which in the ethanolic medium can serve as a precursor of **1**, **2**, and/or **3**.

Tyman and Pickles[2] have reported the preparation of 1-benzoxepin-3,5(2*H*,4*H*)-diones by treatment of 2-acetylphenoxyacetic esters with either ethanolic sodium ethoxide or phosphorous oxychloride in benzene. However, yields apparently were low. The high yield of **4** obtained in our work using sodium ethoxide in toluene is therefore unique, and is dependent on the acidic group ortho to the ketone combined with the aprotic solvent medium (toluene).[6] We attribute the facilitation of benzoxepin formation to the presence of an unsolvated phenolate anion which will deactivate the adjacent ketone to nucleophilic attack. Interaction of the anion formed from the methyl group, adjacent to the ketone, on the ester carbonyl can then predominate.

Experimental Section

Melting points were taken on a Thomas-Hoover Uni-melt apparatus and are uncorrected. Ultraviolet spectra were recorded on a Perkin-Elmer 202 spectrophotometer. Infrared spectra were determined on a Perkin-Elmer 257 spectrophotometer. Nuclear magnetic resonance spectra were obtained with a Varian EM 360 spectrometer with Me_4Si as an internal reference. Mass spectral analyses were provided by Morgan-Schaffer Corp., and elemental microanalyses were carried out by Dr. C. Daessle. The pK_a determination was performed by Mr. S.-C. Ho in these Laboratories.

Cyclization of Ethyl 2-(2-Acetyl-3-hydroxyphenoxy)acetate (5) with Sodium Ethoxide in Ethanol. The compound **5**[1] (23.8 g, 0.1 mol), dissolved in 600 mL of ethanol containing 2.3 g of reacted sodium, was stirred overnight at room temperature. The solution was heated at 80 °C for 3 h and then evaporated. The residue was partitioned between ethyl ether and water. The aqueous fraction was acidified and extracted with diethyl ether, and the ethereal extract was evaporated to give 10.4 g of a brown solid. The solid was triturated with benzene to afford 6.52 g (31%) of semipure 2-acetyl-3-hydroxyphenoxyacetic acid (**2**), mp 183–188 °C. A recrystallization raised the melting point to 193–195 °C (H_2O) (lit.[7] mp 193–194.5 °C); IR (KBr) 1785, 1630, 1605, 1480, 1262, 1213 and 1120 cm^{-1}; NMR (Me_2SO-d_6) δ 2.62 (3 H, s), 4.75 (2 H, s), 6.53 (2 H, m), and 7.4 (1 H, t). Evaporation of the combined benzene and the first ethereal extracts gave 12.2 g of a solid which was chromatographed on silica gel (60–200 mesh). Elution with benzene–ethyl acetate (changing from a ratio of 1:99 to 1:1) afforded three major fractions. The first fraction of 1.02 g (6.9%) was crude 4-hydroxy-3-methylbenzofuran (**3**), which afforded needles: mp 110–112 °C (lit.[1] mp 111 °C) (C_6H_6–petroleum ether); IR (KBr) 3300 (br), 1640, 1620, 1600, 1480, 1470, 1332, 1260, 1220, 1109, 1040, 790, 746; NMR ($CDCl_3$) δ 2.34 (3 H, s), 5.03 (1 H, s) (exchanged with D_2O), 6.52 (1 H, m), 7.03 (1 H, s), and 7.2 (2 D, m). The second fraction afforded 340 mg (2.3%) of 6-hydroxy-1-benzoxepin-3,5(2*H*,4*H*)-dione (**4**): mp 139–141 °C (C_6H_6–petroleum ether); UV (EtOH) λ_{max} 217 nm (ϵ 15 100), 226 (ϵ 14 800), 266 (ϵ 10 235), and 341 (ϵ 4100); IR (KBr) 1740, 1630, 1603, 1555, 1538, 1455, 1232, 1058, 970, 790, and 740 cm^{-1}; NMR ($CDCl_3$) δ 4.32 (2 H, s), 4.50 (2 H, s), 6.78 (2 H, m), 7.45 (1 H, m), and 12.31 (1 H, s) (exchanged with D_2O); mass spectrum *m/e* 192 (M^+), 150 ($M^+ - C_2H_2O$), 121 ($M^+ - C_3H_3O_2$).

Anal. Calcd for $C_{10}H_8O_4$ (192.17): C, 62.50; H, 4.20. Found: C, 62.43; H, 4.33. pK_a = 4.83. A second crop of **4** was obtained in a 280-mg (1.9%) yield, mp 136–139 °C.

The third fraction gave 6.91 g (31.4%) of ethyl 4-hydroxy-3-methyl-2-benzofurancarboxylate (**1**): mp 157–159 °C (lit.[1] mp 155 °C) (C_6H_6–petroleum ether); IR (KBr) 3290, 1690, 1622, 1592, 1460, 1392, 1283, 1190, 1065 and 752 cm^{-1}; NMR (Me_2SO-d_6) δ 1.33 (3 H, t), 2.68 (3 H, s), 4.32 (2 H, q), 6.72 (1 H, m), 7.2 (2 H, m), and 10.28 (1 H, br) (exchanged with D_2O).

The compound **4** (19.2 mg, 0.1 mmol) dissolved in 2 mL of absolute ethanol containing 2.3 mg (0.1 mmol) of sodium was stirred at room temperature for 60 h and then heated at 65 °C for 3 h. Monitoring by TLC indicated no change. The product, isolated by acidification and evaporation, was shown by NMR analysis to be unchanged **4**.

Cyclization of Ethyl 2-(2-Acetyl-3-hydroxyphenoxy)acetate (5) with Sodium Ethoxide in Toluene. The compound **5** (476.4 mg, 2 mmol) was refluxed for 24 h in a suspension of sodium ethoxide (56.5 mg, 2.3 mmol) in 10 mL of toluene. The reaction mixture was evaporated and acidified, and the chloroform extract was washed with 5% sodium bicarbonate solution and then with water, dried (Na_2SO_4), and evaporated to give 300 mg of solid product. The solid gave 221 mg (57.6%) of **4** (C_6H_6–petroleum ether), identical to the sample described in the preceding experiment.

Cyclization of Ethyl 2-(2-Acetylphenoxy)acetate (6) with Sodium Ethoxide in Toluene. Similarly, a mixture of 11.10 g (50 mmol) of **6**,[8] sodium ethoxide (from 1.26 g of sodium), and 50 mL of toluene was refluxed for 1.5 h. The solvent was removed in vacuo and the residue partitioned between water and chloroform. The dried chloroform extract afforded 1.96 g (17.5%) of ethyl 3-methyl-2-benzofurancarboxylate (**8**), mp 48–50 °C (lit.[9] mp 49–51 °C). The aqueous extract was acidified, and the resulting solids were collected and crystallized to give 4.12 g (42.6%) of 3-methyl-2-benzofurancarboxylic acid (**9**), mp 187–190 °C (lit.[9] mp 192–194 °C).

Registry No.—**1**, 3781-69-9; **2**, 3361-22-6; **3**, 3610-15-9; **4**, 63815-26-9; **5**, 6769-65-9; **6**, 63615-27-0; **8**, 22367-82-4; **9**, 24673-56-1.

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Synthesis of Aromatic Hydrocarbons and Alcohols by Tandem Phenylation–Reduction of Esters and Lactones[1]

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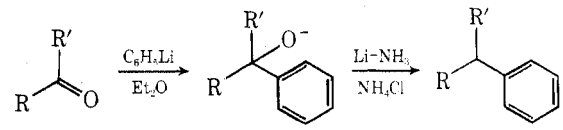
Received June 10, 1977

This laboratory has been exploring the potential applications of tandem alkylation–reduction of aromatic carbonyl systems[3] and phenylation–reduction of aldehydes and ketones[1,4] as a convenient method of preparing aromatic hydrocarbons. The method involves the lithium–ammonia–ammonium chloride reduction of a benzyl alkoxide generated in situ by alkylation. Since the entire sequence is performed in the same reaction vessel without the isolation or purification of intermediates, the total synthesis consumes only a few hours and the isolated yield of the product is usually good. Herein we extend the application of this tandem phenylation–reduction procedure to esters and lactones.



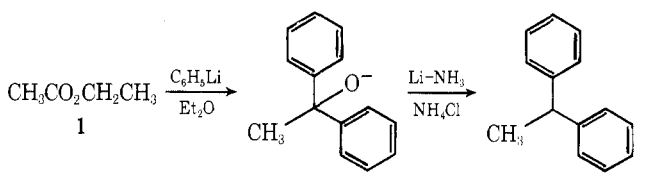
Since subjecting esters and lactones to an excess of phenyllithium results in the formation of a benzyl alkoxide (a 1,1-diphenyl 1-alkoxide), these carbonyl systems seemed appropriate starting materials for the synthesis of 1,1-diphenyl hydrocarbons and alcohols using this tandem sequence. The results are listed in Table I. Esters yield the corresponding 1,1-diphenyl hydrocarbons. Two examples are given. Phenylation–reduction of ethyl acetate (**1**) yielded 1,1-diphenylethane (**9**) and methyl benzoate (**2**) yielded triphenylmethane (**10**).

Phenylation–reduction of lactones, on the other hand, yields the corresponding diphenyl alcohols. For example, γ-butyrolactone (**3**) yielded 4,4-diphenyl-1-butanol (**11**). Related

Table I. Phenylation–Reduction of Esters and Lactones[a]

Ester or lactone	Registry no.	Product[b]	Registry no.	Yield c	Yield d
Ethyl acetate (1)	141-78-6	1,1-Diphenylethane (9)	612-00-0	80	70[e]
Methyl benzoate (2)	93-58-3	Triphenylmethane (10)	519-73-3	89	84[f]
γ-Butyrolactone (3)	96-48-0	4,4-Diphenyl-1-butanol (11)	56740-71-7	92	69[g]
γ-Valerolactone (4)	108-29-2	5,5-Diphenyl-2-pentanol (12)	63797-58-0	70	55[h]
α-Methyl-γ-butyrolactone (5)	1679-47-6	3-Methyl-4,4-diphenyl-1-butanol (13)	63797-59-1	95	45[i]
γ-Phenyl-γ-butyrolactone (6)	1008-76-0	1,1,4-Triphenylbutane (14)	33885-06-2	90	65
Dihydrocoumarin (7)	119-84-6	o-(3,3-Diphenylpropyl)phenol (15)	63797-60-4	95	86
Coumarin (8)	91-64-5	o-(3,3-Diphenylpropyl)phenol (15)		98	78[f]

[a] See Experimental Section for details. [b] Products **9, 10, 14,** and **15** gave satisfactory composition analyses (±0.4% for C, H). [c] Analyzed by GLC (% of volatiles). [d] Isolated by column chromatography unless stated otherwise. [e] Isolated after column chromatography followed by evaporative distillation. [f] Isolated after recrystallization. [g] An inseparable mixture of **11** (98%) and the overreduced dihydro and tetrahydro compounds (ca. 1% each). [h] An inseparable mixture of **12** (90%) and the overreduced dihydro (3%) and tetrahydro (7%) compounds. [i] An inseparable mixture of **13** (96%) and the overreduced dihydro and tetrahydro compounds (ca. 2% each).



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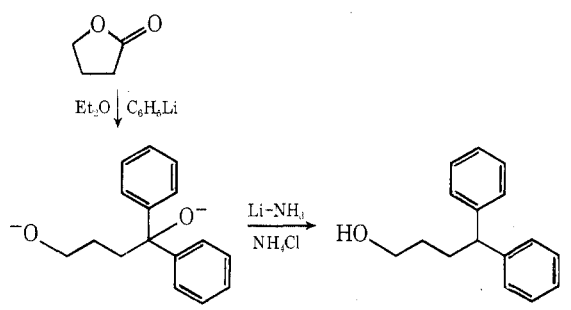
examples appear in Table I. γ-Phenyl-γ-butyrolactone (**6**) yielded the aromatic hydrocarbon 1,1,4-triphenylbutane (**14**) since both alkoxides are benzylic and reduce during the reduction sequence. Only one lactone, α,α-diphenyl-γ-butyrolactone (not shown in Table I), was found not amenable to this procedure. This was evidently because of its resilience to phenylation during the first step for steric reasons. The products from a few of the lactones, notably alcohols **12** and **13**, were contaminated (NMR and GC–MS analyses) with small amounts of overreduction products (see footnotes to Table I).

Phenylation–reduction of the phenolic lactones dihydrocoumarin (**7**) and coumarin (**8**) both resulted in the formation



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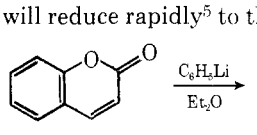
of o-(3,3-diphenylpropyl)phenol (**15**). This result is expected since the intermediate from coumarin is a styrene system that will reduce rapidly[5] to the saturated phenol derivative **15**.



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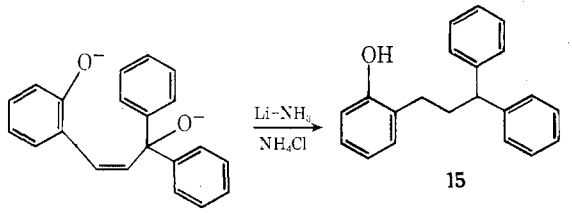

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Although some of the isolated yields of the alcohols and hydrocarbons listed in Table I are only moderate, the availability of the starting materials and efficiency (time, energy, cost) of this one-pot synthesis make this tandem sequence a very useful method for the synthesis of these structural types.

Experimental Section[6]

General Comments. See ref 4 for general experimental comments. Compounds **1–5** were distilled just prior to use. Gas chromatography (GLC) analyses were performed on 120 × 0.2 cm (i.d.) glass columns packed either with 3% silicon gum rubber OV-17 (methylphenyl) or 3% silicon gum rubber SE-30 (methyl) supported on 100–120 mesh HP Chromosorb W (AW, DMCS). Purification of each product by column chromatography was accomplished on chromatographic grade activated alumina (80–325 mesh, Matheson Coleman and Bell) grade I (for the hydrocarbons) and grade III (6% H_2O, for the alcohols) by elution with petroleum ether and petroleum ether–Et_2O. Evaporative distillations, sometimes necessary for microanalyses, were performed in a Kügelrohr oven. The assigned structure of each product was consistent with the spectral data and some were compared with authentic samples. The phenylation–reduction of coumarin (**8**) is described, in detail, to illustrate the procedure.

Phenylation–Reduction of Coumarin (8). o-(3,3-Diphenylpropyl)phenol (15). To a metal–ammonia reaction vessel containing a stirred mixture of 350 mg (50.0 mg-atoms, ca. 25 pieces) of lithium foil in 10 mL of anhydrous ether was slowly added (ca. 10 min)[7] a solution of 1.962 g (12.50 mmol) of bromobenzene in 10 mL of ether. After 50 min, the reaction mixture was diluted with 10 mL of ether and then cooled to ca. −70 °C (dry ice–acetone bath). A solution of 730 mg (5.00 mmol) of coumarin (**8**) in 20 mL of ether was slowly added (ca. 15 min) and after 10 min the cooling bath was removed and the mixture was stirred for 50 min. After a further dilution with 25 mL of ether, ca. 75 mL of ammonia was carefully distilled[8] (15–20 min) into the mixture and after 30 min the dark blue color of the reaction mixture was discharged by the addition[9] (5–10 min) of excess ammonium chloride (ca. 1.8 g). After the ammonia had evaporated the residue was partitioned between ether and brine. The organic phase was dried ($MgSO_4$), filtered, concentrated at water aspirator pressure, and then analyzed (GLC). The crude yellow viscous oil (1.440 g) crystallized as white needles (1.123 g, 78%) from benzene–petroleum ether: mp 65–66 °C; IR (film) 3550, 3440 (br), 1600, 1500, 1460, 750, 700 cm^{-1}; NMR (100 MHz, $CDCl_3$, 25 transients) δ 7.24 (10 H, apparent s), 7.1–6.6 (4 H, complex m), 4.84 (1 H, broad s, exchangeable with D_2O), 3.93 (1 H, t, J = 7.5 Hz), 2.6–2.3 (4 H, complex m); MS m/e (rel intensity) 288 (M^+, 3), 167 (95), 121 (100), 77 (81). Anal. Calcd for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 87.57; H, 7.10.

Acknowledgment. The authors are grateful to Dr. F. Scheidl, Hoffmann–La Roche Inc., Nutley, N.J., for the microanalyses, and the Charles and Johanna Busch Memorial Fund, the Research Council (Rutgers), and N.I.H. (Biomedical Sciences Support Grant) for supporting grants.

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(6) GLC analyses were determined on a Hewlett-Packard Model 7610A (flame detector) chromatograph. The IR spectra were determined with a Beckman Model AccuLab 6 infrared recording spectrophotometer. The ^{1}H NMR spectra were determined at 100 MHz with a JEOL Model JNM-PS-FT-100 fast Fourier Transform NMR spectrometer. The chemical shifts are expressed in δ values (parts per million) relative to a Me_4Si internal standard. The mass spectra were determined with a Finnigan Model 3100D mass spectrometer (70 eV) to which was interfaced a Varian Associates Model 1400 gas chromatograph.
(7) During the addition the exothermic reaction was moderated (18–25 °C, internal thermometer) with a water bath.
(8) To increase the efficiency of the condensation process, the reaction vessel was cooled (dry ice–acetone bath), and to prevent splattering, the apparatus was tilted slightly to allow the condensing ammonia to run down the walls of the flask.
(9) The NH_4Cl is most conveniently introduced by attaching a glass bulb filled with the salt to a side arm by means of tygon tubing. When the salt is to be added, the bulb is raised and tapped gently to smoothly introduce the quenching agent. Should this step start to become violent, the addition and sometimes even the vigorous stirring should be momentarily stopped to avoid an eruption.

Oxidation of Olefins with Silver Chromate–Iodine. A New and Facile Synthesis of α-Iodo Ketones

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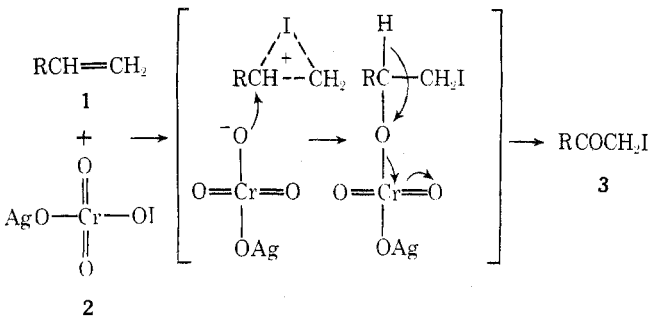
Received April 22, 1977

Our interest in the nucleophilic properties of chromate anion coupled with the recent attention accorded to the oxidation of activated alkyl halides to the corresponding aldehydes[2] prompts this report on the capability of the silver chromate–iodine system for the facile oxidation of double bonds to the corresponding α-iodo ketones.

α-Halo ketones have been regarded as synthetically useful materials and several general methods for their syntheses have been established.[3] In contrast to their chloro or bromo analogues, α-iodo ketones, however, have not been sufficiently studied. This is partly because of their relative instability and that there are only a few satisfactory synthetic methods available, e.g., halogen–iodide interchange[4] and treatment of enol acetates with *N*-iodosuccinimide.[5] Furthermore, both methods appeared to need relatively high reaction temperatures which might cause decomposition of the products. It is, therefore, of value to develop an easy and mild synthetic route to α-iodo ketones.

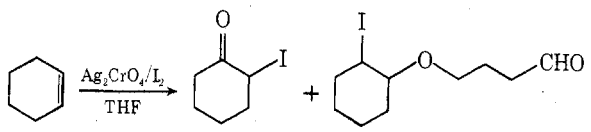
Until now, for one-step oxidations of olefins to α-chloro ketones only two methods have been known, one utilizing nitrosyl chloride[6a,b] and the other chromyl chloride.[6c] On the other hand, oxidation of alkenes with acyl hypoiodite provides an easy way to introduce α-iodo alcohols to double bonds.[7] In an analogy to the well-known Prevost reaction, we considered

Scheme I



that the generation of a hypoiodous–chromic acid mixed anhydride (**2**) under mild conditions would lead to a one-step oxidation of olefins to α-iodo ketones. Scheme I reports a possible mechanism.

Scheme II



We have now found that the treatment of cyclohexene with silver chromate[8] and iodine leads to 2-iodocyclohexanone. A series of experiments was carried out in an effort to find the optimum conditions for the oxidation of cyclohexene. Table I lists the results obtained.

When THF was used as a solvent, a small amount of ether **6**[9] arising from THF was always recovered together with 2-iodocyclohexanone (**5**).

As shown in Table I, the best yield was obtained when dichloromethane was used as a solvent in the presence of 0.5 to 1.0 equiv of pyridine.[10] The reactions summarized in Table II (vide infra) were performed under the optimum conditions found for cyclohexene.

This reaction seemed to have wide applicability. In general, electron-rich olefins gave better results, while electron-deficient ones such as crotononitrile resulted in the recovery of the starting olefins. Aliphatic, alicyclic, and aromatic olefins gave satisfactory yields in the majority of cases. The lower yields observed in the cases of allyl benzoate and 2,3-dihydro-4*H*-pyran are due to the formation of the unidentified by-products which decomposed despite several attempts for isolation. Further, terminal olefins were converted exclusively to the corresponding α-iodo ketones.

Thus, the above results as well as mild reaction conditions make the present method highly useful for the synthesis of α-iodo ketones from olefins.

Further studies utilizing other metal chromates are currently in progress.

Experimental Section

General. All reactions were run under a positive pressure of dry argon. Infrared spectra (IR) were recorded on a Perkin-Elmer 710B spectrometer and are given in cm^{-1}. Nuclear magnetic resonance spectra (NMR) were determined on a Perkin-Elmer R12B spectrometer. Chemical shifts are given in ppm from internal tetramethylsilane. Mass spectra (MS) were taken on a Varian MAT 111 (70 eV). Melting points (mp) which were determined in glass capillaries and boiling points (bp) were uncorrected. Preparative thin-layer chromatography (TLC) was carried out on a glass plate (20 × 20 cm) coated with Merck silica gel HF_{254} (1-mm thick). Column chromatography was performed on Merck silica gel (0.05–0.20 mesh).

Tetrahydrofuran (THF) and dimethoxyethane (DME) were distilled from sodium benzophenone ketyl immediately before use. Benzene was distilled from sodium and stored over it. Dichloromethane was distilled from phosphorus pentoxide and stored over 4-Å molecular sieves. Pyridine was distilled from calcium hydride and stored under argon.

Silver Chromate.[8] A solution of silver nitrate (17.0 g, 100 mmol) in 200 mL of water was added with stirring to a solution of potassium chromate (9.7 g, 50 mmol) in 200 mL of water. Promptly and quantitatively reddish-brown silver chromate precipitated. The precipitate was filtered, washed successively with water, dried in vacuo, finely pulverized, and dried again in vacuo at 90 °C for 5 h.

Unless otherwise indicated, the following α-iodo ketones were prepared according to the general procedure.

Phenacyl Iodide (General Procedure). To a suspension of silver chromate (1.10 g, 3.3 mmol) and 4-Å molecular sieves[11] (1.5 g) in 15 mL of dichloromethane were added iodine (1.14 g, 4.5 mmol) and a solution of pyridine (118 mg, 1.5 mmol) in 0.75 mL of dichloromethane at 0 °C and stirred for 5 min.

A solution of styrene (312 mg, 3.0 mmol) in 5 mL of dichloromethane was added dropwise during 5 min to the ice-cooled suspen-