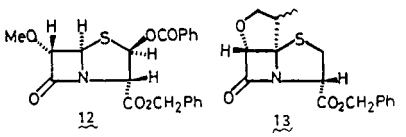
methyl)phenylacetyl (MTPA) derivative [99% ee of (4*S*)-**9a**].[10] In the course of the methylation reaction from (4*S*)-**9** to (4*S*)-**2a**, however, the C4 atom was considerably epimerized [50% ee of (4*S*)-**2a** (400-MHz ^{1}H NMR analysis in the presence of Eu(hfc)$_3$)]. The optical purity of (4*S*)-**2c** was determined to be the same as that of (4*S*)-**2a** by the similar ^{1}H NMR analysis. We employed these optically active and inactive cyclic imino compounds for the following cycloaddition reactions.

In a typical example of methylseleno-promoted ketene–imine cycloaddition reactions, a solution of methoxyacetyl chloride (4.8 mmol) in CH_2Cl_2 (2 mL) was added to a solution of *dl*-**2a** (4 mmol) and Et_3N (8 mmol) in CH_2Cl_2 (2 mL) over a period of 15 min with stirring at 0 °C under N_2. After being stirred at room temperature for 22 h, Et_3N (2 mmol) and a solution of methoxyacetyl chloride (2 mmol) in CH_2Cl_2 (1 mL) were added.[11] The mixture was stirred at room temperature for 14 h and treated as usual[12] to give exclusively *dl*-methyl (3*S**,5*S**,6*S**)-6-methoxy-5-(methylseleno)penam-3-carboxylate (**4a**) (77% yield) as a yellow oil. In the reaction between optically active imine (4*S*)-**2a** (50% ee) or (4*S*)-**2c** (50% ee) and methoxyacetyl chloride, the corresponding chiral penam **4a** [81% yield, $[\alpha]^{27}_D$ +110.1° (*c* 1.0, $CHCl_3$)] or **4d** [52% yield, $[\alpha]^{27}_D$ + 119.3° (*c* 1.0, $CHCl_3$)] having the same optical purity (50% ee) as the starting imines was also obtained exclusively. Similar cycloaddition reactions gave the desired bicyclic products **4** in fairly good yields (see Table I).

Bicyclic products **4** were assigned the stereostructures shown in Scheme I by chemical correlation[13] of *dl*-**4d** to *dl*-**12** whose stereochemistry had been clarified by X-ray analysis.[14] Hence, this cycloaddition reaction may proceed in an extremely high stereoselective fashion via transition state **3**, which is preferred to the other one which would be destabilized by steric repulsion between the C4-alkoxycarbonyl group and the N3-enolate group approaching from the α-side.

The reaction between methoxyacetyl chloride and (4*R*)-**8** or (4*R*)-**11** gave the corresponding bicyclic product in only a moderate yield (58% in (4*R*)-**8**) or in a very poor yield (5% in (4*R*)-**11**). Therefore, a methylseleno group substituent on the imine moiety efficiently promotes this ketene–imine cycloaddition reaction.

Reductive demethylselenation of **4** was carried out by treatment with *n*-Bu_3SnH (ca. 1.2–1.5 equiv) in refluxing THF and CH_3CN or in CH_3CN at 60 °C in the presence of catalytic AIBN to give compound **5** with high stereoselectivity[13,14] and in good yield (Table I). Interestingly, similar demethylselenation of *dl*-**4e** gave tricyclic products *dl*-**13** with a high strain in 62% yield. ^{1}H NMR analysis showed compound **13** to be a 7:3 mixture of diastereoisomers due to a secondary methyl group. This radical cyclization[8,15] offers a unique synthesis of a new type of β-lactams.



We succeeded in synthesizing penam in just a few steps by utilizing a methylseleno-promoted ketene–imine cycloaddition reaction. This new procedure should be useful for large-scale syntheses of various penam-type β-lactams.

Supplementary Material Available: Crystal data of *dl*-**12**, atomic parameters for non-hydrogen atoms, fractional coordinates and isotropic thermal parameters for hydrogen atoms, anisotropic thermal parameters for non-hydrogen atoms, bond lengths, valence angles, and torsion angles, and the perspective view for *dl*-**12** and ^{1}H NMR spectral data of new compounds (9 pages). Ordering information is given on any current masthead page.

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A Novel [3,3]-Rearrangement of 1,2-Dihydro(*N*-arylamino)pyridines: Formation of Unusual Fused Indolines

Summary: Treatment of *N*-(*N*-aryl-*N*-mesylamino)-pyridiniums with base leads to the 1,2-dihydropyridines which undergo a [3,3]-rearrangement and ring closure to give the bridged tetrahydro-α-carbolines **3**, whose structures were established by NMR spectroscopy and single-crystal X-ray crystallography and by reduction to the interesting nine-membered ring compound **8**.

Sir: The addition of suitable bifunctional reagents to pyridine 1-oxides gives the unstable 1,2-dihydropyridine 1-oxides, which rearrange in a number of ways: 1,3-, 1,5-, and 3,5-shifts.[1] *N*-Iminopyridinium ylides give 1,2-dihydropyridine derivatives, which tend to aromatize[2] rather

(10) *cf.* Nagao, Y.; Kumagai, T.; Yamada, S.; Fujita, E.; Inoue, Y.; Nagase, Y.; Aoyagi, S.; Abe, T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2361.
(11) Because the presence of the starting cyclic imino compound **2** was still recognized by TLC analysis even after the reaction for 22 h, more reagents were added. This operation gave a higher yield of **4** than when a large amount of the reagents were added once.
(12) The reaction mixture was successively washed with 5% HCl, saturated aqueous $NaHCO_3$, and brine and evaporated under reduced pressure to give an oily residue. Chromatography on a silica gel column with CH_2Cl_2–AcOEt (25:1) gave the desired penam **4**.
(13) Compound *dl*-**5d** derived from *dl*-**4d** was treated with benzoyl peroxide (4 equiv) in refluxing CCl_4 to give stereoselectively *dl*-**12** as colorless needles (mp 127–128 °C, AcOEt–hexane).
(14) Crystallographic structure of compound *dl*-**12** and its data are available as supplementary material.
(15) Stork, G.; Kahn, M. *J. Am. Chem. Soc.* **1985**, *107*, 500.

(1) Abramovitch, R. A.; Shinkai, I. *Acc. Chem. Res.* **1976**, *9*, 192. Abramovitch, R. A. *Lect. Heterocycl. Chem.* **1979**, *5*, S-15. Abramovitch, R. A.; Shinkai, I.; van Dahn, R. *J. Heterocycl. Chem.* **1976**, *13*, 171. Hisano, T.; Matsuoka, T.; Ichikawa, M.; Muraoka, K.; Komori, T.; Harano, K.; Ida, Y.; Christensen, A. T. *Org. Prep. Proc. Int.* **1978**, *10*, 300. Hisano, T.; Matsuoka, T.; Ichikawa, M.; Hamana, M. *Heterocycles* **1980**, *14*, 19. Abramovitch, R. A.; Kishore, D.; Konieczny, M.; Dauter, Z. *Heterocycles*, in press.

0022-3263/86/1951-4739$01.50/0

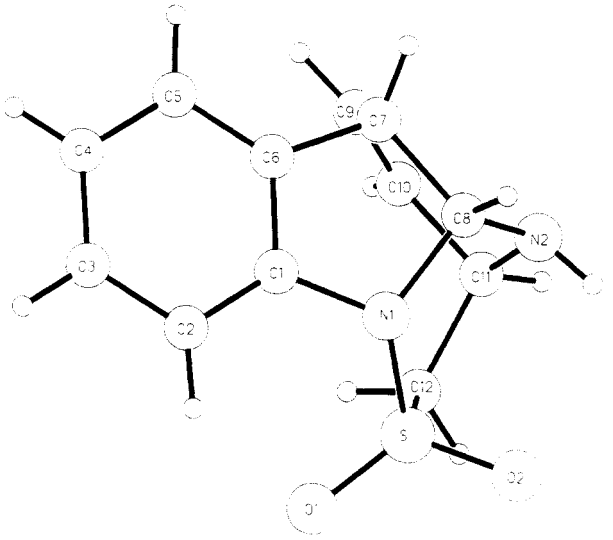


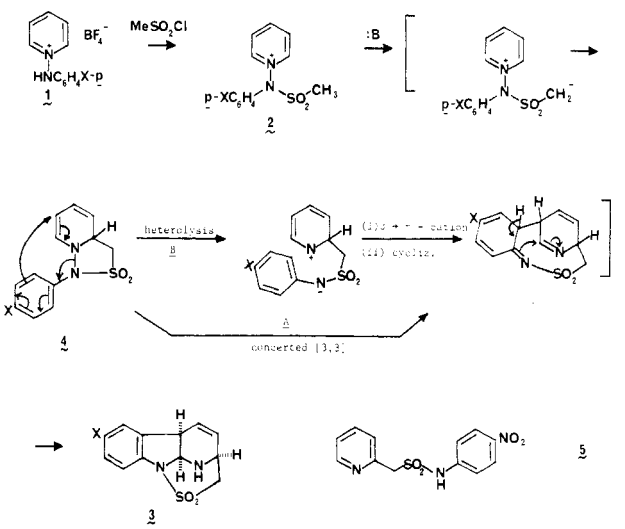
Figure 1. ORTEP diagram of compound 3 (X = H).

than rearrange when the exocyclic nitrogen bears a H, CO_2Et, or SO_2R group, though a few do rearrange. For example, *N*-iminopyridinium ylide reacts with triphenylketeneimine to give a 1,2-dihydropyridine which, unable to aromatize, undergoes a 1,5-sigmatropic shift and dehydrogenation to give a 1*H*-pyrrolo[3,2-*b*]pyridine.[3] 1,2-Dihydro adducts of 1-[(alkoxycarbonyl)imino]-2-methylpyridiniums with acetylene dicarboxylate also underwent rearrangement to 2-methyl-5-(substituted vinyl)pyridines.[4] We anticipated that *N*-(alkylimino)- and *N*-(arylimino)pyridiniums would give 1,2-dihydro derivatives which cannot aromatize.

N-(Phenylamino)pyridinium tetrafluoroborate (**1**, X = H),[5] mp 127–128 °C, gave the *N*-mesyl derivative (**2**, X = H, 67%), mp 156 °C, which, on treatment with Et_3N (excess) in CH_2Cl_2 solution (0 °C → room temperature, 6 h at room temperature) gave **3** (X = H, 60%).[6] The infrared spectrum showed bands for NH (3340 cm^{-1}) and SO_2 (1335, 1140 cm^{-1}), MS peaks at *m/e* (relative intensity) 248 ($M^{\bullet+}$, 41), 184 ($M^{\bullet+} - SO_2$, 2), and 169 ($M^{\bullet+} - SO_2$ – 15, 100), and a complex set of ^1H NMR bands mostly resolved at 400 MHz (atom numbering as in the ORTEP diagram): δ 7.33 (d), 7.25 (d), 7.22 (t), 7.07 (t, 4 H, Ar H), 5.98 (dd, 1 H, $J_{9,10}$ = 9.9 Hz, $J_{10,11}$ = 6.0 Hz, H_{10}), 5.76 (dd, 1 H, $J_{9,10}$ = 9.9 Hz, $J_{7,9}$ = 3.2 Hz, H_9), 5.70 (d, 1 H, $J_{7,8}$ = 6.8 Hz, H_8), 4.04 (looks like br t; irradiation of H_{10} collapses it to a barely resolved q, 1 H, $J_{10,11}$ = 6.0 Hz, $J_{11,12}$ = 9.7 Hz, $J_{11,12'}$ = 2 Hz, H_{11}), 3.86 (m, 1 H, H_7), 3.78 (dd, 1 H, $J_{11,12}$, $J_{12,12'}$ = 13.5 Hz, H_{12}), 3.49 (1 H, exchangeable, NH), 3.14 (dd, 1 H, $J_{12,12'}$ = 2 Hz, $H_{12'}$). The NMR peak assignments were confirmed by proton decoupling.

The structure of **3** (X = H) was established unambiguously by single-crystal X-ray analysis,[7] and one view is given in Figure 1. Compound **3** is a novel tetracyclic ring system incorporating a bridged tetrahydro-α-carboline and a boat 1,2,4-thiadiazine 1,1-dioxide, as well as all-cis ring junctions. The original phenylamino group has been transformed to an indoline ring, and a possible mechanism for its formation, which involves a [3,3]-rearrangement of the 1,2-dihydro derivative **4**, is proposed (Scheme I). It is not known yet whether a concerted (path A) or stepwise (path B) process is taking place. It should be pointed out that if the stepwise process B obtains then heterolysis would be expected to lead either to a σ-cation which would then isomerize to the more stable π-cation (delocalized) or to a π-cation directly if rehybridization of the pyridine N atom accompanies heterolysis. On the other hand, one conformation of **4** brings the *N*-phenyl group below the dihydropyridine and well within the range that would permit a diaza-Cope rearrangement to occur. In any event, this appears to be the first report of this type of interesting transformation.

Scheme I



The rearrangement appears to be a general one. *N*-[*N*-(4-Chlorophenyl)-*N*-mesylamino]pyridinium (**2**, X = Cl, mp 134–135 °C) gives **3** (X = Cl) (62%), mp 207–208 °C.[8] With **2** (X = NO_2), mp 167 °C, the [3,3]-rearrangement appears to slow down somewhat, allowing **4** to undergo stabilization by ring opening and aromatization to **5** (15.7%), mp 217–218 °C,[9] in competition with the rearrangement to **3** (X = NO_2)[10] (28.3%), mp 275–276 °C. This might be taken as some support for path B (Scheme I) since the *p*-NO_2 group would stabilize the anion formed and thus allow some aromatization to the pyridine ring

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(3) Barker, M. W.; McHenry, W. E. *J. Org. Chem.* **1979**, *44*, 1175.

(4) Sasaki, T.; Kanematsu, K.; Kakehi, A. *J. Org. Chem.* **1971**, *36*, 2978.

(5) All new compounds gave the expected microanalytical and spectral data.

(6) Colorless crystals, mp 166–167 °C (from acetone).

(7) The crystals had space group $P2_1/c$ with a = 7.961 (5) Å, b = 10.536 (6) Å, c = 15.04 (1) Å, β = 122.90 (5)°, V = 1058 (1) Å^3; Z = 4; T = −40 °C; diffractometer, Syntex-Nicolet P3; radiation, λ-MoKα, graphite monochromator (λ(Kα) = 0.71069 Å); scan range $2 \le 2\theta \le 44$; ω-scan, $\Delta\omega$ = 1°, 2.4° ≤ ω ≤ 29.3° min^{-1}; 1289 reflections measured, 1110 with $I \ge 2\sigma(I)$; parameters refined, 131 (all hydrogens found by Fourier methods and refined by least squares with $\mu_{isotropic}$ fixed); R_1 = 4.82%, R_2 = 5.07% (solution and refinement: SHEL-XTL).

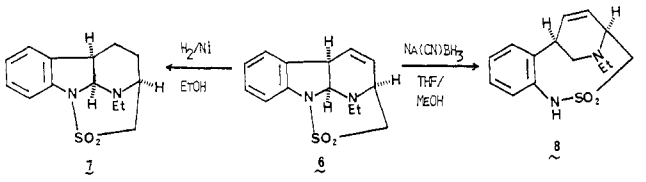
(8) IR (KBr) 3340 (NH), 1345, 1150 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 7.25 (3 H, m, Ar H), 6.0 (dd, 1, CH=), 5.8 (dd, 1, CH=), 5.6 (d, 1 H_7), 4.0 (t, 1), 3.85 (m, 1), 3.6 (dd, 1); MS, *m/e* (relative intensity) 282 ($M^{\bullet+}$, 32), 203 ($M^{\bullet+} - SO_2$ – 15, 100).

(9) IR (KBr) 2900–2600 (br, NH, bonded), 1385, 1145 cm^{-1} (SO_2); NMR (Unisol/Me_2SO) δ 8.51 (d, 1, J = 5.0 Hz, H_6), 8.10 (d, 2, J = 9.3 Hz, H_{ortho}), 7.68 (dt, 1, $J_{3,4}$ = 7.8 Hz, $J_{4,6}$ = 1.8 Hz, H_4), 7.38 (d, 1, $J_{3,4}$ = 7.8 Hz, H_3), 7.32 (d, 2 H, J = 9.3 Hz, H_{meta}), 7.26 (m, 1, H_5), 4.58 (s, 2, CH_2), 2.40 (br, NH).

(10) IR (KBr) 3340 (NH), 1330, 1140 cm^{-1} (SO_2); NMR (Unisol/Me_2SO) δ 8.25, 8.10 (2, $H_{o\text{-}NO_2}$), 7.30 (d, 1 H_2), 6.00 (dd, 1, CH=), 5.85 (t, 1, CH=), 5.70 (m, 1, H_7), 4.25 (br, 1, NH), 4.1 (t, 1), 3.90 (br s, 1), 3.85 (dd, 1), 3.0 (d, 1); MS, *m/e* (relative intensity) 293 ($M^{\bullet+}$), 215 ($M^{\bullet+} - SO_2$ – 14, 100), 214 ($M^{\bullet+} - SO_2$ – 15, 73).

before coupling could occur. On the other hand, it is known[11] that para electron-withdrawing groups decrease the rate of the Claisen rearrangement. A decision concerning the mechanism will have to await further results.

Compound **3** (X = H) can be N-ethylated (Et_3O^+ BF_4^-) to the hydrofluoroborate salt (94%), mp 186 °C, which gives **6**, mp 158–159 °C, with alkali. The tertiary amine can be reduced to one of two products, depending on the reducing agent: H_2/Ni in ethanol gives the tetracyclic piperidine derivatives **7** (40%), mp 174 °C, while NaCN-(BH_4) in THF/MeOH gives **8** (75%), mp 107–108 °C.



The structure of the latter is assigned on the basis of its spectral properties[12] and by analogy with the cleavage of 5-substituted 3-(diethylamino)-1,2-benzothiazepine 1,1-dioxide with $LiAlH_4$.[13] Similar reduction of **3** (X = H) itself gave the corresponding **8** (NH instead of NEt), which exhibited only NH groups (no NH_2) in its IR spectrum, confirming the proposed direction of ring cleavage. Compounds **8** are novel bridged nine-membered sultam rings whose properties are being studied.

Acknowledgment. This work was supported by NSF Latin/American Cooperative Science Grant INT-8111977 (to R.A.A.) and by a grant from CNPq (Brazil) (to J.M.), for which we are grateful.

Registry No. **1** (X = H), 105019-32-7; **1** (X = Cl), 105019-34-9; **1** (X = NO_2), 105019-36-1; **2** (X = H), 105019-38-3; **2** (X = Cl), 105019-40-7; **2** (X = NO_2), 105019-42-9; **3** (X = H), 105019-43-0; **3** (X = Cl), 105019-44-1; **3** (X = NO_2), 105019-45-2; **5**, 105019-50-9; **6**, 105019-46-3; **6**·(H^+·BF_4^-), 105088-02-6; **7**, 105019-47-4; **8**, 105019-48-5; **8** (NH deriv.), 105019-49-6; $MeSO_2Cl$, 124-63-0.

Supplementary Material Available: Single-crystal X-ray analytical data (temperature factors, atomic coordinates, bond lengths and angles) for compound **3** (10 pages). Ordering information is given on any current masthead page.

(11) Gilchrist, T. L.; Storr, R. C. *Organic Reactions and Orbital Symmetry*, 2nd ed.; Cambridge University: Cambridge, 1979; p 273.
(12) IR ($CHCl_3$) 3380 (NH), 1320, 1130 cm^{-1} (SO_2); ^1H and ^{13}C NMR ($CDCl_3$) suggests the molecule exists in two conformations in solution.
(13) Abramovitch, R. A.; More, K. M.; Shinkai, I.; Srinivasan, P. C. *Heterocycles* **1976**, *5*, 95.

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Synthetic Elaboration of Diosphenols: Replacement of Hydroxyl by Halogen

Summary: Replacement of the enolic oxygen of diosphenols by chlorine or bromine may be achieved by treating the derived dimethylthiocarbamate with lithium chloride or bromide in hot acetonitrile/acetic acid.

Sir: In connection with applications of the diosphenol Claisen rearrangement[1] to natural products synthesis we sought to convert the products of this reaction, namely α-hydroxy-α,β-unsaturated ketones, to α-halo-α,β-unsaturated ketones.[2] Traditional reagents[3] (e.g., $SOCl_2$, $POCl_3$, PCl_5) for replacing hydroxyl by chloro or for preparing vinyl chlorides from monoketones utterly fail for diosphenols; after the fact this is not surprising since nucleophilic displacements at unactivated sp^2 carbon are very difficult, even with very good leaving groups.[4] We now report a new and very mild procedure for this transformation which we believe is based on the ability of the thiocarbamoyloxy group to function as both nucleofuge and nucleophile. The method is illustrated in (Scheme I) for the conversion of 1,2-cyclopentanedione into the known[5] 2-chloro-2-cyclopenten-1-one in 80% overall yield.

Thiocarbamoylation can be effected under several conditions (all under nitrogen): (a) sequential treatment at room temperature of a THF or DME solution of the diosphenol with 1.1 equiv of sodium hydride and 1.2 equiv of dimethylthiocarbamoyl chloride; (b) sequential treatment of a 1 M acetone solution of the diosphenol with 1 equiv of 10 M aqueous sodium hydroxide solution and 1 equiv of solid dimethylthiocarbamoyl chloride followed by heating at reflux for 30 min; (c) dropwise addition at room temperature of a concentrated chloroform solution of 1.2 equiv of dimethylthiocarbamoyl chloride to a solution of diosphenol in 1.2 equiv of 1 M aqueous lithium hydroxide solution. The last two procedures are more convenient than the first and give 70–85% yields of crystalline derivatives after a rapid filtration chromatography.

Replacement of oxygen by halogen is effected by treating 0.2 M solutions of dimethylthiocarbamates in acetonitrile/acetic acid 9:1 with 3 equiv of lithium bromide or chloride and heating at reflux (80 °C) for 5–24 h.[6] Workup consists of evaporation of most of the solvent, dilution with

(1) (a) Ponaras, A. A. *Tetrahedron Lett.* **1980**, *21*, 4803. (b) Dauben, W. G.; Ponaras, A. A.; Chollet, A. *J. Org. Chem.* **1980**, *45*, 4413. (c) Ponaras, A. A. *Tetrahedron Lett.* **1983**, *24*, 3. (d) Ponaras, A. A. *J. Org. Chem.* **1983**, *48*, 3866.
(2) The synthetic utility of this array is well documented: (a) Kowalski, C. J.; Weber, A. E.; Fields, K. W. *J. Org. Chem.* **1982**, *47*, 5088. (b) Smith, A. B., III; Branca, S. J.; Pilla, N. N.; Guaciaro, M. A. *J. Org. Chem.* **1982**, *47*, 1855 and references therein. (c) Deprés, J.-P.; Greene, A. E. *J. Org. Chem.* **1980**, *45*, 2036 and references therein. (d) Wender, P. A.; Hillemann, C. L.; Szymonifka, M. J. *Tetrahedron Lett.* **1980**, *21*, 2205. (e) Balci, M.; Jones, W. M. *J. Am. Chem. Soc.* **1980**, *102*, 7607. (f) Kočor, M.; Kroszcyński, W. *Synthesis* **1976**, 813.
(3) (a) Brown, G. S. In *The Chemistry of the Hydroxyl Group*; Patai, S., Ed.; Wiley-Interscience: New York, 1971; Part 1, p 593. (b) Stroh, R. In *Houben-Weyl Methoden der Organischen Chemie*; Müller, E., Ed.; Georg Thieme: Stuttgart, 1962; Vol. 5/3, p 830 ff.
(4) If the leaving group is activated by conjugation to an electron-withdrawing group (as in 1,3-dicarbonyl compounds and their derivatives) then substitution by addition–eleimination can occur. Diosphenols are somewhat analogous to phenols where, without activation, hydroxyl can be replaced by halogen only under drastic conditions: Schaefer, J. P.; Higgins, J. *J. Org. Chem.* **1967**, *32*, 1607 and references therein.
(5) Mitsuhashi, K.; Nomura, K. *Chem. Pharm. Bull.* **1965**, *13*, 951.
(6) The use of less solvent is recommended for large-scale reactions. Inferior yields of 2-halo enones are obtained if either zinc or tetraethylammonium halides are used or if the reaction is conducted in pure acetic acid at 80 °C. The chief side reaction under these circumstances is O–S interchange (thiono–thiolo rearrangement—cf. the Newman–Kwart reaction, ref 7).
(7) (a) Newman, M. S.; Karnes, H. A. *J. Org. Chem.* **1966**, *31*, 3980. (b) Kwart, H.; Evans, E. R. *J. Org. Chem.* **1966**, *31*, 410.

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