Lithium Aluminum Hydride Reduction of Phenacyl Halides. An Aryl Rearrangement Pathway[1]

LEONARD H. SCHWARTZ AND RICHARD V. FLOR

Department of Chemistry,
The City College of The City University of New York,
New York, New York 10031

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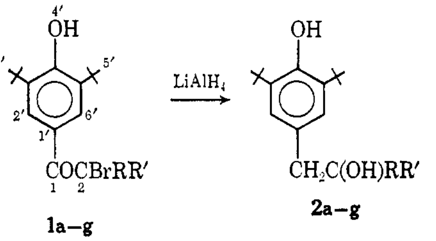
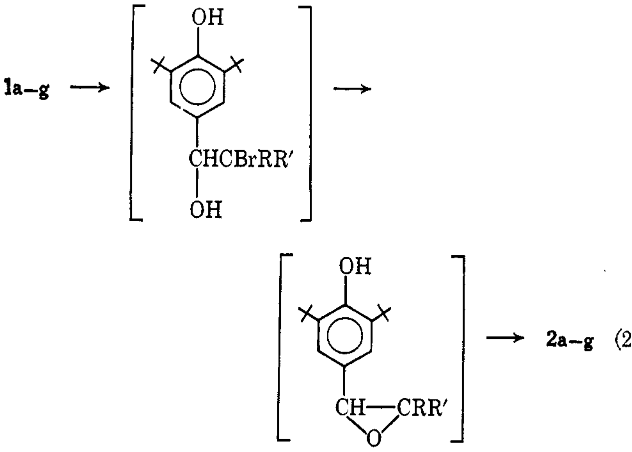
The reduction of phenacyl halides with $LiAlH_4$ has been the subject of a number of previous studies. The earlier work showed these reactions to proceed normally and to yield 1-aryl-1-ethanols[2–4] and 1-aryl-2-halo-1-ethanols.[4] The formation of the former products was favored by an excess of $LiAlH_4$. More recently, it was reported that the reduction of a series of 2-substituted 2-bromo-4′-hydroxy-3′,5′-di-*t*-butylacetophenones (**1a-g**) with excess $LiAlH_4$ proceeded abnormally (eq 1).[5]



(1)

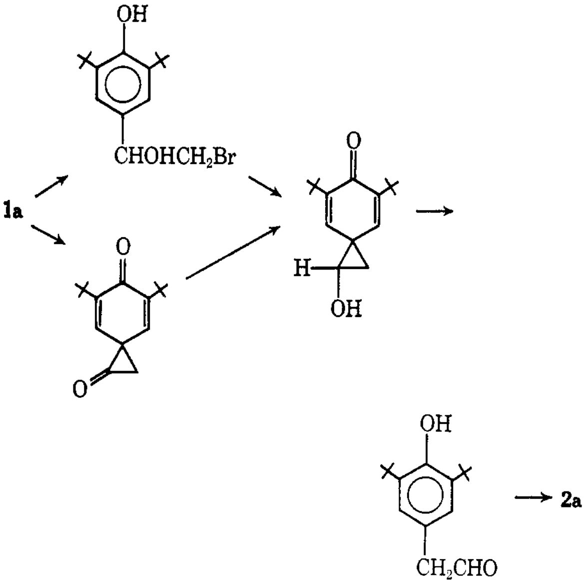
R, R′: **a**, H, H; **b**, H, CH_3; **c**, H, C_2H_5; **d**, H, *n*-Pr;
e, H, *i*-Pr; **f**, H, C_6H_5; **g**, CH_3, CH_3

The products, 1-substituted 2-(4-hydroxy-3,5-di-*t*-butylphenyl)ethanols (**2a-g**), were suggested to arise by way of a hydride attack on an epoxide intermediate (eq 2).[6]



(2)

We recently reported our findings of a study of the reduction of 2-bromo-4′-hydroxy-3′,5′-di-*t*-butylacetophenone (**1a**) with $LiAlD_4$.[7] The product of this reaction, 1,1-dideuterio-2-(4-hydroxy-3,5-di-*t*-butylphenyl)ethanol (**3**), is inconsistent with the reaction pathway previously postulated (eq 2).[5] To explain the formation of **3**, we suggested an aryl rearrangement pathway (eq 3).[6,8] For the substituted phenacyl bromides previously studied,[5] this mechanism predicts the formation of 2-substituted 2-(4-hydroxy-3,5-di-*t*-butylphenyl)ethanols (**4**) rather than the previously suggested products (**2b-g**).



(3)

It was not apparent to us why the presence of substituents at C_2 of **1** should cause a change in mechanism, from eq 3 to eq 2. We, therefore, decided to reinvestigate the earlier work. Bromides **1b**, **1c**, **1f**, and **1g** were synthesized from the corresponding 2-substituted acetophenones[9] by reaction with cupric bromide in ethyl acetate–chloroform.[10] In each case, the structure of the bromide was established by elemental analysis and nmr spectroscopy (Table I). The bromides were reduced with excess $LiAlH_4$. In each case, nmr spectroscopy of the crude reaction product (chemical shift of the methylene group and a triplet for the aliphatic OH proton in DMSO-d_6) indicated the product to be a 2-substituted 2-(4-hydroxy-3,5-di-*t*-butylphenyl)ethanol (**4**) (Table II) in essentially pure form, rather than a 1-substituted 2-(4-hydroxy-3,5-di-*t*-butylphenyl)ethanol (**2**) as previously reported.[5] We conclude that the reduction of 2-bromo-4′-hydroxy-3′,5′-di-*t*-butylacetophenones (**1**) with $LiAlH_4$ proceeds by way of an

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[1] Support of this work by the National Science Foundation (GP 6404), The City University of New York, and The General Faculty Research Committee of The City College of New York is gratefully acknowledged.

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[5] V. V. Ershov, A. A. Volod'kin, and N. V. Portnykh, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1632 (1966); A. A. Volod'kin, N. V. Portnykh, and V. V. Ershov, *ibid.*, 1352 (1967).

[6] For simplicity of representation, the various alkoxide ions present throughout the reaction scheme are shown as neutral hydroxyl groups.

[7] L. H. Schwartz and R. V. Flor, *Chem. Commun.*, 1129 (1968).

[8] The alternate routes shown in eq 3 cannot be distinguished by this work. Efforts to distinguish between these pathways are in progress.

[9] N. V. Portnykh, A. A. Volod'kin, and V. V. Ershov, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 2181 (1966).

[10] L. C. King and C. K. Ostrum, *J. Org. Chem.*, **29**, 3459 (1964).

TABLE I

PHYSICAL PROPERTIES AND YIELDS OF 2-BROMO-4′-HYDROXY-3′,5′-DI-*t*-BUTYLACETOPHENONES (1)

			Found, %			Calcd, %			Nmr,[a] δ				
R, R′	% yield	Mp, °C	C	H	Br	C	H	Br	2′,6′-ArH	3′,5′-*t*-Bu	4′-OH	R	R′
H, CH_3	57	133–134	59.85	7.37	23.54	59.83	7.38	23.41	8.00	1.50	5.86	5.33 (q)[b]	1.89 (d)[b]
H, C_2H_5	80	126–127	60.84	7.63	22.49	60.85	7.66	22.49	7.99	1.50	5.86	5.10 (t)[b]	2.22 (p)[b] (CH_2) 1.08 (t)[b] (CH_3)
H, C_6H_5	83	119–120	65.37	6.79	19.94	65.51	6.75	19.81	7.94	1.43	5.80	6.40	7.24–7.74 (m)
CH_3, CH_3	82	141–142	61.00	7.73	22.48	60.85	7.66	22.49	8.21	1.48	5.76	2.07	2.07

[a] Unless otherwise specified, all absorptions are singlets: d, doublet; t, triplet; q, quartet; p, quintet; m, multiplet. In each case, integration was consistent with the proposed assignment. [b] J = 7 cps.

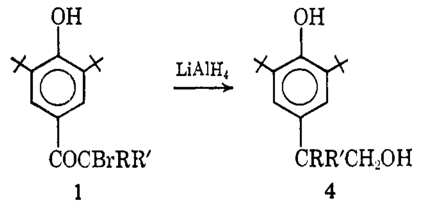
TABLE II

CHARACTERIZATION OF 2-SUBSTITUTED 2-(4-HYDROXY-3,5-DI-*t*-BUTYLPHENYL)ETHANOLS (4)

		Found, %		Calcd, %		Nmr,[a,b] δ							
R, R′	Mp, °C	C	H	C	H	ArH	*t*-Bu	ArOH	CH_2	ROH	ROH[c]	R	R′
H, CH_3	93.2–94.5	77.11	10.80	77.23	10.67	7.06	1.45	5.13	3.66 (d)[d]	1.62	4.54 (t)[e]	2.85 (s)[d]	1.28 (d)[d]
H, C_2H_5	86.0–86.5	77.73	10.92	77.65	10.86	7.01	1.45	5.11	3.71 (d)[d]	1.52	4.46 (t)[e]	2.59 (p)[d]	1.76 (m) (CH_2) 0.85 (t)[d] (CH_3)
H, C_6H_5	107–108	80.70	9.13	80.94	9.26	7.10	1.42	5.11	4.11	1.58	4.70 (t)[f]	4.11	7.31
CH_3, CH_3	149.8–150.3	77.85	10.82	77.65	10.86	7.24	1.47	5.14	3.57	1.47	4.54 (t)[e]	1.32	1.32

[a] Unless otherwise specified, all absorptions are singlets: d, doublet; t, triplet; p, quintet; s, sextet; m, multiplet. In each case, integration was consistent with the proposed assignment. [b] For comparison, 2-(4-hydroxy-3,5-di-*t*-butylphenyl)ethanol (R, R′ = H, H) has the following absorptions: 7.05 (ArH), 1.45 (*t*-Bu), 5.11 (ArOH), 1.77 (ROH), 3.82 (t)[d] (CH_2O), 2.78 (t)[d] ($ArCH_2$). [c] Spectrum taken in DMSO-d_6. [d] J = 7 cps. [e] J = 5.5 cps. [f] J = 5.0 cps.

aryl rearrangement pathway (eq 4) and is independent of the substitution at C_2.[11]



(4)

Experimental Section

Melting points are corrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Unless otherwise specified, nmr spectra were determined in $CDCl_3$ solution using a Varian Associates A-60 spectrometer. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane as zero.

2-Bromo-4′-hydroxy-3′,5′-di-*t*-butylacetophenones (1).—The acetophenone (0.29 mol), cupric bromide (0.67 mol) (the preparation of **1b** is best accomplished with 0.58 mol), 330 ml of ethyl acetate, and 220 ml of chloroform were heated at reflux, with stirring, for 1.25 hr (the preparation of **1g** required 1.75-hr heating time). The cooled reaction mixture was filtered and the solvent was removed by evaporation. The dark residue was dissolved in excess $CHCl_3$–hexane and repeatedly treated with charcoal until a light colored solution was obtained. Recrystallization from hexane or $CHCl_3$–hexane yielded the product 1 (Table I).

Reduction with $LiAlH_4$.—To 0.020 mol of the phenacyl bromide (1) in 200 ml of anhydrous ether, cooled to 0°, was rapidly added 0.045 mol of powdered $LiAlH_4$ with vigorous stirring. The reaction mixture was heated at reflux for 3 hr with vigorous stirring. Addition of 30 ml of H_2O and 100 ml of 10% H_2SO_4, followed by drying and evaporation of the ether layer, yielded the crude product in essentially quantitative yield. In each case, nmr spectroscopy indicated the crude product to be essentially pure. Crystallization was effected from hexane to yield the pure product 4 (Table II).

Registry No.—Lithium aluminium hydride, 1302-30-3; **1b,** 17055-13-9; **1c,** 17055-14-0; **1f,** 17055-17-3; **1g,** 17055-18-4; **4b,** 19510-15-7; **4c,** 19598-29-9; **4f,** 19598-30-2; **4g,** 19598-31-3.

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The Reaction of Iodobenzene and Nickel Carbonyl in the Presence of Olefins

E. YOSHISATO, M. RYANG, AND S. TSUTSUMI

Department of Chemical Technology, Faculty of Engineering, Osaka University, Yamadakami, Suita, Osaka, Japan

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In the course of our study of the reactions of organo transition metal complexes with unsaturated compounds, we observed that organo transition metal complexes derived from the reaction of transition metal carbonyls with organolithiums or active halides are reactive toward acetylenes and/or olefins.[1-3]

Bauld[4] reported that nickel carbonyl reacted with iodobenzene at 50–60° to form benzoylnickel carbonylate, $C_6H_5CoNi(CO)_nI$, as an intermediate complex, and its thermal decomposition or alcoholysis gave benzil or esters of benzoic acid, respectively.

On the other hand, acetylene insertion between the acyl and metal carbonyl groups in acyl metal carbonyls

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[11] Preliminary results by R. V. Flor indicate that the substituents at C_3' and C_5' have a profound effect on the course of the reaction.

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(4) N. L. Bauld, *Tetrahedron Lett.*, 1841 (1963).