chloric acid, and the steroids were recovered with ethyl acetate. The ethyl acetate solution was washed with sodium bicarbonate and water, dried, and concentrated *in vacuo*. The residue was crystallized from aqueous methanol to yield prisms: m.p.[13] 257–261° (loss of water at 110°) (lit.[10] m.p. 274–276°); ν_{max} 3550, 1727 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{40}O_5$: C, 72.19; H, 9.32. Found: C, 72.14: H, 9.14.

Hecolo Lactone Acetate XI.—A mixture of hecogenin acetate (650 mg.), *t*-butyl alcohol (30 ml.), selenium dioxide (50 mg.), and hydrogen peroxide (50%, 1.5 ml.) was refluxed for 10 hr. Processing of the reaction mixture gave acidic (312 mg.) and neutral (250 mg.) residues.

The neutral residue crystallized from methanol to yield the lactone XI (200 mg.): m.p. 290–292° (lit.[11b] m.p. 290–295°); ν_{max} 1728, 1243, 1158, 983, 922, 897 cm.$^{-1}$.

The acidic residue was dissolved in methanol (2.5 ml.) and 1 *N* sodium hydroxide (2.5 ml.), and the mixture was refluxed for 1 hr. in an atmosphere of nitrogen. After the usual work-up, the seco acid XII was obtained and showed a double m.p. 185–189° and 242–252° (lit.[11b] m.p. 187° and 253–258°); ν_{max} 3400, 2600 (broad), and 1700 cm.$^{-1}$.

Condensation of 2-Aryl-1,3-dioxolanes with Alkyllithium Reagents. A New Synthesis of Alkyl Aryl Ketones from Aromatic Aldehydes[1]

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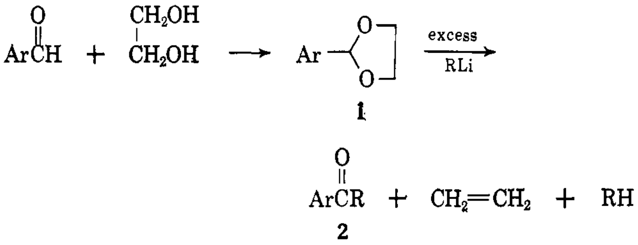
1,3-Dioxolanes of aromatic aldehydes have been found to react with alkyllithium reagents to give alkyl aryl ketones in good yield. The over-all process is thus replacement of hydrogen in the aromatic aldehyde by an alkyl substituent. An inverse addition of butyllithium to a dioxolane produced several compounds including butane which suggests initial hydrogen–metal exchange to yield an alicyclic carbanion. A mechanism is postulated in which the carbanion formed undergoes ring opening to give a β-arylcarboxyethyl anion. Decay of this anion is postulated to explain the products.

Facile conversion of one functional group to another is extremely valuable in synthetic problems. Results are now available which demonstrate that aromatic aldehydes can be smoothly transformed into alkyl aryl ketones through the following sequence.[4] Syntheses



1a, Ar = C_6H_5
b, Ar = p-$CH_3OC_6H_4$
c, Ar = p-$CH_3C_6H_4$

2a, Ar = C_6H_5, R = C_4H_9
b, Ar = C_6H_5, R = C_6H_{11}
c, Ar = p-$CH_3OC_6H_4$, R = C_4H_9
d, Ar = p-$CH_3C_6H_4$, R = C_4H_9

of 1,3-dioxolanes **1** are conventionally achieved by condensation of the appropriate aldehyde with a 1,2-diol in the presence of *p*-toluenesulfonic acid as a catalyst.[5] Although noted for marked stability to alkali bases,[6] 1,3-dioxolanes of aromatic aldehydes are conceivably vulnerable to attack by removal of a benzylic proton in analogy with the Wittig rearrangement involving the reaction of phenyllithium with benzyl ethers to give alcohols.[7,8]

In a typical experiment 2-phenyl-1,3-dioxolane (**1a**) in cyclohexane was slowly added to butyllithium in ether–cyclohexane under nitrogen. When the addition was complete (the temperature was maintained below 35°), the mixture was slowly heated to 60° (1 hr.). A large quantity of gelatinous precipitate was formed and gas was evolved. After an additional 1.5 hr. at 60°, the mixture was decomposed with water. Distillation of the organic layer gave *n*-valerophenone (**2a**) identified by infrared and n.m.r. spectroscopy. *n*-Hexyllithium and **1a** gave *n*-heptanophenone (**2b**), *n*-butyllithium and 2-*p*-methoxyphenyl-1,3-dioxolane (**1b**) gave *p*-methoxy-*n*-valerophenone (**2c**), and *n*-butyllithium and 2-*p*-tolyl-1,3-dioxolane (**1c**) gave *p*-methyl-*n*-valerophenone (**2d**) as shown in Table I. In all cases the ratio of lithium reagent to dioxolane was greater than 3. Butane and ethylene were produced in major quantity and were trapped over salt water and identified by infrared analysis. These observations imply that a nucleophilic attack by butyllithium on a carbon atom of the cyclic acetal is unlikely. In contrast the stability of benzylic anions is well known,[9] and loss of a benzylic proton from **1a** would produce such an anion.

TABLE I

ALKYL ARYL KETONES

Ketone	Yield, %	$\lambda_{max}^{C=O}$, μ
2a	87.5	5.95
2b	66.5	5.92
2c	78.0	5.98
2d	80.0	5.96

Fission of a carbon–oxygen bond in the carbanion **3** could occur to give **4** which may decompose to **5** and

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[2] Dow Chemical Co. Predoctoral Fellow, 1963–1964.

[3] College Teacher Research Participant supported by the National Science Foundation, summer 1964; National Science Foundation Faculty Fellow, 1964–1965.

[4] After this work was submitted, a paper appeared describing similar results from the reaction of 2-phenyl-1,3-dioxolane with phenyllithium: see P. S. Wharton, G. A. Hiegel, and S. Ramaswami, *J. Org. Chem.*, **29**, 2441 (1964). The one reaction studied did not provide a method of synthetic value nor was the postulated mechanism substantiated by the interception of benzoic acid. Neither was reference made to the earlier report of L. J. Nehmsman (ref. 8) who discovered the same reaction recently. In neither case was firm evidence provided for the existence of the anion **3**.

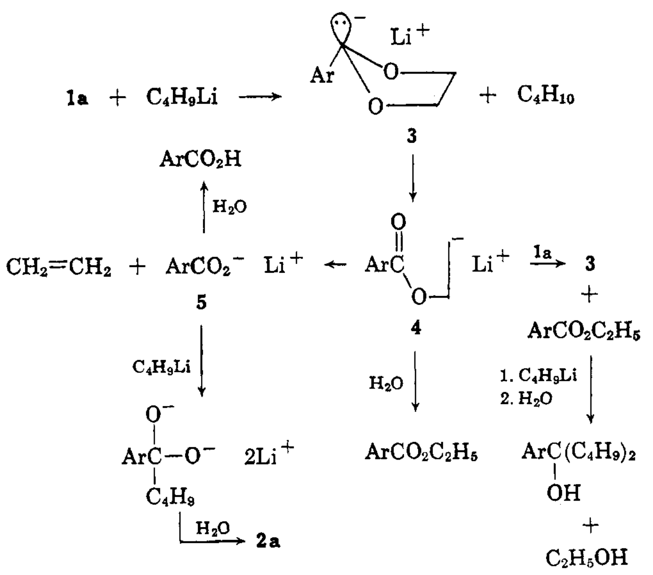
[5] M. Renoll and M. S. Newman, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 502.

[6] R. C. Fuson, "Reactions of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1962, p. 401.

[7] G. Wittig, R. Mangold, and G. Felletschin, *Ann.*, **560**, 116 (1948).

[8] Phenyllithium is reported to react with 2-phenyl-1,3-dioxolane to give benzophenone, tritanol, and ethylene as major products: see L. J. Nehmsmann, *Dissertation Abstr.*, **23**, 1929 (1962).

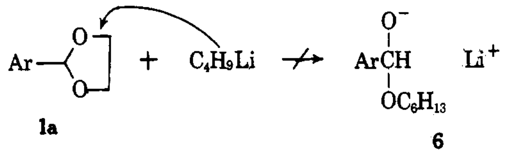
[9] G. A. Russell, *J. Am. Chem. Soc.*, **81**, 2017 (1959).



ethylene. The driving force for ring opening may well be due to creation of the π-bond in **4**, although any inherent strain in **3** cannot be evaluated at present. It is noteworthy that the reaction to produce ethylene is slow at room temperature and only when the mixture is heated to 60° does the gas begin to evolve in quantity. Although not identified specifically in our work, the carboxylate salt **5** is logical and has been postulated in the condensation involving the action of lithium reagents on carboxylic acids to give ketones.[10,11] Assuming nearly 1 mole of butyllithium is converted to butane in the initial metal exchange with **1a**,[12] more than 2 moles of butyllithium are still available so that the classical reaction with **5** may proceed. In the example with **1a**, a small amount of benzoic acid was identified in the aqueous and organic phases of the decomposition mixture. The most reasonable precursor of benzoic acid is **5**.

Since presumably the first mole of lithium reagent was destroyed in the formation of **3**, it was anticipated that an inverse addition of butyllithium to **1a** (1:1 molar ratio) should provide opportunity to witness the decay pattern of **3** in the absence of excess lithium reagent. Benzoic acid was found in high yield along with smaller amounts of **2a**, ethanol, ethyl benzoate, and 5-phenyl-5-nonanol. Some starting material was also recovered. In view of the identification of **2a** and 5-phenyl-5-nonanol, it is presumed that the carboxylate anion **5** and ethyl benzoate, respectively, can compete with **1a** for the butyl anion. This competition probably becomes more effective as the reaction proceeds and the molar ratio of **5** to **1a** rises. Moreover, 5-phenyl-5-nonanol and ethanol would be expected from attack of butyllithium on ethyl benzoate. This evidence suggests that ring opening occurs to give **4** which can collapse to yield **5** and ethylene or remove a proton, probably from the dioxolane **1a** (and thus compete with butyllithium) to give ethyl benzoate. The latter process would be favored when a deficiency of butyllithium existed as in the inverse addition. When **1a** is added to excess butyllithium, **3** is formed and opens to give **4** which loses ethylene to form **5**.

The argument arises that a nucleophilic displacement on **1a** is reasonable but this appears less acceptable in view of the isolation of butane. In addition, if the ring opened to the hemiketal **6**, preservation of its structure might be anticipated under the basic conditions of the reaction. Hydrolysis of **6** would be expected to yield hexanol, the absence of which was substantiated by gas chromatography. More pertinent perhaps is the observation that the tertiary hydrogen in *n*-valeraldehyde dimethyl acetal is not sufficiently acidic to react with butyllithium under the conditions described. Only starting material was recovered. This observation supports the conclusion that a nucleophilic displacement on carbon to give an alkoxide ion is untenable.



Advantages of the method are the mild conditions required, simplicity of product isolation, and high yields of ketones. In view of the ease of preparation of 1,3-dioxolanes from aromatic aldehydes, the method may be limited only by the availability of the lithium reagent and multiplicity of its reaction with other reactive functional groups in the aldehyde.

Experimental[13]

2-Aryl-1,3-dioxolanes 1a, 1b, and 1c.—The procedure used for the preparation of **1a**, **1b**, and **1c** was essentially that of Sulzbacher and co-workers.[14] **1a** had b.p. 228–231° (747 mm.), n^{32}_{D} 1.5212 (lit.[15] b.p. 225°, n^{20}_{D} 1.5269[14]). **1b** had b.p. 121–125° (2.2 mm.), $n^{26.5}_{D}$ 1.5328 (lit.[14] b.p. 158–160° at 17 mm., $n^{19.5}_{D}$ 1.5362). **1c** had b.p. 82–84° (0.9 mm.), $n^{31.4}_{D}$ 1.5188 (lit.[16] b.p. 128° at 14 mm., n^{20}_{D} 1.5247).

Reaction of Butyllithium with 1a.—The method described was typical for the other examples investigated. Addition of a solution of **1a** (3.45 g., 0.023 mole) in 60 ml. of cyclohexane to butyllithium (0.076 mole)[17] in 215 ml. of ether was slightly exothermic. The mixture was heated to reflux under nitrogen, and some ether was allowed to escape until the temperature of the mixture reached 60° (0.5 hr). Cyclohexane (40 ml.) was added to dilute the mixture (a gelatinous precipitate had formed) which was then stirred for an additional 0.2 hr. at room temperature. Water (60 ml.) was added dropwise to effect decomposition. The aqueous phase was extracted with cyclohexane, and the extracts and original organic layer were combined, dried over magnesium sulfate, and distilled to give **2a**: b.p. 237–240° (740 mm.), 2,4-dinitrophenylhydrazone (2,4-DNP) m.p. 166° (lit.[18] b.p. 242°, 2,4-DNP m.p. 166°), yield 3.26 g.

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[10] H. Gilman and P. R. Van Ess, *J. Am. Chem. Soc.*, **55**, 1258 (1933).

[11] C. K. Bradsher and S. T. Webster, *ibid.*, **79**, 393 (1957).

[12] In an analogous reaction it was found that ortho esters react with butyllithium to give butane. The resulting anion, $(RO)_3C^-$, undergoes a series of cleavage reactions involving carbon–oxygen bonds to give internal olefins: see K. D. Berlin and B. S. Rathore, *Tetrahedron Letters*, 2547 (1964).

[13] All melting points are corrected. All boiling points are uncorrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. The g.l.c. analyses were performed on columns of silicone rubber on Chromosorb W with a Hy Fi A-550 hydrogen flame unit by Wilkens Instrument and Research, Inc. The n.m.r. spectrum was determined on a Varian A-60 high-resolution spectrometer. Tetramethylsilane was used as internal standard with its scale as 0 in δ-units.

[14] M. Sulzbacher, E. Bergmann, and E. R. Pariser, *J. Am. Chem. Soc.*, **70**, 2827 (1948).

[15] H. Hibbert and J. A. Timm, *ibid.*, **46**, 1283 (1924).

[16] E. J. Salmi and K. Kyrki, *Suomen Kemistilehti*, **19B**, 97 (1946); *Chem. Abstr.*, **41**, 5480 (1947).

[17] The preparation was essentially that found in A. J. Vogel, "A Textbook of Practical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1959, p. 932.

[18] N. D. Cheronis and J. B. Entrikin, "Semiqualitative Organic Analysis," Interscience Publishers, Inc., New York, N. Y., 1960, p. 665.

***n*-Hexyllithium.**—The reagent was prepared by a procedure in the literature.[19]

Inverse Reaction of *n*-Butyllithium with 2-Phenyl-1,3-dioxolane (Ia).—2-Phenyl-1,3-dioxolane (2.25 g., 0.015 mole) was dissolved in 50 ml. of cyclohexane and the system was swept with nitrogen. *n*-Butyllithium (0.0146 mole) in 140 ml. of ether was added dropwise over a 0.5-hr. period (a small rise in temperature was noted). A heavy white precipitate was formed during this period.

The reaction was heated gradually for 2 hr. until the temperature reached 57°. Water (150 ml.) was carefully added to hydrolyze the mixture and additional ether (final volume 250 ml.) was added to dissolve the remaining solids. The organic layer was dried over anhydrous sodium sulfate, and approximately one-half of the sample (*ca.* 100 ml.) was concentrated to a volume of 10 ml. which was used for subsequent g.l.c. analysis.

The water layer was acidified with 6 *N* hydrochloric acid and extracted with three 100-ml. portions of ether. After drying over anhydrous sodium sulfate, 100 ml. of the ether extract was concentrated to 5 ml. and examined by gas chromatography.

G.l.c. analysis was made using a column of SE-30 (5%) on Chromosorb W (80/100), 6 ft. × 0.125 in., on an Aerograph Hy Fi Model A-550 unit with a hydrogen flame ionization detector; the temperature range examined was 112–215°; H_2 flow, 20 cc./min.; N_2 flow, 30 cc./min. The following compounds were identified by the mixed injection technique: 2-phenyl-1,3-dioxolane, benzaldehyde, valerophenone, ethyl benzoate, benzoic acid, octane, and 5-phenyl-5-nonanol.

Preparation of 5-Phenyl-5-nonanol.—The butyl Grignard reagent was prepared in the usual manner from 12.16 g. (0.5 g.-atom) of magnesium, 68.52 g. (0.5 mole) *n*-butyl bromide and 200 ml. of anhydrous ether. To the Grignard reagent was added 37.54 g. (0.25 mole) of ethyl benzoate dissolved in 50 ml. of absolute ether. During addition, which required 0.75 hr., the temperature rose five degrees. After the addition was complete the reaction was heated under reflux for 2 hr.

Hydrolysis was effected with 250 ml. of 20% aqueous ammonium chloride. The mixture was acidified with dilute hydrochloric acid and the organic layer was separated. The aqueous layer was washed with three 100-ml. portions of ether. After the extract had been combined with the organic layer and dried over anhydrous magnesium sulfate, it was distilled to give 33.55 g. (61%) of 5-phenyl-5-nonanol: b.p. 90.8–91.5° (1.5–2 mm.), $n^{25.8}$D 1.4993 (lit.[20] b.p. 130–132° at 7–8 mm., n^{18}D 1.50602); λ_{max}^{film} 3448 (O-H), 3010 (aromatic C-H), 2915 and 2857 (aliphatic C-H), and 700 cm. (C_6H_5–). The n.m.r. (in CCl_4) showed resonance frequencies at δ 0.75 (multiplet), 1.12 (multiplet), 1.75 (multiplet), 2.35 (singlet, O-H), and 7.24 (singlet, aromatic protons).

***n*-Valeraldehyde Dimethyl Acetal.**—The procedure was that found in the literature[21]: b.p. 131° (739 mm.); λ_{max}^{film} 1060 and 1440 cm.$^{-1}$; yield 48%.

Reaction of *n*-Butyllithium with *n*-Valeraldehyde Dimethyl Acetal.—*n*-Butyllithium (0.1 mole) and the acetal (2.24 g., 0.02 mole) were heated at reflux in ether–hexane (60°). After 2 hr., the reaction mixture was decomposed with water. Analysis by gas chromatography of the organic solution indicated primarily unreacted acetal.

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(19) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn, and L. S. Miller, *J. Am. Chem. Soc.*, **71**, 1499 (1949).

(20) A. D. Petrov, A. P. Bardanov, N. N. Zakotin, and P. I. Suntsov, *J. Gen. Chem. USSR.*, **9**, 509 (1939); *Chem. Abstr.*, **34**, 388 (1940).

(21) C. Morel, *Soap Perfumery Cosmetics*, **27**, 279 (1954); *Chem. Abstr.*, **48**, 6654 (1954).

The Hofmann Elimination of 9-Methyl-3,9-diazabicyclo[4.2.1]nonan-4-one Methiodide. Nature of the Product and Mechanism[1]

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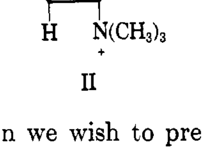
The Hofmann elimination of 9-methyl-3,9-diazabicyclo[4.2.1]nonan-4-one methiodide (IV) has been found to afford the α,β-unsaturated amide VI. Evidence in support of this structure has been obtained from ultraviolet and n.m.r. data, and from studies of the behavior of the monocyclic and tetradeuterated analogs, XV and XX, respectively. The elimination of the quaternary nitrogen center has been shown by proper deuterium labeling to occur most probably *via* an E1cb mechanism.

The thermal decomposition of a quaternary hydroxide to give an olefin and an amine has proven itself not only a useful procedure for degradation and synthesis,[4] but has been found to vary mechanistically upon the demand of the particular system under study. For example, simple alkylammonium hydroxides which possess a β-hydrogen atom that can readily attain *trans* coplanarity with the positively charged nitrogen function in the transition state undergo elimination *via* the E2 mechanism.[5,6] However, the quaternary hydroxide I, wherein the β-hydrogen atom cannot become *trans* and coplanar because of steric factors, has been found to eliminate by the *cis*-ylide mechanism.[7] Additional work has demonstrated that *trans*-2-phenylcyclohexyltrimethylammonium hydroxide (II) reacts exclusively by means of the two-step β-carbanion (E1cb) mechanism to yield only 1-phenylcyclohexene.[8-10]

I



II

In the present communication we wish to present a study of the Hofmann elimination of a bicyclic quaternary hydroxide wherein the nitrogen function is attached as the bridging atom simultaneously β-oriented to both the carbonyl and nitrogen moieties of an amide group (see IV). Such a system as IV is capable of the normal E2 *trans* elimination, for Dreiding models indicate that the appropriate hydrogens lie *trans* coplanar to the nitrogen function (as illustrated below). Alternatively, one can visualize an E1cb

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(1) Part XI of the series Unsaturated Heterocyclic Systems. For part X, see L. A. Paquette, *J. Org. Chem.*, **29**, 3447 (1964).

(2) Department of Chemistry, The Ohio State University, to whom inquiries should be addressed.

(3) Taken in part from the M.S. Thesis of L. D. W., The Ohio State University, 1964.

(4) For an excellent review of the Hofmann elimination reaction, see A. C. Cope and E. R. Trumbull, *Org. Reactions*, **11**, 317 (1960).

(5) V. G. Shiner and M. L. Smith, *J. Am. Chem. Soc.*, **80**, 4095 (1958).

(6) A. C. Cope, N. A. LeBel, P. T. Moore, and W. R. Moore, *ibid.*, **83**, 3861 (1961).

(7) A. C. Cope and A. S. Mehta, *ibid.*, **85**, 1949 (1963).

(8) J. Weinstock and F. G. Bordwell, *ibid.*, **77**, 6706 (1955).

(9) A. C. Cope, G. A. Berchtold, and D. L. Ross, *ibid.*, **83**, 3859 (1961).

(10) G. Ayrey, E. Buncel, and R. N. Bourns, *Proc. Chem. Soc.*, 458 (1961).