent was removed by evaporation under reduced pressure. The residue was neutralized with 5% NaOH under ice-cooling and extracted with EtOAc. The extract was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The residue was purified by column chromatography [eluent: hexane–EtOAc (2:1)] to give **31** (320 mg, 31%) as an oil. IR ν max (film) cm^{-1}: 3400 (OH). ^{1}H-NMR δ: 1.50—2.20 (6H, m, C_3- and C_4-H_2, and $C\underline{H}_2CH_2OH$), 2.95 (2H, m, C_5-H_2), 3.45 (1H, m, C_2-H), and 3.70 (2H, t, J=6 Hz, CH_2O). MS m/z: 132 (M^+). HRMS Calcd for $C_6H_{12}OS$: 132.0608. Found: 132.0608.

***O*-Phenyl *O*-2-(2-Tetrahydrothienyl)ethyl Thionocarbonate (32)** Phenyl chlorothionoformate (0.07 ml, 0.51 mmol) was added to a solution of **31** (67 mg, 0.51 mmol), 4-DMAP (6 mg, 0.05 mmol) and pyridine (0.04 ml, 0.51 mmol) in acetonitrile (3 ml). Work-up as described for the preparation of **4** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (9.7:0.3)] to give **32** (101 mg, 74%) as an oil. IR ν max (film) cm^{-1}: 1200 (C=S). ^{1}H-NMR δ: 1.50—2.30 (6H, m, C_3- and C_3-H_2, and $C\underline{H}_2CH_2O$), 2.90 (2H, m, C_5-H_2), 3.50 (1H, m, C_2-H), 4.50—4.70 (2H, m, OCH_2), and 7.05—7.50 (5H, m, Ar-H). MS m/z: 268 (M^+). HRMS Calcd for $C_{13}H_{16}O_2S_2$: 268.0590. Found: 268.0568.

Pyrolysis of 32 A solution of **32** (152 mg, 0.57 mmol) in *o*-dichlorobenzene (5 ml) was refluxed for 5 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (9.7:0.3)] to give an oil (36 mg, 31%), which was found to be a mixture of 4-phenoxythiepane (**33**) and 2-(2-phenoxyethyl)tetrahydrothiophene (**34**) in the ratio of 33:67 from the ^{1}H-NMR spectrum, from the first fraction. The ^{1}H-NMR spectral data of **33** were obtained from the spectrum of the mixture of these two compounds: δ 1.50—2.42 (6H, m, C_3-, C_5- and C_6-H_2), 2.75 (4H, m, C_2- and C_7-H_2), 4.58 (1H, m, OCH), 6.78—7.49 (5H, m, Ar-H). MS m/z of the mixture: 208 (M^+). The second fraction of the eluate gave *O*-phenyl *S*-2-(2-tetrahydrothienyl)ethyl thiolcarbonate (**35**) (80 mg, 53%) as an oil. IR ν max (film) cm^{-1}: 1710 (C=O). ^{1}H-NMR δ: 1.45—2.22 (6H, m, C_3- and C_4-H_2, $C\underline{H}_2CH_2S$), 2.60—3.10 (4H, m, C_5-H_2 and SCH_2), 3.45 (1H, m, C_2-H), and 7.10—7.50 (5H, m, Ar-H). MS m/z: 268 (M^+). HRMS Calcd for $C_{13}H_{16}O_2S_2$: 268.0591. Found: 268.0593.

Alternative Synthesis of 2-(2-Phenoxyethyl)tetrahydrothiophene (34) TsCl (114 mg, 0.6 mmol) was added to a solution of **31** (66 mg, 0.5 mmol), 4-DMAP (6 mg, 0.05 mmol), and triethylamine (0.07 ml, 0.6 mmol) in tetrahydrofuran (THF) (3 ml), and the mixture was stirred for 20 h at room temperature. After removal of the solvent, the residue was extracted with EtOAc. The extract was washed with H_2O, dried over anhydrous Na_2SO_4, and evaporated. The residue was purified by column chromatography [eluent: hexane–EtOAc (9:1)] to give the tosylate (38 mg, 27%) as an oil. ^{1}H-NMR δ: 1.39—2.17 (6H, m, C_3- and C_4-H_2, $C\underline{H}_2CH_2O$), 2.40 (3H, s, CH_3), 2.79 (2H, m, C_5-H_2), 3.35 (1H, m, C_2-H), 3.90—4.25 (2H, m, OCH_2), 7.32 and 7.77 (each 2H, each d, J=8 Hz, Ar-H). MS m/z: 286 (M^+). A solution of the tosylate, thus obtained, (38 mg, 0.133 mmol) in acetone (3 ml) was added to a suspension of phenol (15 mg, 0.16 mmol) and K_2CO_3 (55 mg, 0.4 mmol) in acetone (3 ml), and the mixture was refluxed for 6 h with stirring. After removal of the solvent, the residue was extracted with EtOAc. The extract was washed with brine, dried over anhydrous Na_2SO_4, and evaporated. The residue was purified by column chromatography [eluent: hexane–EtOAc (7.5:2.5)] to give **34** (16 mg, 57%) as an oil. ^{1}H-NMR δ: 1.50—2.36 (6H, m, C_3- and C_4-H_2, and $C\underline{H}_2CH_2O$), 2.87 (2H, br s, C_5-H_2), 3.56 (1H, m, C_2-H), 4.0 (2H, m, OCH_2), and 6.80—7.40 (5H, m, Ar-H). MS m/z: 208 (M^+). HRMS Calcd for $C_{12}H_{16}OS$: 208.0921. Found: 208.0924.

***S*-Phenyl *O*-2-(2-Tetrahydrothienyl)ethyl Dithionocarbonate (36)** Phenyl chlorodithioformate (0.08 ml, 0.5 mmol) was added to a solution of **31** (66 mg, 0.5 mmol), 4-DMAP (6 mg, 0.05 mmol), and triethylamine (0.07 ml, 0.5 mmol) in acetonitrile. Work-up as described for the preparation of **9** gave a crude oil, which was purified by column chromatography [eluent: hexane–EtOAc (9.7:0.3)] to give **36** (33 mg, 23%) as oil. IR ν max (film) cm^{-1}: 1220 (C=S). ^{1}H-NMR δ: 1.37—2.13 (6H, m, C_3- and C_4-H_2, and $C\underline{H}_2CH_2O$), 2.80 (2H, m, C_5-H_2), 3.20 (1H, m, C_2-H), 4.40—4.70 (2H, m, OCH_2), 7.30—7.70 (5H, m, Ar-H). MS m/z: 284 (M^+). HRMS Calcd for $C_{13}H_{16}OS_3$: 284.0362. Found: 284.0367.

Pyrolysis of 36 A solution of **36** (44 mg, 0.155 mmol) in *o*-dichlorobenzene (3 ml) was refluxed for 4 h. After removal of the solvent, the residue was purified by column chromatography [eluent: hexane–EtOAc (9.7:0.3)] to give 2-(2-phenylthioethyl)tetrahydrothiophene (**37**) (26 mg, 74%) as an oil. ^{1}H-NMR δ: 1.45—2.13 (6H, m, C_3- and C_4-H_2, and $C\underline{H}_2CH_2S$), 6.20—3.10 (4H, m, C_5-H_2 and SCH_2), 3.48 (1H, m, C_2-H), and 7.08—7.58 (5H, m, Ar-H). MS m/z: 224 (M^+). HRMS Calcd for $C_{12}H_{16}S_2$: 224.0693. Found: 224.0694.

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