41263-09-6; IIIn, 41263-10-9; IIIo, 41263-11-0; IIIp, 41263-12-1; IIIq, 41263-13-2; IIIr, 41263-14-3; IIIs, 41263-15-4; N-aminocamphorimide, 37710-30-8; methanesulfonyl chloride, 124-63-0; acetic anhydride, 108-24-7; p-toluenesulfonyl chloride, 98-59-9; benzoyl chloride, 98-88-4; p-toluoyl chloride, 933-88-0; m-toluoyl chloride, 1711-06-4; o-toluoyl chloride, 933-88-0.

Supplementary Material Available.—Tables of nmr, analytical, and ir data and figures showing the nmr of IIIa, IIIc, IIIf, IIIj,

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O-(1-Alkyl- or -arylthioalkyl)hydroxylamines.
A New Class of Oxime Reagents, Their Preparation and Synthetic Utility

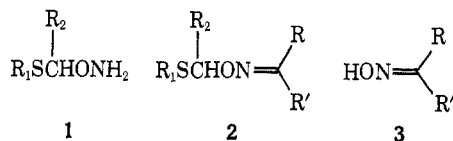ISIDOROS VLATTAS,* LAURENCE DELLAVECCHIA, AND JOHN J. FITT

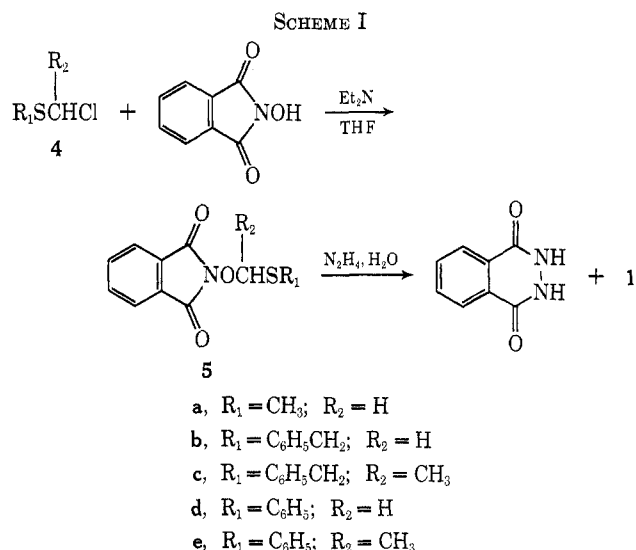*Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, Summit, New Jersey 07901*

O-(1-Methyl-, -benzyl-, and phenylthioalkyl)hydroxylamines 1a–e were synthesized by solvolysis of the corresponding N-(1-methyl-, benzyl-, and -phenylthioalkoxy)phthalimides 5a–e. The (1-methyl-, -benzyl-, and -phenylthioalkoxy) oximes, 7a–e, of the cyclopentanone were prepared, and their stability in acidic, basic, reductive, and oxidative media was determined. The mercury(II)-promoted hydrolysis of 7a–e to the corresponding hydroxy ketoxime 10 is described.

In connection with the synthesis and chemical transformations of the E prostaglandins, the masking and unmasking of the reactive β-ketol moiety in the cyclopentane ring has been a challenging problem for the organic chemist. Oxime reagents have already been used to stabilize the β-ketol functionality;[1-3] however, the regeneration of prostaglandins from them, in good yield, has so far only been achieved in the case of the O-unsubstituted ketoxime derivative.[3] However, the sensitivity of the labile hydroxy ketoximes to acidic and oxidative media[4] substantially limits their role as synthetic intermediates.

In this paper we wish to report on the development of a new class of oxime reagents, namely the O-(1-alkyl- and -phenylthioalkyl)hydroxylamines 1, to demonstrate the synthetic versatility of such ketoxime derivatives 2[5] and describe the hydrolysis of 2, under mild conditions, to the corresponding free oxime derivatives 3.

$$R_1SCHONH_2 \qquad R_1SCHON{=}\!\!\big\langle\genfrac{}{}{0pt}{}{R}{R'} \qquad HON{=}\!\!\big\langle\genfrac{}{}{0pt}{}{R}{R'}$$

$$\overset{R_2}{|} \qquad\qquad \overset{R_2}{|}$$

$$\mathbf{1} \qquad\qquad \mathbf{2} \qquad\qquad \mathbf{3}$$

The synthesis of the hydroxylamine derivatives 1a–e was accomplished as outlined in Scheme I. The chloroalkylthio ethers, 4a–e, were prepared by the method of Bohme, et al.[6] The crude reaction products of 4c and 4e were unstable to fractional distillation[7] and were used without further purification. Reaction of N-hydroxyphthalimide and triethylamine with 4a–e in refluxing tetrahydrofuran gave the crystalline

SCHEME I

$$R_1SCHCl \;+\; \text{(phthalimide)}{-}NOH \xrightarrow[\text{THF}]{Et_3N}$$
$$\overset{R_2}{|}$$
$$\mathbf{4}$$

$$\text{(phthalimide)}{-}NOCHSR_1 \xrightarrow{N_2H_4, H_2O} \text{(o-phthalimide)}\genfrac{}{}{0pt}{}{NH}{NH} \;+\; 1$$
$$\overset{R_2}{|}$$
$$\mathbf{5}$$

a, $R_1 = CH_3$; $R_2 = H$
b, $R_1 = C_6H_5CH_2$; $R_2 = H$
c, $R_1 = C_6H_5CH_2$; $R_2 = CH_3$
d, $R_1 = C_6H_5$; $R_2 = H$
e, $R_1 = C_6H_5$; $R_2 = CH_3$

phthalimide derivatives 5a–e[8] in good yield. Solvolysis of 5a–e with hydrazine hydrate in refluxing ethanol produced the hydroxylamine derivatives 1a–e as stable distillable liquids. Although the free bases could be stored indefinitely at 0°, their addition salts (e.g., hydrochlorides) slowly decomposed on standing at room temperature.

The hydroxylamine derivatives 1a–e were treated with the model cyclopentanone 6[9] in pyridine, in the presence of equivalent amounts of pyridine hydrochloride at room temperature, to give the oximes 7a–e quantitatively (Scheme II). A variety of conditions were employed in the mercury(II)-promoted hydrolysis of the oximes 7a–e. By far the best results were obtained when 7a–e were treated in glacial acetic acid with excess of mercuric chloride and sodium acetate as buffer. Under these conditions acidolysis of 7a–e resulted in the formation of the stable O-acetoxyme-

(1) K. Green, *Chem. Phys. Lipids*, **3**, 254 (1969).
(2) N. Finch and J. J. Fitt, *Tetrahedron Lett.*, 5649 (1969).
(3) J. E. Pike, F. H. Lincoln, and W. P. Schneider, *J. Org. Chem.*, **34**, 3552 (1969).
(4) The authors' unpublished observations.
(5) Acid-catalyzed reactions of o-(methylthiomethyl)benzophenone oxime have been reported by J. W. Jones, D. A. Kerr, and D. A. Wilson, *J. Chem. Soc. C*, 2591 (1971).
(6) H. Bohme, H. Fisher, and R. Frank, *Justus Liebigs Ann. Chem.*, **563**, 54 (1949).
(7) An alternative synthesis of 4e has been described by D. L. Tuleen and T. B. Stephens, *Chem. Ind. (London)*, 1555 (1966).

(8) Compound 5a was reported during the course of this work by V. Lerch and J. G. Moffat, *J. Org. Chem.*, **36**, 3391 (1971).
(9) (a) J. F. Bagli, T. Bogri, R. Deghenghi, and K. Weisner, *Tetrahedron Lett.*, 465 (1966); (b) N. Finch, J. J. Fitt, and I. H. C. Hsu, *J. Org. Chem.*, **36**, 3191 (1971).

SCHEME II

1a–e +

6   7a–e

NOH   NOCHOAc
10   8, R₂ = H
                                                 9, R₂ = CH₃

11a, b, d
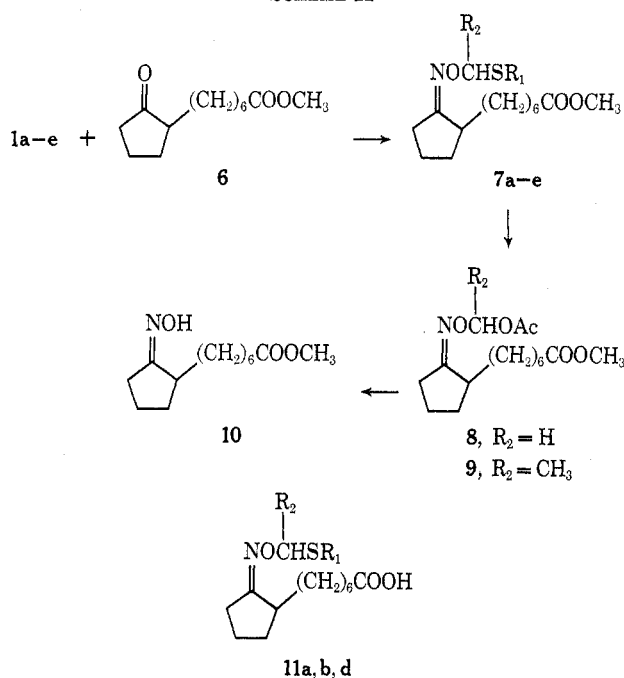
thoxy oximes **8** or **9**, in good yields.   The reaction conditions are given in Table I.

TABLE I

MERCURY(II)-PROMOTED ACIDOLYSIS OF *O*-ALKYL- OR
-ARYLTHIOALKYL OXIMES IN ACETIC ACID

Compd	Mole ratio HgCl₂/HgO	Reaction temp, °C	Reaction time, hr	Product
7a	5:0	50	48	8
7b	5:0	50	48	8
7c	5:0	25	1	9
7d	5:0	50	48	8
7e	5:0	25	1	9
7d	5:2	25	0.5	8

From these data it is apparent that the methyl, benzyl, or phenyl substituent (R₁) in **7a**, **7b**, and **7d**, respectively, had virtually no effect on the rate of solvolysis.   On the other hand, the methyl substituent (R₂) in **7c** and **7d** markedly increased the cleavage rate as would be expected considering the intermediacy of the carbonium ion **12**. In an effort to optimize

12
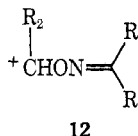
further the conditions for the acidolysis of **7a–e**, it was found that the presence of mercuric oxide dramatically increased the rate of solvolysis,[10] as is indicated in the case of the oxime **7d**.

Finally, mild treatment of **8** or **9** with aqueous potassium carbonate in methanol at room temperature for 5 min gave the oxime **10** quantitatively.

The keto protecting groups in **7a**, **7b**, and **7d** were found to be stable in dilute aqueous hydrochloric acid, while those in **7c** and **7e** were found to hydrolyze slowly to the oxime **10**. Hydrolysis of **7a**, **7b**, and **7d**

with aqueous potassium carbonate to the acids **11a**, **11b**, and **11d** and reesterification of the latter to **7a**, **7b** and **7d** in refluxing methanol and *p*-toluenesulfonic acid further demonstrated the stability of the corresponding keto protecting groups to basic or acidic media.

In order to determine the stability of the most promising keto protecting groups in **7a** or **7d** toward reductive or oxidative media, the esters **7a** and **7d** were reduced at room temperature with lithium aluminum hydride in ether to alcohols **13a** and **13d** in good yield (Scheme III). By subjecting **13a** to a modified Moffat oxida-

SCHEME III

7a, d $\xrightarrow{\text{LiAlH}_4}$

13a, d   14a, d
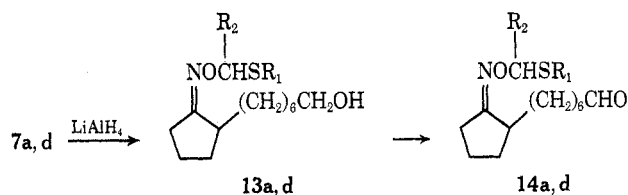
tion,[11] the substrate was overoxidized, presumably at the S atom, and only small amounts (5–10%) of a substance tentatively identified as the aldehyde **14a** (on the basis of its ir spectrum) were recovered from the reaction mixture. Similar results were obtained by subjecting **13a** to a Collins oxidation reaction.[12] However the phenyl group in the oxime **13d** markedly decreased the tendency of the S atom to be oxidized, and this substance could now be oxidized to the aldehyde **14d** in good yield, by employing the conditions of the Collins oxidation reaction.[12a]

The *O*-(phenylthiomethyl)hydroxylamine **1d** was thus found to be a versatile oxime reagent for the protection of carbonyl groups. Oximes derived thereof, which are stable against a broad spectrum of hydrolytic reductive, and oxidative reagents, can be hydrolyzed *via* the corresponding hydroxy oximes to ketones in good yields and under mild conditions. The synthetic utility of this keto protecting group was further demonstrated by its use in our total synthesis of prostaglandin E₁.[13]

Experimental Section[14]

(10) For a recent discussion on related mercury(II)-promoted hydrolysis of 1,3-dithiane derivatives, see E. J. Corey and B. W. Erickson, *J. Org. Chem.*, **36**, 3553 (1971).

(11) K. E. Pfitzner and J. G. Moffat, *J. Amer. Chem. Soc.*, **87**, 5661, 5670 (1965).

(12) (a) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).   (b) A mild oxidation method which might be suitable for the oxidation of **13** has been recently reported by E. J. Corey and C. V. Kim, *J. Amer. Chem. Soc.*, **94**, 7586 (1972).

(13) N. Finch, L. DellaVecchia, J. J. Fitt, R. Stephani, and I. Vlattas, submitted for publication in *J. Org. Chem.*

(14) Melting points were obtained in a Thomas-Hoover melting point apparatus and are uncorrected. Nmr were obtained on a Varian A-60 instrument as CDCl₃ solutions.

analogous manner described in the preparation of **5a**. Crystallization from methylene chloride–ether gave an analytical sample: mp 102–104°; ir (KBr) 1784, 1724 cm^{-1}; nmr δ 7.81 (s, 4, Ar), 7.35 (s, 5, Ar), 5.17 (s, 2, SCH$_2$O), 4.07 (s, 2, SCH$_2$ Ph).

Anal. Calcd for C$_{16}$H$_{13}$NO$_3$S: C, 64.21; H, 4.38; N, 4.68. Found: C, 64.39; H, 4.31; N, 4.67.

N-Phenylthiomethoxyphthalimide (5d) was synthesized from chloromethyl phenyl sulfide and N-hydroxyphthalimide following the procedure described for the preparation of **5a**. Crystallization from methylene chloride–ether gave an analytical sample: mp 88–89.5°; ir (KBr) 1785, 1725 cm^{-1}; nmr δ 7.9–7.1 (m, 9, Ar), 4.48 (s, 2, SCH$_2$O).

Anal. Calcd for C$_{15}$H$_{11}$NO$_3$S: C, 63.16; H, 3.89; N, 4.91. Found: C, 62.90; H, 3.91; N, 4.86.

Benzyl 1-Chloroethyl Sulfide (4c).—Benzyl mercaptan (61.37 g, 0.44 mol) was cooled to 0° and mixed with acetaldehyde (39.17 g, 0.89 mol). The mixture was stirred at 0° for 15 min and cooled to −15°; dry hydrogen chloride was bubbled through at such a rate so that the temperature remained at 0° for 1 hr. After hydrogen chloride was bubbled through at room temperature for 3 hr, calcium chloride (15 g) was added and dry nitrogen was bubbled through the mixture for 15 hr. The solids were filtered and the yellowish oily filtrate was used in the next step without further purification since attempts to vacuum distil this material led to extensive decomposition: nmr δ 7.28 (s, 5, Ar), 4.95 (q, 1, *J* = 7 Hz, SCHCl), 3.9 (q, 2, PhCH$_2$S), 1.73 (d, 3, *J* = 7 Hz, CH$_3$).

N-(1-Benzylthioethoxy)phthalimide (5c).—To a mixture of the crude chloroethyl thioether **4c** (86 g, 0.46 mol) and N-hydroxyphthalimide (91 g, 0.56 mol) in tetrahydrofuran (1000 ml) was added dropwise triethylamine until a faint yellow coloration persisted in the reaction mixture. Additional triethylamine (54 g, 0.53 mol) was then added at once and the mixture was refluxed for 15 hr. The reaction mixture was cooled to room temperature, the solids were filtered, and the filtrates were evaporated under vacuum. The residue was dissolved in methylene chloride and the solution was washed several times with 10% potassium bicarbonate, dried (MgSO$_4$), decolorized with charcoal, and evaporated. The residue was crystallized from methylene chloride–ether to give 56 g of **5c** as white crystals: mp 74–76°; ir (KBr) 1785, 1725 cm^{-1}; nmr δ 7.9–7 (m, 9, Ar), 5.6 (q, 1, *J* = 7 Hz, OCHS), 4.05 (q, 2, SCH$_2$Ph), 1.65 (d, 3, *J* = 7 Hz, CH$_3$).

Anal. Calcd for C$_{17}$H$_{15}$NO$_3$S: C, 65.17; H, 4.82; N, 4.47. Found: C, 65.52; H, 4.92; N, 4.46.

1-Chloroethyl phenyl sulfide (4e) was prepared according to the procedure employed for the preparation of **4c**. As in the case of **4c**, the crude reaction product **4e** was unstable to vacuum distillation [lit.[7] bp 75–78° (0.4 mm)] and was used in the next step without purification: nmr δ 7.7–7.1 (m, 5, Ar), 5.35 (q, 1, *J* = 7 Hz, SCHCl), 1.75 (d, 3, *J* = 7 Hz, CH$_3$).

N-(1-Phenylthioethoxy)phthalimide (5e) was synthesized from the crude chloroethyl sulfide **4e** and N-hydroxyphthalimide according to the procedure employed for the preparation of **5c**. Crystallization from methylene chloride–ether gave an analytical sample: mp 65–67.5°; ir (KBr) 1785, 1725 cm^{-1}; nmr δ 7.7–7.0 (m, 9, Ar), 5.9 (q, 1, *J* = 7 Hz, SCHO), 1.65 (d, 2, *J* = 7 Hz, CH$_3$).

Anal. Calcd for C$_{16}$H$_{13}$NO$_3$S: C, 64.4; H, 4.38; N, 4.68. Found: C, 64.81; H, 4.64; N, 4.83.

O-(Methylthiomethyl)hydroxylamine (1a).—A mixture of N-methylthiomethoxyphthalimide (**5a**, 40 g), hydrazine hydrate (9.42 g), 95% ethanol (350 ml), and water (9.2 ml) was refluxed for 2.5 hr. The reaction mixture was cooled to room temperature, the solids were filtered, and the filtrates were evaporated under aspirator pressure at 40° to a small volume. More solids were formed and were filtered. The filtrate was distilled under aspirator pressure to give 10 g of the amine **1a** as a colorless oil: bp 54–55° (15 mm); nmr δ 5.5 (broad s, 2, NH$_2$), 4.79 (s, 2, SCH$_2$O), 2.15 (s, 3, CH$_3$). The amine **1a** gave a crystalline hydrochloride on treatment with methanolic hydrochloric acid in methanol and subsequent dilution with ether, mp 135° dec.

Anal. Calcd for C$_2$H$_8$ClNOS: C, 18.53; H, 6.22; N, 10.81. Found: C, 18.44; H, 6.41; N, 10.52.

By a similar procedure to that described for the preparation of **1a**, the amines **1b–e** were prepared[15] from the corresponding phthalimides **5b–e**.

O-(Benzylthiomethyl)hydroxylamine (**1b**): bp 87–89° (0.1 mm); nmr δ 7.33 (s, 5, Ar), 5.43 (broad s, 2, NH$_2$), 4.7 (s, 2, SCH$_2$O), 3.8 (s, 2, PhCH$_2$S). *Anal.* Calcd for C$_8$H$_{11}$NOS: C, 56.79; H, 6.55; N, 8.28. Found: C, 57.19; H, 6.69; N, 8.12.

O-(1-Benzylthioethyl)hydroxylamine (**1c**): bp 100–107° (0.1 mm); nmr δ 7.21 (s, 5, Ar), 5.2 (s, 2, NH$_2$), 4.75 (q, 1, *J* = 7 Hz, SCHO), 3.75 (s, 2, PhCH$_2$S), 1.37 (d, 2, *J* = 7 Hz, CH$_3$). The amine **1c** was further analyzed as the corresponding oxalate, mp 115–116°. *Anal.* Calcd for C$_{10}$H$_{14}$NO$_3$S: C, 52.62; H, 6.19; N, 6.14. Found: C, 52.99; H, 6.28; N, 5.97.

O-(Phenylthiomethyl)hydroxylamine (**1d**): bp 84–87° (0.1 mm); nmr δ 7.6–7.1 (m, 5, Ar), 5.56 (s, 2, NH$_2$), 5.05 (s, 2, SCH$_2$O). *Anal.* Calcd for C$_7$H$_9$NOS: C, 54.19; H, 5.85; N, 9.03. Found: C, 54.40; H, 5.99; N, 9.16.

O-(Phenylthiomethyl)hydroxylamine hydrochloride was prepared by treatment of **1d** in ether with ethereal hydrogen chloride: mp 110–112° dec. *Anal.* Calcd for C$_7$H$_{10}$ClNOS: C, 43.86; H, 5.26; N, 7.31. Found: C, 43.93; H, 5.39; N, 7.41.

O-(1-Phenylthioethyl)hydroxylamine (**1e**): bp 73–74° (0.1 mm); nmr δ 7.7–7 (m, 5, Ar), 5.43 (s, 2, NH$_2$), 5.05 (q, 1, *J* = 7 Hz, SCH$_2$O), 1.38 (d, 3, *J* = 7 Hz, CH$_3$). *Anal.* Calcd for C$_8$H$_{11}$NOS: C, 54.19; H, 5.88; N, 9.03. Found: C, 54.40; H, 5.99; N, 9.16.

General Procedures.—The preparation of the oximes **7a–e** from methyl 2-oxocyclopentaneheptanoate **6** and the corresponding amines **1a–e** were carried out using one of the following procedures.

A.—A mixture of cyclopentanone **6** (1 mmol) the amine **1** (1.5 mmol), pyridine (2 ml), and anhydrous pyridine hydrochloride (1.5 mmol) was stirred at room temperature for 15 hr. The pyridine was removed under vacuum; the residue was extracted with ether, washed with water, dried (MgSO$_4$), and evaporated. The residue was purified by preparative tlc on silica gel, followed by bulb-to-bulb distillation.

B.—Same as in A, except that freshly prepared amine hydrochlorides were used in the place of free amine **1** and pyridine hydrochloride.

Methyl 2-(methylthiomethoxyimino)cyclopentaneheptanoate (7a): bp 145–155° (0.1 mm); ir (CHCl$_3$) 1735 cm^{-1}; nmr δ 5.1 (s, 2, OCH$_2$S), 3.65 (s, 3, OCH$_3$), 2.35 (m, 5), 2.23 (s, 3, SCH$_3$), 2.1–1 (m, 14). *Anal.* Calcd for C$_{15}$H$_{27}$NO$_3$S: C, 59.78; H, 9.03; N, 4.65. Found: C, 60.1; H, 9.21; N, 4.35.

Methyl 2-(benzylthiomethoxyimino)cyclopentaneheptanoate (7b): bp 195–205° (0.1 mm); ir (CHCl$_3$) 1735 cm^{-1}; nmr δ 7.36 (s, 5, Ar), 5.05 (s, 2, OCH$_2$S), 3.87 (s, 2, CH$_2$Ph), 3.63 (s, 3, OCH$_3$), 2.3 (m, 5), 2.1–1 (m, 14). *Anal.* Calcd for C$_{21}$H$_{31}$NO$_3$S: C, 66.82; H, 8.28; N, 3.71. Found: C, 66.94; H, 8.49; N, 3.57.

Methyl 2-(1-benzylthioethoxyimino)cyclopentaneheptanoate (7c): ir (CHCl$_3$) 1735 cm^{-1}; nmr δ 7.3 (m, 5, Ar), 5.3 (q, 1, OCHS), 3.9 (q, 2, PhCH$_2$), 3.64 (s, 3, OCH$_3$), 2.26 (m, 5), 2.1 (m, 17). *Anal.* Calcd for C$_{22}$H$_{33}$NO$_3$S: C, 67.49; H, 8.50; N, 3.58. Found: C, 67.52; H, 8.34; N, 3.22.

Methyl 2-(phenylthiomethoxyimino)cyclopentaneheptanoate (7d): ir (CHCl$_3$) 1735 cm^{-1}; nmr δ 7.6–7 (m, 5, Ar), 5.45 (s, 2, OCH$_2$S), 3.6 (s, 3, OCH$_3$), 2.25 (m, 5), 2–1 (m, 14). *Anal.* Calcd for C$_{20}$H$_{29}$NO$_3$S: C, 66.09; H, 8.04; N, 3.85. Found: C, 65.69; H, 8.05; N, 4.03.

Methyl 2-(1-phenylthioethoxyimino)cyclopentaneheptanoate (7e): ir (CHCl$_3$) 1735 cm^{-1}; nmr δ 7.68–7.1 (m, 5, Ar), 5.6 (m, 1, OCHS), 3.65 (s, 3, OCH$_3$), 2.3 (m, 5), 2.1 (m, 17). *Anal.* Calcd for C$_{21}$H$_{31}$NO$_3$S: C, 66.82; H, 8.28; N, 3.71. Found: C, 67.17; H, 7.98; N, 3.70.

Hydrolysis and Reesterification of 7a.—A mixture of the ester **7a** (585 mg), methanol (20 ml), and 10% aqueous potassium carbonate (5 ml) was refluxed for 1 hr. The solvent was removed under vacuum and residue was dissolved in water (20 ml). The aqueous solution was extracted twice with ether and the extracts were discarded. The aqueous layer was acidified with 2 N hydrochloric acid and extracted twice with ether. The ether extracts were washed with water, dried (MgSO$_4$), and evaporated. The residue was dissolved in absolute methanol (30 ml), *p*-toluenesulfonic acid (30 mg) was added, and the mixture was refluxed for 24 hr. The methanol was evaporated under vacuum, the residue was dissolved in ether and the ether solution was washed with 10% aqueous potassium bicarbonate and water, dried (MgSO$_4$), and evaporated to give 510 mg of the original ester **7a**.

(15) During fractional distillation of the crude reaction products **1b–e**, overheating should be avoided or decomposition of these compounds might occur.

Lithium Aluminum Hydride Reduction of 7a.—To a suspension of lithium aluminum hydride (100 mg) in ether (25 ml) was added a solution of the ester 7a (750 mg) in ether (15 ml) with stirring and ice-water cooling over a period of 15 min. After 1 hr of stirring at room temperature, the excess of the hydride was destroyed with water, the salts were filtered, and the filtrates were evaporated. The residue was extracted with ether washed with water, dried (MgSO₄), and evaporated to give 543 mg of 2-(methylthiomethoxyimino)cyclopentaneheptanol 13a as a viscous oil: nmr δ 5.07 (s, 2, OCH₂S), 3.55 (t, 2, CH₂O), 2.35 (m, 3), 2.17 (s, 3, OCH₃), 2–1 (m, 16).

In a similar manner, lithium aluminum hydride reduction of ester 7d gave 2-(phenylthiomethoxyimino)cyclopentaneheptanol (13d) as a colorless, viscous oil. Bulb-to-bulb distillation of this compound gave an analytical sample: bp 165° (0.1 mm); nmr δ 7.61–7.1 (m, 5, Ar), 5.45 (s, 2, OCH₂S), 3.6 (t, 2, CH₂O), 2.3 (m, 3), 2.1–1 (m, 16).

Anal. Calcd for C₁₉H₂₉NO₂S: C, 68.02; H, 8.71; N, 4.15. Found: C, 67.79; H, 8.85; N, 4.04.

Moffat Oxidation[11] of the Alcohol 13a.—A solution of the alcohol 13a (250 mg) in benzene (5 ml) and dimethyl sulfoxide (5 ml) was cooled to 0°; pyridine (93 μl), trifluoroacetic acid (75 μl), and 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-*p*-toluenesulfonate (0.8 g) were added; and the mixture was stirred at 4° for 48 hr. The mixture was poured into cold water and extracted three times with ether. The ether extracts were washed with water, dried (MgSO₄), and evaporated to give 30 mg of an oily substance: ir (CHCl₃) 2725 (weak), 1720 cm⁻¹.

Collins Oxidation of the Alcohol 13d.—To a solution of the alcohol 13d (130 mg) in dry methylene chloride (50 ml) was added chromium trioxide–pyridine complex[12a] (600 mg) at once, and the mixture was stirred at room temperature for 10 min. The mixture was poured into water; the methylene chloride layer was washed once more with water, dried (MgSO₄), decolorized with charcoal, and evaporated. The oily residue was subjected to bulb-to-bulb distillation and gave 104 mg of 2-(phenylthiomethoxyimino)cyclopentaneheptanal (14d) as a clear viscous oil: bp 145° (0.1 mm); ir (CHCl₃) 2725, 1720 cm⁻¹; nmr δ 10.7 (t, 1, CHO), 7.8–7.1 (m, 5, Ar), 5.5 (s, 2, OCH₂S), 2.7–2.2 (m, 5), 2.1–1 (m, 14).

Anal. Calcd for C₁₉H₂₇NO₂S: C, 68.44; H, 8.16; N, 4.20. Found: C, 68.15; H, 7.88; N, 4.03.

Mercuric Chloride Promoted Acidolysis of Methylthiomethoxy Oxime 7a.—Mercuric chloride (270 mg) and potassium acetate (250 mg) were added to a solution of the oxime 7a (230 mg) in acetic acid (11 ml), and the mixture was stirred at 50° for 48 hr. The precipitate was filtered and the filtrate was treated with hydrogen sulfide gas. The black mercuric sulfide was filtered and the filtrates were evaporated to dryness under vacuum. The residue was extracted with ether and the extracts were washed with water, dried (MgSO₄), and evaporated to give 180 mg of methyl 2-(acetoxymethoxyimino)cyclopentaneheptanoate (8) as a yellowish oil. Further purification by preparative thin layer chromatography (silica gel, methylene chloride–ether 5:95, *R*ᵢ 0.65) gave an analytical sample: ir (film) 1755 (sh), 1740 cm⁻¹; nmr δ 5.68 (q, 2, OCH₂S), 3.65 (s, 3, OCH₃), 2.3 (m, 5), 2.08 (s, 3, COCH₃), 2.0–1.0 (m, 14).

Anal. Calcd for C₁₆H₂₇NO₅: C, 61.32; H, 8.68; N, 4.47. Found: C, 61.62; H, 8.68; N, 4.61.

Under similar acidolysis conditions, the phenylthiomethoxyoximes 7b, and 7d gave, after 24 hr, the acetate 8 in 75% yield.

Mercuric Chloride Promoted Acidolysis of Phenylthioethoxy Oxime 7e.—Mercuric chloride (136 mg) and potassium acetate (128 mg) were added to a solution of the oxime 7e (114 mg) in acetic acid (32 ml), and the mixture was stirred at room temperature for 1 hr. The mixture was diluted with acetone (30 ml) and treated with hydrogen sulfide gas; the salts were filtered. The filtrates were evaporated under vacuum, the residue was extracted with ether, and the extracts were washed with water, dried (MgSO₄), and evaporated. Preparative thin layer chromatography of the residue (silica gel, methylene chloride–ethyl acetate 95:5, *R*ᵢ 0.51) gave 98 mg of ethyl 2-(1-acetoxyethoxyimino)cyclopentaneheptanoate (9) as a yellowish viscous oil: ir (film) 1740 cm⁻¹; nmr δ 6.35 (q, 1, OCHS), 3.6 (s, 3, OCH₃), 2.3 (m, 5), 2.0 (s, 3, COCH₃), 2.0–1.0 (m, 17).

Anal. Calcd for C₁₇H₂₉NO₅: C, 62.36; H, 8.93; N, 4.28. Found: C, 62.42; H, 9.23; N, 4.35.

Under similar acidolysis conditions, the benzylthioethoxy oxime 7c gave the acetate 9 quantitatively.

Mercuric Chloride–Mercuric Oxide Promoted Acidolysis of 7d.—A mixture of mercuric chloride (456 mg, 1.68 mmol), mercuric oxide (120 mg, 0.56 mmol), potassium acetate (412 mg, 4.2 mmol), and acetic acid (10 ml) was added at once to a solution of the oxime 7d (200 mg, 0.56 mmol) in acetic acid (20 ml); the mixture was stirred at room temperature for 0.5 hr. The mixture was diluted with acetone (30 ml), treated with hydrogen sulfide gas, and filtered. The filtrates were evaporated under vacuum, the residue was extracted with ether, and the extracts were washed with water, dried (MgSO₄), and evaporated to give 150 mg of the acetate 8.

Methyl 2-(hydroxyimino)cyclopentaneheptanoate (10). 1. From the Acetate 8.—To a solution of 150 mg of the acetate 8 in 1 ml of methanol was added 50 μl of 10% aqueous potassium carbonate, and the mixture was stirred at room temperature for 5 min. The mixture was diluted with 50 ml of ether, washed with water, dried (MgSO₄), and evaporated to give the title compound 10 quantitatively: bp 133–138° (0.2 mm); ir (film) 3270, 1740 cm⁻¹.

Anal. Calcd for C₁₃H₂₃NO₃: C, 64.70; H, 9.61; N, 5.80. Found: C, 64.34; H, 9.45; N, 5.57.

2. From the Acetate 9.—The acetate 9 was hydrolyzed in a similar manner to give the oxime 10 quantitatively.