This is the first stereospecific synthesis of pure *endo*-norbornyl chloride. It appears to provide the basis for a general procedure for the synthesis of such *endo*-bicyclic chlorides.

Experimental Section

The melting and boiling points are uncorrected. The ^1H NMR and ^{13}C NMR spectra were recorded on Varian T-60 and Varian FT-80A spectrometers, respectively.

Preparation of 2,2-Dichloronorbornane (1). 2,2-Dichloronorbornane was made, following the reported procedure,[10] in 60% yield, bp 70–72 °C (14 mm) [lit.[10] bp 65–68 °C (12–12.4 mm)].

Preparation of 2-Chloronorbornene (4). This was made by a modification of the reported procedure.[11] In an oven-dried, nitrogen-flushed, 250-mL round-bottom flask fitted with a septum inlet, a magnetic stirring bar, and a reflux condenser topped with a connecting tube leading to a mercury bubbler was placed potassium *tert*-butoxide (16.8 g, 150 mmol). Dry THF (100 mL) was added. To this well-stirred solution was added 2,2-dichloronorbornane (16.6 g, 100 mmol). This mixture was heated under reflux for 1 h (the reaction was complete as indicated by the absence of the peak due to 2,2-dichloronorbornane in the GC analysis of an aliquot). The reaction mixture was cooled, poured into water (200 mL), and extracted with pentane (3 × 100 mL). The combined organic layers were washed with water (5 × 100 mL) and dried over anhydrous sodium sulfate. Solvent was removed, and the residue was distilled to provide pure 2-chloronorbornene in a yield of 90% (11.6 g), bp 62–63 °C (57 mm) [lit.[11] bp 72–73 °C (69 mm)].

***endo*-Norbornyl Chloride (5).** The hydrogenation of 2-chloronorbornene was carried out using the Ace Brown hydrogenator.[12] In the reactor flask was placed 2-chloronorbornene (1.29 g, 10 mmol), ethyl acetate (20 mL), and platinum oxide[14] (100 mg). Hydrogen was generated using a solution of sodium borohydride in Me_2SO (~1 M) added to aqueous acetic acid. After the absorption of hydrogen ceased, the catalyst was removed by filtration through a sintered glass funnel. The solvent was then removed, and the residue was distilled to provide the pure *endo*-norbornyl chloride: bp 88–90 °C (110 mm); mp 44–45 °C [lit.[3] bp 51–53 °C (17 mm), mp 34–36 °C].

Anal. Calcd for $C_7H_{11}Cl$: C, 64.12; H, 8.4; Cl, 27.48. Found: C, 64.40; H, 8.63; Cl, 27.46.

The hydrogenation was carried out at 25, 0, −10, and −25 °C. The results are summarized in Table I.

Registry No.—1, 19916-65-5; 4, 694-93-9.

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(1) Postdoctoral research associate on a grant provided by the Exxon Research and Engineering Co., Linden, N.J.
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(14) Suppliers: Aldrich Chemical Co.

New Synthetic Approaches to 4(1*H*)-Pyridinone Derivatives. 3.[1] 2-Bromoacetylated Enamines as Pyridine Ring Synthons

Riaz F. Abdulla,* Kenneth H. Fuhr, and James C. Williams, Jr.

Lilly Research Laboratories, Division of Eli Lilly & Company, Greenfield, Indiana 46140

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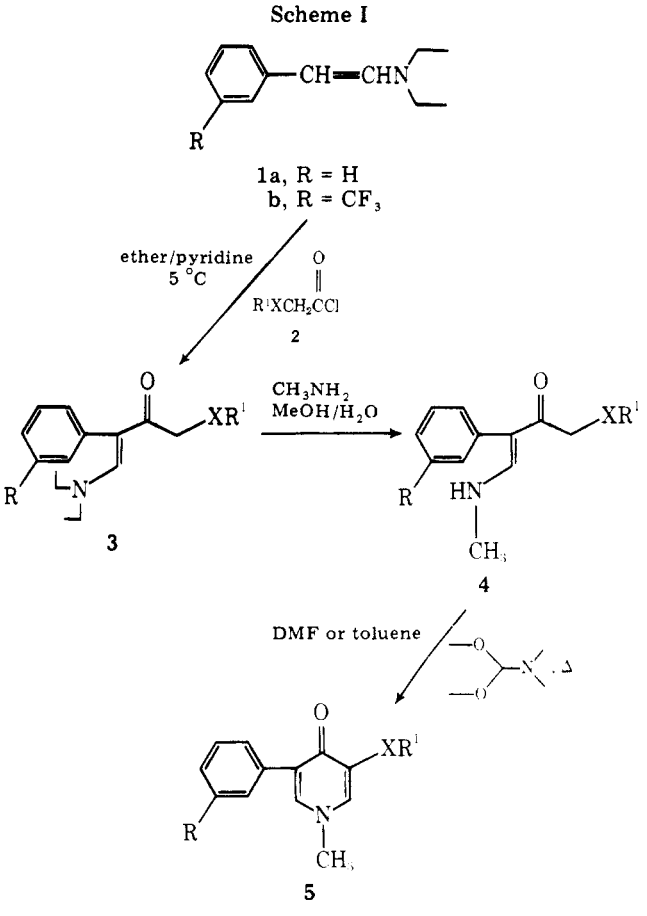
The synthesis of highly functionalized pyridines by conceptually differing routes continues to draw the attention of numerous research groups.[2-10] We[1] and others[11] have recently described methods for synthesizing 3,5-disubstituted-4(1*H*)-pyridinone compounds. This paper describes the synthesis of pyridinone rings bearing heteroatoms (O, S, N, Cl, and Br) in the 3 position.

Scheme I



	R	R^1	X	mp, °C	yield, %[12]
5a	H	C_6H_5	S	164–165	18
5b	CF_3	C_6H_5	S	151–152	16
5c	H	C_6H_5	O	176–177	19
5d	CF_3	C_6H_5	O	144–145	17
5e	H	CH_3	O	153–155	23
5f	CF_3	CH_3	O	173–175	18

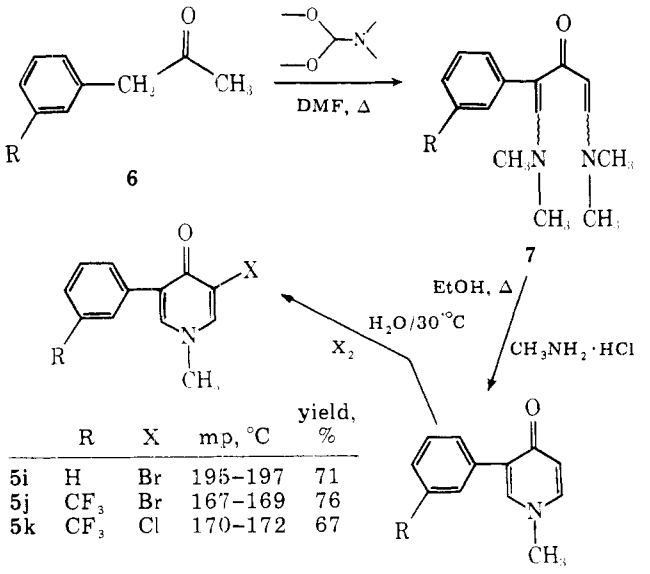
Acylation of a dialkylstyrylamine (1) with an acid chloride (2) R^1XCH_2COCl in anhydrous ether (Linde 4Å sieves) in the presence of pyridine, at 5 °C over a 4-h period, gave enaminone **3**. Enamine exchange with aqueous methanolic methylamine in 40 min to 2 h gave the *N*-methylenaminones **4**, which were cyclized by refluxing with *N,N*-dimethylformamide dimethyl acetal, neat or in DMF or toluene, to the pyridinones **5** (Scheme I).

We next turned our attention toward preparing 3-substituted pyridinones starting with phenylacetone derivatives.

The process of Scheme II was applied to the synthesis of 3-bromo- and 3-chloro-4(1*H*)-pyridinones. Pyridinones **5g** and **5h** were obtained in 26 and 16% overall yields based on the corresponding phenylacetones **6**. Though **5g** and **5h** could be readily halogenated with aqueous halogen at 30 °C to give the pyridinones **5i–5k** in moderate to good yields, the halogen atoms in the 3 position were quite recalcitrant to nucleophilic displacement.[13] However, bromoacylation of diethylstyrylamines readily afforded the bromoacetylated enamines **8** in excellent yields (85–90% in 2 h at 5–10 °C, ether solvent, without special precautions). The bromine atom in **8** was readily displaced by a variety of alkylthio anions and by secondary amines to give the enaminones **9**, which were readily

0022-3263/79/1944-1349$01.00/0

Scheme II



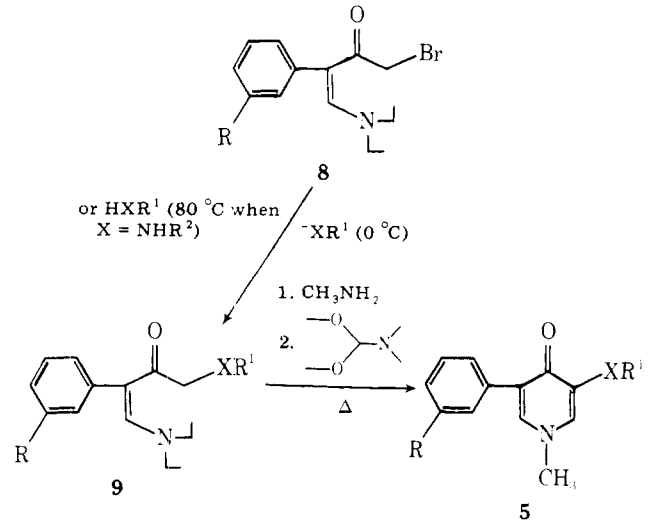
	R	X	mp, °C	yield, %
5i	H	Br	195–197	71
5j	CF_3	Br	167–169	76
5k	CF_3	Cl	170–172	67

	R	mp, °C	yield, %
5g	H	123–125	26
5h	CF_3	122–123	16

cyclized to the pyridinones **5l–5q** (Scheme III). The overall yields were poorest for the amino compound **5q,** while an approximately 40% overall yield could be obtained consistently for the (alkylthio)pyridinones **5l** and **5m.** Though the yields of materials have not been optimized and though some yields are poor, the process of Scheme III is nevertheless a convenient laboratory preparative method for the synthesis of pyridinone compounds.

In summary, we have designed a synthesis of the pyridin-4(1*H*)-one ring from a styrylamine and a substituted acetyl halide already bearing the 3 substituent of the pyridinone ring or an α-bromine atom which can be displaced by nucleophiles in the intermediate (bromoacetyl)enamines (e.g., 8, Scheme III). Owing to the ease and efficiency of the acylation of enamines with bromoacetyl bromide, the latter process is the route of choice for the synthesis of pyridinones bearing heteroatom (O, N, S) substituents on C_3.

Scheme III. Bromoacylated Enamines as Synthons for Pyridinones



	R	R^1	X	mp, °C	yield, %
5l	H	C_2H_5	S	94–95	40
5m	CF_3	C_2H_5	S	84–85	39
5n	CF_3	CF_3	S	122–124	21
5o	CF_3	C_6H_5	NCH_3	64–65	18
5p	CF_3	C_2H_5	NC_2H_5	64–66	20
5q	CF_3	C_2H_5	NCH_3	oil	4

Experimental Section

Acylation of *N,N*-Diethyl-*m*-(trifluoromethyl)styrylamine (1b).[1] To 12.1 g (0.05 mol) of **1a** was added 200 mL of anhydrous (Linde 4Å sieves) diethyl ether followed by 4.5 g (0.056 mol) of anhydrous (KOH dried and distilled) pyridine. Under the absence of moisture and with vigorous mechanical stirring was added dropwise a solution of 10.0 g (0.05 mol) of bromoacetyl bromide dissolved in 200 mL of dry ether. An immediate precipitate of pyridine hydrobromide separated. Any exotherm was controlled by cooling the reaction in an ice–water bath. A convenient temperature for the acylation is about 10 °C. The addition was completed in 2.0 h. The solution was immediately filtered, and the filtrate was washed with 1 N HCl solution followed by saturated $NaHCO_3$ solution. The ether was dried over anhydrous $MgSO_4$, and the ether was removed under reduced pressure on a rotary evaporator to give 18.0 g (100%) of **8** (R = CF_3) as a red liquid: IR (Nujol) $\bar{\nu}$ 1655 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.01 (t, 6 H), 3.03 (q, 4 H), 3.70 (s, 2 H), 7.53 (broad s, 4 H), 7.75 (s, 1 H); M^+ *m/e* = 362.

Displacement of Bromine in 8 with Ethanethiol Anion. To 24.3 g (0.01 mol) of **8** (R = CF_3) dissolved in 50.0 mL of toluene was added a prepared solution of ethanethiol anion (0.01 mol of ethanethiol and 0.01 mol of sodium methoxide in 25 mL of methanol, under nitrogen with ice-bath cooling) over 5 min. TLC analysis showed complete reaction in less than 180 s after addition was complete. The reaction was stirred for 2 h after the addition, the reaction mixture was then washed with 1 N HCl solution and saturated $NaHCO_3$ solution, dried, and filtered, and a small portion was stripped to give **9** (R = CF_3, X = S, R^1 = CH_2CH_3) as a thick brown oil: IR (Nujol) $\bar{\nu}$ 1652 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.8–1.6 (two triplets, 9 H), 2.4–3.4 (two quartets and one singlet at δ 3.18, 8 H), 7.20 (broad s, 4 H), 7.78 (s, 1 H); M^+ *m/e* = 345.

Enamine Exchange on Compound 9 (R = CF_3, X = S, R^1 = CH_2CH_3) and Cyclization to Pyridinone 5n. Methylamine gas was added from a cylinder to the ethanethioacetylated compound **9** dissolved in the toluene from the preceding experiment. The solution was stirred overnight. TLC monitoring indicated that the reaction was completed, and the solution was stripped to 25 mL.[14] To this solution was added 13.0 g of *N,N*-dimethylformamide dimethyl acetal, and the solution was refluxed under a nitrogen atmosphere for 5 h. TLC analysis showed that the reaction was complete. Upon removal of volatile solvents from the reaction mixture, a thick brown oil was produced. Trituration under 5.0 mL of diisopropyl ether gave a tan solution which suddenly deposited a mass of crystalline **5n** upon cooling and stirring. The yield of **5n** was 1.20–1.25 g per run (38–40%): IR (Nujol) $\bar{\nu}$ 1645 cm^{-1}; NMR ($CDCl_3$) δ 1.23 (t, 3 H), 2.83 (q, 2 H), 3.70 (s, 3 H), 7.2–8.2 (m, 6 H); M^+ *m/e* = 313. Anal. Calcd for $C_{15}H_{14}F_3NOS$: C, 57.51; H, 4.50; N, 4.47; F, 18.19; S, 10.21. Found: C, 57.71; H, 4.70; N, 4.59; F, 18.47; S, 10.51.

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Registry No.—**1a,** 56672-27-6; **1b,** 64468-58-2; **2** (R^1 = C_6H_5, X = S), 7031-27-8; **2** (R^1 = C_6H_5, X = O), 701-99-5; **2** (R^1 = CH_3, X = O), 38870-89-2; **5a,** 59757-64-1; **5b,** 69257-99-4; **5c,** 59757-65-2; **5d,** 67098-20-8; **5e,** 59757-68-5; **5f,** 69258-00-0; **5g,** 59757-28-7; **5h,** 59757-31-2; **5i,** 59757-29-8; **5j,** 59757-30-1; **5k,** 59757-32-3; **5l,** 69258-01-1; **5m,** 69246-49-7; **5n,** 69246-50-0; **5o,** 69258-02-2; **5p,** 69258-03-3; **5q,** 69258-04-4; **6** (R = H), 103-79-7; **6** (R = CF_3), 21906-39-8; **8** (R = H), 69258-05-5; **8** (R = CF_3), 69246-48-6; **9** (R = CF_3, X = S, R^1 = CH_2CH_3), 69258-06-6; **10,** 69258-07-7; bromoacetyl bromide, 598-21-0; ethanethiol anion, 20733-13-5.

Supplementary Material Available: Full NMR data for compounds **5a–q** (Table I) (2 pages). Ordering information is given on any current masthead page.

References and Notes

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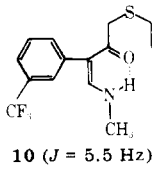
(12) These refer to *isolated yields* of chromatographically homogeneous materials based on starting enamine. All pyridinones described in this communication were fully characterized by combustion analysis, mass spectral fragmentation spectra, and infrared and proton magnetic resonance spectra. Liquid intermediates were purified by column chromatography on Woelm silica gel using dichloromethane/ethyl acetate gradient elution and characterized by infrared, proton magnetic resonance spectra, and mass spectral fragmentation analysis.
(13) Fused sodium acetate at 300 °C led to recovered starting material. In addition, we were unable to generate hetarynes from these compounds via the use of *tert*-butoxide in anhydrous *tert*-butyl alcohol. Therefore, the 3-halogenated pyridinones would not serve as intermediates for the synthesis of the 3-alkylthio and 3-substituted aminopyridinones or of the 3-oxypyridinones we had already obtained via Scheme I.
(14) In one run an aliquot of the toluene solution was stripped to dryness to give **10** as a viscous oil that crystallized under pentane to an orange solid: mp 47–48 °C; IR (Nujol) $\bar{\nu}$ 3175 (broad), 1645 cm^{-1}; NMR ($CDCl_3$) δ 1.17 (t, 3 H), 2.53 (q, 2 H), 3.05 (d, 3 H), 3.17 (s, 2 H), 6.80 (d, J = 12 Hz, 1 H), 7.40 (broad s, 4 H). Compound **10** could also be prepared using methanol in place of toluene and 40% aqueous methylamine.



10 (J = 5.5 Hz)

Convenient Method for the Preparation of Reactive Oxiranes by Direct Epoxidation

Mitsuru Imuta and Herman Ziffer*

Laboratory of Chemical Physics, National Institute of Arthritis, Metabolism, and Digestive Diseases, National Institutes of Health, Bethesda, Maryland 20014

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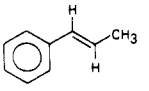
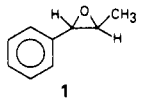
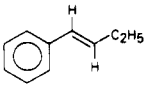
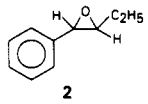
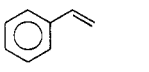
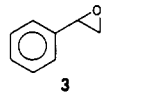
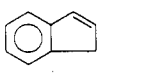
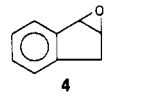
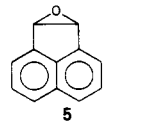
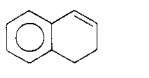
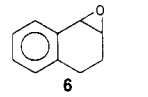
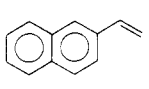
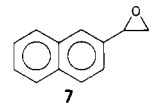
As part of another study we recently required pure samples of *trans*-β-methylstyrene oxide, **1**, and *trans*-β-ethylstyrene oxide, **2**. Related oxides, such as styrene oxide, **3**, are usually prepared from the olefin via an intermediate halohydrin; when this reaction sequence was used for *trans*-β-methylstyrene and β-ethylstyrene, mixtures of cis and trans oxides were obtained. Similar results were recently reported by Marshall and Prager,[1] who prepared their halohydrin intermediate by sodium borohydride reduction of the corresponding ketone. As these oxides were intended to be starting materials in a study of the stereochemistry of ring openings of oxides, a tedious separation of these sensitive compounds into the constituent isomers did not appear practical. Pure cis and trans oxides have been prepared by direct epoxidation of the appropriate olefin; however, aryl oxides are very sensitive to acids and therefore unstable under the usual epoxidizing conditions.[2a] Several methods[2b] have been employed to minimize the amount of acid present; we wish to report here the successful preparation of **1**, **2**, **3**, and several other related reactive oxides using a two-phase system similar to one described by Anderson and Veysoglu.[3]

Although samples of **1** and **2** were required, we were also interested in the methodology associated with the preparation of related labile aryl oxiranes. The reactivity of one such oxirane, indene oxide, **4**, has been studied in some detail by Berti et al.[4] Consequently this compound was chosen as our initial target molecule. Berti et al. have shown that **4** is easily opened by weak acids to yield mixtures of cis and trans diols.[5] In order to minimize destruction of **4**, we chose therefore to examine two-phase systems, dichloromethane and aqueous phosphate buffer (pH 8).[6] On oxidizing indene with 1 equiv of *m*-CPBA in dichloromethane in the presence of the phosphate buffer, reaction was not complete; however, when a second equivalent of *m*-CPBA was added, all the indene present was consumed and very little, if any, ring-opened product formed. If two or more equivalents of *m*-CPBA were added initially in one portion, epoxidation was not complete.

Epoxidation of *trans*-β-methylstyrene and *trans*-β-ethylstyrene with 2 equiv of *m*-CPBA in the two-phase system developed for indene yielded the trans oxides, in each case in high yield (90%) and uncontaminated by the cis isomer. In addition to the two styrene derivatives, 2-vinylnaphthalene, styrene, and 1,2-dihydronaphthalene were oxidized to the respective oxiranes in high yield (see Table I).

Although acenaphthene can be oxidized to 1,2-epoxyacenaphthene[8,9] under carefully controlled conditions using *m*-CPBA by a procedure using only one solvent, the reported yield was relatively low (35%). Furthermore, formation of acenaphthenone and other compounds complicated the isolation of the oxirane. We therefore subjected acenaphthene to the above-mentioned two-phase oxidation and obtained

Table I. Summary of Results from Two-Phase Epoxidations [c,d]

Aryl Olefin	Product	Reaction Time (hr.)	Yield (%)[a]
	 **1**	10	90[b]
	 **2**	11	90[b]
	 **3**	7	95[11]
	 **4**	10	100[12]
	 **5**	8	100[7]
	 **6**	14	95[13]
	 **7**	9	90[14]

[a] Determined by NMR. [b] The yields of these oxiranes prepared via bromohydrin are given in the Experimental Section. [c] Registry no. for the aryl olefins from top to bottom: 873-66-5; 1005-64-7; 100-42-5; 95-13-6; 208-96-8; 447-53-0; 827-54-3. [d] Registry no.—**1**, 23355-97-7; **2**, 69140-50-7; **3**, 96-09-3; **4**, 768-22-9; **5**, 22058-69-1; **6**, 2461-34-9; **7**, 20861-99-8.