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(18) Acyl migration in lysophosphatidylcholine is known to occur; see B. Serdarevich, *J. Am. Oil Chem. Soc.*, **44**, 381 (1967). The extent to which acyl migration might have occurred in our experiment has not been determined.
(19) Infrared spectra were recorded with either a Beckman IR-5 or IR-7 spectrophotometer. NMR spectra were recorded on a Varian XL-100 high-resolution spectrometer in $CDCl_3$, and only the characteristic peaks are reported. Chemical shifts are reported in parts per million (δ) downfield from internal Me_4Si. Mass spectra (70 eV) (*m/e*) are given followed by the relative peak height in parentheses and were determined on a CEC 110-2B double-focusing mass spectrometer equipped with a direct inlet. Elemental analyses were performed at the University of Oregon by Dr. R. Wielesek. Ultraviolet spectra were determined on a Cary 15 UV spectrometer. Unless otherwise noted, all silica gel column chromatography was done with Baker 60–200 mesh silica gel packed dry and eluted in the usual fashion. Preparative thin-layer chromatography (TLC) was done on Analtech 1000 silica gel plates with the fluorescent indicator. Analytical TLC used EM silica gel F-254 plates. Solvents were routinely distilled. Commercial reagents were used as received.
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Notes

Synthesis of 3-Carboethoxyoxindoles

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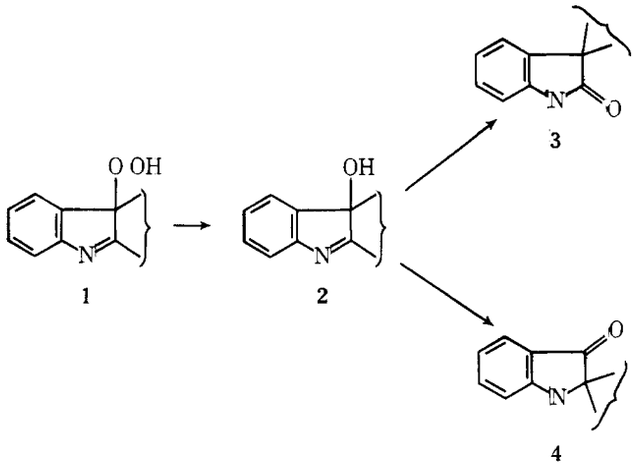
Indoles have been converted to 3-hydroperoxyindolenines **1** on autoxidation or peracid oxidation. Selective reduction of the hydroperoxy group in **1** gives 3-hydroxyindolenines **2**, which can rearrange to either oxindole **3**[1] or indoxyl **4**[2] de-



rivatives. Unfortunately, peracid oxidation can often be troublesome as a result of competitive N-oxide formation.[3] Other methods that circumvent this problem involve reaction of indoles with *tert*-butyl hypochlorite[4] or *N*-bromosuccinimide[5] to give 3-haloindolenines, and these can be converted to oxindoles. However, halogenation of the indole benzene ring[5] can sometimes be competitive with 3-haloindolenine formation (vide infra). In this paper, we present a new, high-yield method for oxindole preparation, which is based on the photosynthesis of 3-hydroxyindolines **6** and their oxidative rearrangement to oxindoles **9**.

We have reported that *N*-methyl-3-hydroxyindolines can be prepared in excellent yield by photocyclization–rearrangement of 2-(*N*-methylanilino)acetoacetates.[6] For example, irradiation of **5a** in *n*-pentane in the presence of suspended sodium carbonate gives 3-hydroxyindoline **6a** in quantitative yield. In similar fashion, indolines **6b** and **6c** also are prepared. Treatment of these 3-hydroxyindolines **6a–c** with lead tetraacetate (1.1 equiv) and pyridine (1.1 equiv) in benzene solution at room temperature results in a high-yield conversion to oxindoles **10a–c** (Table I).

In order to unambiguously establish the structure of the lead tetraacetate oxidation product, we attempted to prepare **10a** by treatment of *N*-methyl-2-carboethoxy-3-methylindole with *tert*-butyl hypochlorite using literature procedures.[4] Under these conditions, products resulting from chlorination of the benzene ring as well as the C(3) methyl substituent in the indole were obtained. Oxindole **10a** was eventually pre-

Scheme I

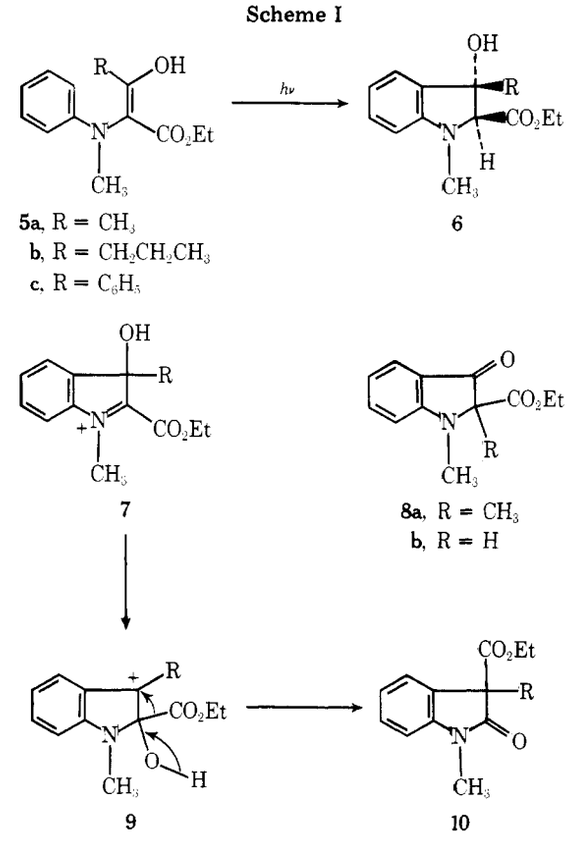


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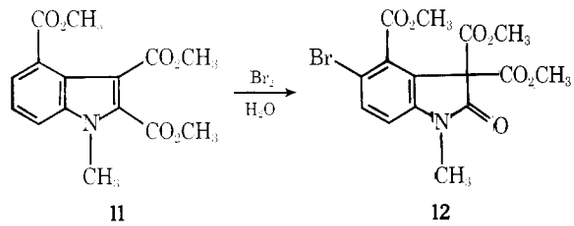
Table I. Oxidation-Rearrangement of 3-Hydroxyindolines 6 to Oxindoles 10

compd	R	yield, %[a]	Mp, °C
10a	CH_3	80	67.5–68.5
10b	$CH_2CH_2CH_3$	76	83–84
10c	C_6H_5	70	109–110

[a] Isolated yield of crystallized product based on the two-step sequence from **5**.

pared in low yield by reaction of *N*-methyloxindole with lithium diisopropylamide–ethyl chloroformate in THF followed by alkylation with sodium ethoxide–methyl iodide in ethanol. The material thus obtained was found to be identical with that isolated from oxidative rearrangement of **6a**. Indoxyl **8a** was prepared from previously reported **8b**[7] by alkylation with sodium hydride–methyl iodide in THF. The absence of **8a** from reaction mixtures of **6a** with lead tetraacetate was confirmed by comparison of appropriate ^1H NMR spectral data.

A reasonable mechanism for oxidative rearrangement of **6** requires lead tetraacetate oxidation to iminium ion **7**, from which rearrangement to carbonium ion **9** occurs. A 1,2 shift of the ethoxycarbonyl group in **9** with loss of a proton gives the oxindole **10**. Migration of an alkoxycarbonyl group to an electron deficient carbon is well-documented,[8] and we note the relevant rearrangement of **11** to **12** reported by Acheson and coworkers.[9]



11 **12**

As a result of our study of substituents compatible with photocyclization of 2-anilino keto acetates,[6,10] we feel confident that oxindoles with a variety of substituents in the benzene ring will be available by utilization of the methodology reported here.

Experimental Section

General. ^1H NMR spectra were obtained on a Varian A-60A or EM-390 NMR spectrometer (tetramethylsilane standard, deuteriochloroform solvent). Infrared spectra were recorded on a Perkin-Elmer 137B infrared spectrometer and melting points were measured on a calibrated Thomas-Hoover capillary melting point apparatus and are uncorrected. Ultraviolet spectra were taken on a Cary 14 spectrometer. The light source for irradiation was a 450-W Ace-Hanovia medium pressure, mercury vapor lamp. Mass spectra were obtained on a Finnigan 3300 gas chromatograph–mass spectrometer.

Ethyl 2-(*N*-methylanilino)acetoacetate (5a). A solution of ethyl 2-bromoacetoacetate (36.34 g, 0.173 mol) and *N*-methylaniline (37.24 g, 0.348 mol) in 95% ethanol (85 mL) was refluxed for 5.5 h. After cooling, the solvent was removed in vacuo and the residue dissolved in ether (300 ml) which was washed successively with 1 N hydrochloric acid (4 × 75 mL), 1 N sodium bicarbonate solution (1 × 50 mL), and water (3 × 100 mL) and dried over anhydrous magnesium sulfate. Removal of solvent in vacuo and distillation gave **5a** (31.05 g, 76%, bp 93–95 °C at 0.03 mm): IR ($CHCl_3$) 6.05, 6.25, 6.70 μm; ^1H NMR δ 1.10 (3 H, triplet, J = 7.5 Hz), 1.97 (3 H, singlet), 3.04 (3 H, singlet), 4.11 (2 H, quartet, J = 7.5 Hz), 6.50–7.38 (5 H, multiplet), 12.28 (1 H, singlet); UV (benzene) λ_{max} 295 nm (ε 2940); electron impact mass spectrum, *m/e* 235, 189, 161, 118.

Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.34; H, 7.32.

Ethyl 2-(*N*-methylanilino)butyroylacetate (5b). Prepared from ethyl 2-chlorobutyroylacetate and *N*-methylaniline by the method described for **5a** (52%, bp 100–102 °C at 0.04 mm): IR (neat) 6.05, 6.25, 6.70 μm; ^1H NMR δ 0.90 (3 H, triplet, J = 7.5 Hz), 1.09 (3 H, triplet, J = 7.0 Hz), 1.61 (2 H, sextet, J = 7.5 Hz), 2.32 (2 H, triplet, J = 7.5 Hz), 3.02 (3 H, singlet), 4.11 (2 H, quartet, J = 7.0 Hz), 6.58–6.80 (3 H, multiplet), 7.10–7.31 (2 H, multiplet), 12.40 (1 H, singlet).

Ethyl 2-(*N*-methylanilino)benzoylacetate (5c). Prepared from ethyl 2-chlorobenzoylacetate and *N*-methylaniline by the method described for **5a**; purified by medium-pressure liquid chromatography on silica gel using benzene/hexane (1:1) as eluent (50% yield): IR ($CHCl_3$) 6.09, 6.25, 6.70 μm; ^1H NMR δ 1.07 (3 H, triplet, J = 7.5 Hz), 2.91 (3 H, singlet), 4.14 (2 H, quartet, J = 7.5 Hz), 6.55–6.86 (3 H, multiplet), 7.03–7.40 (5 H, multiplet), 7.62–7.84 (2 H, multiplet).

Ethyl 1,3-Dimethyloxindole-3-carboxylate (10a). A solution of **5a** (4.01 g, 17.1 mmol) and sodium carbonate (18 mg, 0.17 mmol) in dry pentane (300 mL) was purged with argon for 30 min and irradiated with Uranyl glass-filtered light, while a slow stream of argon was bubbled through the solution. After 5.3 h, the solution was filtered and solvent removed in vacuo at room temperature to give ethyl 1,3-dimethyl-3-hydroxyindoline-2-carboxylate (**6a**) as a colorless oil: IR (neat) 2.90, 5.75, 6.20 μm; ^1H NMR δ 1.30 (3 H, triplet, J = 7.5 Hz), 1.44 (3 H, singlet), 2.78 (3 H, singlet), 2.7 (1 H, broad singlet, disappears upon addition of deuterium oxide), 3.97 (1 H, singlet), 4.28 (2 H, quartet, J = 7.5 Hz), 6.40–7.35 (4 H, multiplet).

A solution of **6a** in dry benzene (18 mL, 18.5 mmol) was cooled to 5 °C and lead tetraacetate (8.35 g, 18.5 mmol) was added in portions. After stirring for 4.5 h, water (10 mL) was added and the solution extracted with ether (3 × 30 mL). The combined ether extracts were washed successively with 1 N sodium hydroxide (5 × 20 mL), 1 N hydrochloric acid (3 × 29 mL), and water (3 × 20 mL) and dried over anhydrous magnesium sulfate. Rotoevaporation of solvent and recrystallization from ether/hexane gave **10a** (3.17 g, 80%, mp 67.5–68.5 °C): IR ($CHCl_3$) 5.75, 5.83, 6.18, 6.70, 6.80, 7.25 μm; ^1H NMR δ 1.14 (3 H, triplet, J = 7.0 Hz), 1.63 (3 H, singlet), 3.24 (3 H, singlet), 4.12 (2 H, quartet, J = 7.0 Hz), 6.80–7.46 (4 H, multiplet); electron impact mass spectrum *m/e* 233 (16), 161 (25), 160 (100).

Anal. Calcd for $C_{13}H_{15}NO_3$; C, 66.94; H, 6.48. Found: C, 67.01; H, 6.43.

Alternate Preparation of 10a. Ethyl 1-methyloxindole-3-carboxylate was prepared by adding a solution of 1-methyloxindole (95 mg, 0.72 mmol) in THF (0.3 mL) to a stirred solution of lithium diisopropylamide (0.72 mmol from *n*-BuLi and diisopropylamine) in THF (0.5 mL) at −78 °C. After stirring for 30 min at −78 °C, ethyl chloroformate (0.07 mL, 79 mg, 0.73 mmol) was added and the solution was stirred at −78 °C for an additional 4 h. Ether (25 mL) and 1 N hydrochloric acid (0.5 mL) were added and the resulting solution was washed successively with 1 N hydrochloric acid (3 × 5 mL) and water (3 × 5 mL) and dried over anhydrous magnesium sulfate. Rotoevaporation of solvent and recrystallization from hot petroleum ether gave ethyl 1-methyloxindole-3-carboxylate (23 mg, 15%, mp 96–97 °C): IR (neat) 5.72, 5.80, 6.06, 6.15 μm; ^1H NMR δ 1.26 (3 H, triplet, J = 7.5 Hz), 3.24 (3 H, singlet), 4.25 (2 H, quartet, J = 7.5 Hz), 4.42 (1 H, singlet), 6.70–7.40 (4 H, multiplet).

A solution of ethyl 1-methyloxindole-2-carboxylate (23 mg, 0.11 mmol), methyl iodide (20 mg, 0.14 mmol), and sodium ethoxide (11 mg, 0.14 mmol) in absolute ethanol (0.2 ml) was heated to reflux temperature for 4 h. After cooling, water (1.0 mL) was added and the solution was extracted with ether (3 × 10 mL). The combined ether extracts were washed successively with 1 N sodium hydroxide (3 × 5 mL) and water (3 × 5 mL) and dried over anhydrous magnesium sulfate. Rotoevaporation of solvent gave **10a** (11 mg, 43%, mp 68 °C).

Ethyl 1-Methyl-3-*n*-propyloxindole-3-carboxylate (10b). 10b was prepared from **5b** by the method described for **10a**, purified by column chromatography on silica gel using methylene chloride as eluent, and recrystallized from ethyl acetate/hexane (76%, mp 83–84 °C): IR ($CHCl_3$) 5.75, 5.85, 6.19, 6.70, 6.81, 7.30, 7.44 μm; ^1H NMR δ 0.83 (5 H, multiplet), 1.14 (3 H, triplet, J = 7.0 Hz), 2.11–2.34 (2 H, multiplet), 3.24 (3 H, singlet), 4.13 (2 H, quartet, J = 7.0 Hz), 6.80–7.48 (4 H, multiplet).

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33. Found: C, 68.89; H. 7.24.

Ethyl 1-Methyl-3-phenyloxindole-3-carboxylate (10c). 10c was prepared from **5c** by the method described for **10a.** Recrystallization from hexane gave **10c** (70%, mp 109–110 °C); IR ($CHCl_3$) 5.72, 5.81, 6.19, 6.70, 6.80, 7.30, 7.41 μm; ^1H NMR δ 1.19 (3 H, triplet, J = 7.0 Hz), 3.22 (3 H, singlet), 4.22 (2 H, quartet, J = 7.0 Hz), 6.88–7.57 (4 H, multiplet), 7.34 (5 H, singlet).

Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80. Found: C, 73.06; H, 5.69.

Ethyl 1,2-Dimethylindoxyl-2-carboxylate (8a). A solution of ethyl 1-methylindoxyl-2-carboxylate[7] (1.21 g, 5.5 mmol) and sodium

hydride (132 mg, 5.5 mmol) in tetrahydrofuran (8 mL) was stirred at room temperature for 2 h. Methyl iodide (0.44 mL, 1.00 g, 7.1 mmol) was added and the solution refluxed for 2 h. After cooling, ether (30 mL) was added and the solution was washed with 1 N sodium hydroxide (3 × 10 mL) and water (3 × 10 mL) and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo and the residue was separated by preparative thick layer chromatography on silica gel using ether/methylene chloride (1:9) as eluent to give **8a** (0.87 g, 68%, mp 63–64 °C): IR (neat) 5.74, 5.88, 6.18 μm; ^{1}H NMR δ 1.20 (3 H, triplet, J = 7.5 Hz), 1.55 (3 H, singlet), 2.96 (3 H, singlet), 4.17 (2 H, quartet, J = 7.5 Hz), 6.70–6.88 (2 H, 3 singlets), 7.36–7.70 (2 H, multiplet).

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Registry No.—**5a,** 67271-23-2; **5b,** 67271-24-3; **5c,** 67271-25-4; **6a,** 61838-88-8; **6b,** 67271-26-5; **6c,** 67271-27-6; **8a,** 67271-28-7; **10a,** 67271-29-8; **10b,** 67271-30-1; **10c,** 67271-31-2; *N*-methylaniline, 100-61-8; ethyl 2-bromoacetoacetate, 609-13-2; ethyl 2-chlorobutyroylacetate, 67271-32-3; ethyl 2-chlorobenzoylacetate, 41381-97-9; 1-methyloxindole, 61-70-1; ethyl chloroformate, 541-41-3; ethyl 1-methyloxindole-3-carboxylate, 39478-72-3; ethyl 1-methylindoxyl-2-carboxylate, 67271-33-4.

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Condensation Reactions of Carbanions and Ylides Derived from α-Halo Sulfoximines

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The homologation of aldehydes and ketones is a classic problem in organic chemistry with many practical solutions. The limitations and disadvantages of the known methods are sufficient to warrant development of new methods. We have recently described the first preparations of α-halo sulfoximines[1] and we envisioned in their chemistry a carbonyl homologation scheme (Scheme I).

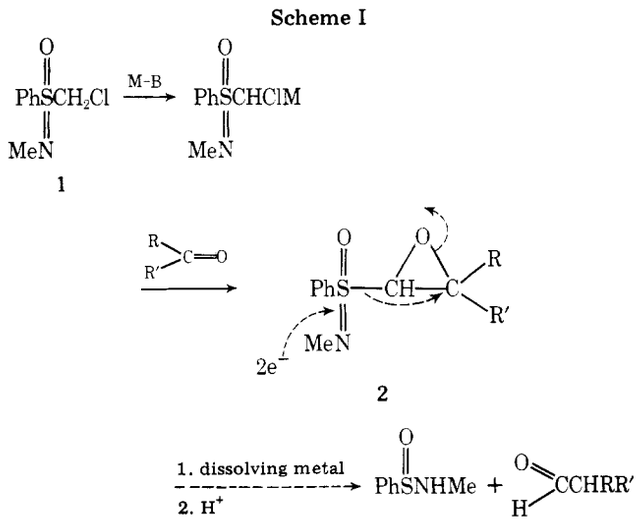
After considerable experimentation, the most effective condition which we found for the condensation of **1** with carbonyl compounds involved potassium *tert*-butoxide in a mixture of dimethyl sulfoxide (Me_2SO) and tetrahydrofuran (THF) at 0 °C to room temperature. Table I lists the epoxy sulfoximines produced in this manner. The use of symmetrical ketones simplified product analysis by restricting the diastereomers to two in each case. Chromatography on basic alumina was found to be acceptable for the isolation of the epoxy sulfoximines. Attempts to condense **1** with *p*-nitrobenzaldehyde and 2-propenal under the above conditions were unsuccessful. The diastereomeric alcohols **3** and **4** were obtained in good yield by using sodium hydride in THF at 0 °C. All four diastereomeric α-chloro-β-hydroxy sulfoximines (**3**) were separated and characterized by NMR spectroscopy. All attempts to effect ring closure of **3** and **4** to epoxy sulfoximines have been unsuccessful.

Table I. Condensation of 1 with Carbonyl Compounds

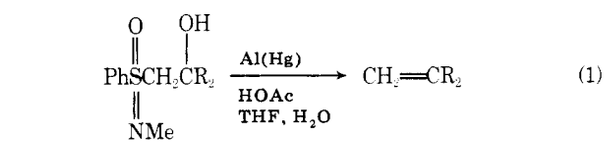
carbonyl compound	registry no.	product	R	R′	yield, %	diastereomeric ratio[a]
acetone	67-64-1	**2a**	CH_3	CH_3	81	29/72
cyclohexanone	108-94-1	**2b**	$-(CH_2)_5-$		75	32/68
4-*tert*-butylcyclohexane	98-53-3	**2c**	$-(CH_2)_2-CH(t\text{-Bu})-(CH_2)_2-$		50	*b*
benzaldehyde	100-52-7	**2d**	H	Ph	75	44/56

[a] Diastereomers due to contiguous chiral centers at S and the α-C. [b] Mixture of four diastereomers due to chiral centers at S and the α-C plus cis–trans ring isomers. The diastereomers with the *tert*-butyl and oxide cis accounted for 90% of the product.

Scheme I



Aluminum amalgam in the presence of acetic acid in aqueous THF has been found effective for the reductive elimination of β-hydroxy sulfoximines to yield alkenes (eq 1).[2]



(1)

When the epoxy sulfoximines **2a** and **2b** were treated under the above conditions no isobutyraldehyde or cyclohexanecarboxaldehyde could be detected by gas chromatography. Thin-layer chromatography indicated rapid loss of the starting material. From the reaction of **2b,** cyclohexylmethanol was isolated. In the absence of acetic acid **2b** is slowly reduced to **5** (eq 2). Although the above experiments are not exhaustive we have concluded that Scheme I is not likely to provide a practical method for homologation of aldehydes and ketones.

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