[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Reduction of Mixed Hindered Benzils

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The reduction of simple benzils with metal-acid combinations or phosphorus and iodine generally leads to the formation of a desoxybenzoin and it is believed that enediols and benzoins are formed as intermediates. The reduction of mixed benzils with metal-acid combinations or with hydrogen iodide has not been extensively investigated. In particular, only two examples of the reduction of mixed *hindered* benzils (with a metal-acid combination and with hydrogen iodide) have been reported. Mesityl phenyl diketone was observed to undergo reduction with zinc and acetic acid to give phenyl 2,4,6-trimethylbenzyl ketone in practically quantitative yields.[2] It was reported later that phenyl 2,4,6-triisopropylbenzyl ketone could be obtained in a 90% yield by the reduction of phenyl triisopropylphenyl diketone with hydrogen iodide.[3] In both instances it was found to be the hindered carbonyl group that was ultimately reduced to a methylene group.

This seemingly anomalous manner of reaction has been observed in the present study with five other mixed, hindered benzils (listed in Table III). The reductions were carried out in glacial acetic acid with 47% hydrogen iodide solution. The product of each reaction was the desoxybenzoin in which the methylene group is adjacent to the hindered radical.

Although the mechanism of such reductions is not known, it seems clear from the foregoing results that steric hindrance is not an important factor. The expected differences in electrical effects, however, correspond with the facts. The carbon atom attached to a polymethylphenyl radical would be richer in electrons than that attached to a phenyl group and as a consequence might be expected to lose oxygen more readily.

Experimental[4]

Synthesis of Desoxybenzoins

The desoxybenzoins prepared in this work are listed in Table I together with other data including an indication of the method of synthesis. The first synthetic method (A) was employed only in the preparation of benzyl 4-methoxy-2,6-dimethylphenyl ketone and consisted in the condensation of phenylacetyl chloride with 4-methoxy-2,6-dimethylphenylmagnesium bromide. The second (B) involved Friedel-Crafts condensations of phenylacetyl chloride with appropriate aromatic compounds and is exemplified by the preparation of benzyl 2,4,6-triethylphenyl ketone. The third method (C), illustrated by the synthesis of phenyl 2,3,5,6-tetramethylbenzyl ketone, involved the use of organocadmium compounds. The acids from which the acid chlorides were derived were known substances and were prepared by hydrolysis of the corresponding nitriles or reduction of the appropriate glycolic acids.

Benzyl 4-Methoxy-2,6-methylphenyl Ketone.—Twenty-five grams of 4-methoxy-2,6-dimethylbromobenzene was added dropwise to 1.32 g. of magnesium turnings in 50 ml. of ethyl ether. A small amount of ethyl bromide was added to start the reaction. To this Grignard reagent was added dropwise 10 g. of freshly distilled phenylacetyl chloride, and the mixture was heated under reflux, with stirring, for three hours. It was decomposed with ice and hydrochloric acid and the ether layer was separated. After being washed successively with dilute hydrochloric acid, 10% sodium hydroxide and water it was dried over calcium chloride. The ether was evaporated and the residue distilled *in vacuo*. The benzyl 4-methoxy-2,6-dimethylphenyl ketone was a pale yellow oil boiling at 178–180° (2 mm.).

Benzyl 2,4,6-Triethylphenyl Ketone.—To a mixture of 16.2 g. of 2,4,6-triethylbenzene, 16.0 g. of anhydrous aluminum chloride and 50 ml. of dry carbon disulfide was added dropwise, and with stirring at room temperature, 15.5 g. of freshly distilled phenylacetyl chloride. The mixture was stirred overnight and decomposed with ice and hydrochloric acid. The carbon disulfide layer was removed and washed with dilute hydrochloric acid, 10% sodium hydroxide and water. The solution was dried over calcium chloride and the solvent evaporated. The benzyl 2,4,6-triethylphenyl ketone was distilled *in vacuo;* b. p. 168–170° (2 mm.); $n^{20}\text{D}$ 1.5508.

Phenyl 2,3,5,6-Tetramethylbenzyl Ketone.—To a Grignard reagent prepared from 1.7 g. of magnesium turnings, 100 ml. of absolute ether and 22 g. of bromobenzene was added 13.2 g. of anhydrous cadmium chloride. The mixture was stirred rapidly with gentle refluxing for three hours. A solution of 11 g. of freshly distilled durylacetyl chloride in 20 ml. of dry ether was then added dropwise over a period of one and one-half hours. The mixture was stirred and refluxed an additional three hours and decomposed with a hydrochloric acid-ice mixture. The ether layer was washed successively with dilute hydrochloric acid, 10% sodium hydroxide and water, and dried over calcium chloride. The phenyl 2,3,5,6-tetramethylbenzyl ketone, left when the ether was evaporated, weighed 12 g. It crystallized from benzene in white needles.

Preparation of the Benzils

The benzils listed in Table II were prepared from the desoxybenzoins listed in Table I by oxidation with selenium dioxide in dioxane. The description of the preparation of phenyl 2,4,6-triethylphenyl diketone will serve to illustrate the procedure.

Phenyl 2,4,6-Triethylphenyl Diketone.—Fourteen grams of benzyl 2,4,6-triethylphenyl ketone, 5.5 g. of selenium dioxide (unsublimed) and 150 ml. of wet dioxane were placed in a 200-ml. three-necked, round-bottomed flask equipped with a stirrer and condenser. The mixture was heated under reflux with stirring for six hours. The dioxane was decanted from the precipitated selenium and removed by distillation. The diketone was distilled *in vacuo* from a modified Claisen flask; b. p. 179–182° (3 mm.).

The Reduction of the Benzils

All of the benzils were reduced in refluxing glacial acetic acid with commercial hydrogen iodide solution (47%, sp. gr. 1.5), a large excess of the hydrogen iodide being employed. The reduction products are listed in Table III. The description of the reduction of isoduryl phenyl diketone illustrates the procedure.

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(2) Weinstock and Fuson, THIS JOURNAL, **58**, 1233 (1936).

(3) Fuson, Armstrong, Chadwick, Kneisley, Rowland, Shenk and Soper, *ibid.*, **67**, 386 (1945).

(4) Melting points are corrected unless otherwise indicated.

TABLE I

Procedure	Ketone	Reaction solvent	Recrystallization solvent	Melting point, °C.	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
A	Benzyl 4-methoxy-2,6-dimethylphenyl				29	80.26	79.87	7.14	7.16
B	Benzyl 2,4,6-triethylphenyl[a]				89	85.63	85.25	8.62	8.73
B	Benzyl bromomesityl[b]	Carbon disulfide	Ethanol	64.65	66	64.36	64.54	5.40	5.19
B	Benzyl duryl[c]			108.5–109.5	51	...	...	..	..
B	Benzyl isoduryl[d]			60–61	59	...	...	..	..
C	Phenyl 2,4,6-triethylbenzyl	Benzene	Methanol	71.5–72.5	33	85.67	85.91	8.59	8.80
C	3-Bromo-2,4,6-trimethylbenzyl phenyl	Ether	Benzene	180–181	87	64.36	64.50	5.40	5.54
C	Phenyl 2,3,5,6-tetramethylbenzyl	Ether	Benzene	214–215	93	86.01	85.90	7.62	8.11
C	Phenyl 2,4,5,6-tetramethylbenzyl	Benzene	Ethanol	183–184	47	86.01	85.88	7.62	7.97

[a] B. p. 168–170 (2 mm.); n^{20}_D 1.5508. The *p*-chlorobenzal derivative melted at 113–114° (uncor.). *Anal.* Calcd. for $C_{27}H_{27}ClO$: C, 80.47; H, 6.76. Found: C, 80.50; H, 7.01. [b] The *p*-chlorobenzal derivative melted at 109–110° (uncor.). *Anal.* Calcd. for $C_{24}H_{30}BrClO$: C, 65.54; H, 4.58. Found: C, 65.24; H, 4.49. [c] Foster and Fuson, THIS JOURNAL, **65**, 913 (1943). [d] Riebsomer, *ibid.*, **60**, 2974 (1938).

TABLE II

Desoxybenzoin oxidized	Diketone	Melting point, °C.	Recrystallization solvent	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Benzyl 4-methoxy-2,6-dimethylphenyl ketone	4-Methoxy-2,6-dimethylphenyl phenyl	82–83	Petroleum ether	..	76.10	76.41	6.01	6.26
Benzyl 2,4,6-triethylphenyl ketone	Phenyl 2,4,6-triethylphenyl	47–48	Methanol	75	81.59	80.84	7.53	7.29
Benzyl bromomesityl ketone	Bromomesityl phenyl	56–57	Ethanol	75	63.08	62.99	4.56	4.55
Benzyl duryl ketone	Duryl phenyl[a]	76–77	Ethanol	51	...	...	..	..
Benzyl isoduryl ketone	Isoduryl phenyl[a]	59–61	Methanol	59	...	...	..	..

[a] Fuson, Byers, Sperati, Foster and Warfield, *J. Org. Chem.*, **10**, 69 (1945).

TABLE III

Diketone	Ketone	Melting point, °C.	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
4-Methoxy-2,6-dimethyl phenyl	4-Hydroxy-2,6-dimethylbenzyl phenyl	178–180	..	79.97	80.23	6.71	6.75
Phenyl 2,4,6-triethylphenyl	Phenyl 2,4,6-triethylbenzyl	71.5–72.5	92	85.67	85.91	8.59	8.80
3-Bromomesityl phenyl	Bromo-2,4,6-trimethylbenzyl phenyl	181–182	71				
Duryl phenyl	Phenyl 2,3,5,6-tetramethylbenzyl	215–216	83				
Isoduryl phenyl	Phenyl 2,4,5,6-tetramethylbenzyl	183–184	92				

Reduction of Isoduryl Phenyl Diketone.—A solution of 3.0 g. of isoduryl phenyl diketone, 100 ml. of glacial acetic acid and 40 ml. of hydrogen iodide solution was heated under reflux, with stirring, for two hours. The reduction mixture was diluted with water and the white, crystalline solid collected on a filter and washed with a dilute solution of sodium bisulfite and with water. The 2,4,5,6-tetramethylbenzyl phenyl ketone weighed 2.6 g. It was recrystallized from ethyl alcohol.

Summary

Five mixed, hindered benzils have been reduced to the corresponding desoxybenzoins by the action of hydriodic acid. In every instance it was found that the carbonyl group involved was that joined to the hindering radical.

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