[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF HOWARD UNIVERSITY]

# THE ACETYLATION OF SOME DESOXYBENZOINS

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In 1899 Thiele (1) found that an acetic anhydride solution of benzil in the presence of zinc dust and a little sulfuric acid gave rise to two stereoisomeric forms of diphenylacetylene glycol diacetate, each of which upon hydrolysis with alcoholic potash yielded benzoin. He concluded therefore that the reduction of benzil occurred by way of diphenylacetylene glycol according to the following scheme:

$$\begin{array}{ccc} C_{6}H_{5}CO & \longrightarrow & \begin{bmatrix} C_{6}H_{5}COH \\ & & \\ C_{6}H_{5}CO & & \begin{bmatrix} C_{6}H_{5}COH \\ & & \\ C_{6}H_{5}COH \end{bmatrix} & \longrightarrow & C_{6}H_{5}CO \\ & & C_{6}H_{5}CHOH \end{array}$$

Nef (2) also in 1899 found that the product of the action of metallic sodium on an anhydrous ethereal solution of benzil when treated with acetic anhydride yielded a product which was identical with one of the stereoisomeric diphenylacetylene glycol diacetates which Thiele (1) had obtained.

In 1909 Wren (3) reported that when l-benzoin was boiled for one-half hour with alcoholic potash the recovered benzoin was optically inactive. He interpreted the racemization as having taken place thus:

$$\begin{array}{ccc} C_{6}H_{5}CHOH \longrightarrow & C_{6}H_{5}COH \rightleftharpoons & C_{6}H_{5}CO \\ \downarrow & & \downarrow \\ C_{6}H_{5}CO & & C_{6}H_{5}COH & C_{6}H_{5}CHOH \\ active & inactive & inactive \end{array}$$

Later McKenzie, Roger, and Wills (4) discovered that the racemization of *l*-benzoin could be effected much less drastically. Thus almost complete racemization was brought about by the use of a mere trace of potash in alcoholic solution in the cold in the course of twenty-four hours.

It was Jenkins (5) who in 1931 was first to effect the conversion of a mixed benzoin into its isomer. By treatment of an alcoholic solution of *alpha-p*-dimethylamino-p'-chlorobenzoin with potassium cyanide, he obtained the isomeric *beta-p*-dimethylamino-p'-chlorobenzoin:



Margaret Luis (6) followed Jenkins' work with the conversion of r-4'-dimethylaminobenzoin and anisbenzoin into r-4-dimethylaminobenzoin and benzanisoin, respectively, by means of alcoholic potash at room temperature, and showed

<sup>1</sup> Part of this work was done by Mr. Harold Delaney in partial fulfillment of the requirements for the Master's degree.

that the reverse change did not occur under those conditions. During the same year Julian and Passler (7) reported a partial transformation of anisbenzoin into benzanisoin by distillation.

In their investigation of isomeric benzoins, Weinstock and Fuson (8) found that an equilibrium mixture resulted when either 2,4,6-trimethylbenzoin (I) or 2',4',6'-trimethylbenzoin (II) was heated with sodium acetate in alcoholic solution. They also found that 2,4,6-trimethylbenzoin on boiling for five hours with acetic anhydride yielded a monoacetate, whereas the 2',4',6'-trimethylbenzoin upon treatment under the same conditions gave the diacetate.



In all of these isomerizations it is assumed that under the influence of alkali or heat the rearrangement takes place through the unstable ene-diol, -C—OH. -C—OH

More recently still, Barnes and Tulane (9) have presented a mechanism for the interconversion of mixed benzoins; and Barnes and Lucas (10, 11) have also pointed out the stabilizing effect of the methoxyl group on ene-diols.

It is the purpose of this paper to report a series of acetates of enolic modifications of monoketones and to relate the behavior of the methoxyl substituted monoketones to the mechanism for the interconversion of mixed benzoins (9). Thus, we have prepared and acetylated (12) the following desoxybenzoins:





The ease with which alkyl desoxybenzoins are formed (13, 14), is indicative of the formation of metallic enolates. And so it does not seem strange that, under the proper conditions, O-acetyl derivatives of these enolates may result.

The ease with which acetylation is effected is reflected in the variations in the time of refluxing in the various cases. The fact that p-hydroxydesoxybenzoin (V) is practically completely converted into the acetate in one hour, whereas the p-methoxydesoxybenzoin (X) is not completely converted in four hours, seems very highly significant in the light of the mechanism presented on the rearrangement of mixed benzoins (9). The effect of the p-methoxyl group is to make the methylenic carbon relatively negative as compared with the carbonyl carbon:



Thus there is little tendency for the methylenic hydrogen to give rise to the enolic modification. It seems therefore that the p-hydroxyl group is no more effective in this regard than is a similarly placed hydrogen, for the ketone (V) is as easily acetylated as is desoxybenzoin (III).

On the other hand, one would predict that p'-hydroxydesoxybenzoin (VI) would be as easily acetylated as desoxybenzoin (III) or p-hydroxydesoxybenzoin (V). In like manner, one would predict that the p'-methoxydesoxybenzoin (XI), because of the effect of the methoxyl in rendering the methylenic carbon relatively positive as compared with the carbonyl carbon, would tend to expel a methylenic hydrogen, thereby giving rise to the enolic modification with subsequent quantitative acetylation:



These predictions are fulfilled in that both compounds (VI) and (XI) are quantitatively acetylated in thirty minutes.

When one applies these considerations to the behavior of desoxyanisoin (VII); its behavior becomes perfectly clear. It is acetylated quantitatively in one hour, for the opposing effects of 4,4'-methoxyls render this compound of the order of activity of desoxybenzoin, whereas in the case of anisoin (10), in which a perfectly symmetrical ene-diol results as an intermediate, there is no acetylation, as predicted. Neither steric hindrance nor the inhibiting effect on enolization by substitution of methylenic hydrogen, which is so pronounced in *alpha* and *beta* diketones and esters, seems to play a very important part in connection with the acetylation of these compounds, for phenyldesoxybenzoin (VIII) is practically quantitatively acetylated in one hour; desoxymesitoin (IX) in four hours; and benzyldesoxybenzoin (IV) in six hours. On the other hand, methyl desoxymesitoin (XIV) is the only compound investigated which was recovered unchanged even after a period of thirty-seven hours of refluxing. This behavior



of methyldesoxymesitoin is in keeping with the findings of Fuson and coworkers (15).

The p'-nitrodesoxybenzoin (XII) and the p'-aminodesoxybenzoin (XIII) are quantitatively acetylated in thirty minutes, which indicates an activating effect of both the nitro group and the amino nitrogen.

All of these desoxybenzoin acetates hydrolyze smoothly in acid medium to the parent desoxybenzoin.

This explanation applies not only to the rearrangement of Margaret Luis' r-4'-dimethylaminobenzoin since the dimethylamino group also possesses a strong tendency toward electron-release, but particularly well to the rearrangement of Jenkins' *alpha-p*-dimethylamino-p'-chlorobenzoin, for in this case also the -T-effect of the dimethylamino group and the +I-effect of the halogen atom act in the same direction and hence reinforce each other.

In relation to the findings of Weinstock and Fuson (8), it seems significant that the 2', 4', 6'-trimethylbenzoin (II) gives rise to a diacetate, whereas its isomer yields the monoacetate solely. For, since interconversion or diacetylation must occur by way of the ene-diolic modification, the equilibrium point must be far toward (I). This ene-diolic system is identical with that pictured for the ene-diolic modification of anisbenzoin (9), the driving force here being an inductive effect (16, 17, 18, 19, 20) of the methyl groups. This is in keeping with the report that the mesityl nucleus acts against enolization towards itself, but promotes enolization away from itself (21).

## EXPERIMENTAL

p'-Methoxydesoxybenzoin (XI). Two grams of p'-hydroxydesoxybenzoin was suspended in 30 cc. of water, to which 2 g. of dimethyl sulfate was added. To this suspension, 1.6 g. of sodium hydroxide dissolved in 10 cc. of water was added drop-wise with vigorous shaking. The solution turned yellow. The reaction mixture became warm, and a pale yellow solid separated on the walls of the reaction flask. The reaction mixture was warmed and shaken for thirty minutes, chilled, filtered, washed with water, and recrystallized from methanol yielding 1.5 g. of pale yellow leaves, melting at 98°.

Anal. Calc'd for C15H14O2: OCH3, 13.7. Found: OCH3, 13.7.

Acetylation. Each of the desoxybenzoins was refluxed with twice its weight of freshly fused potassium acetate and sufficient boiling acetic anhydride to effect solution of the

ACETATE	FORM	м.р. °С	FORMULA	ANALYSIS	
				Calc'd	Found
$C_{\delta}H_{\delta}CH = CC_{\delta}H_{\delta}^{\delta}$	Pale yellow needles	101	C <sub>16</sub> H <sub>14</sub> O <sub>2</sub>	C, 80.67 H, 5.88	80.66 6.2
$\begin{array}{c} C_{6}H_{5}C \xrightarrow{} CC_{6}H_{5}^{c} \\   &   \\ CH_{2}C_{6}H_{5} & OCOCH_{3} \end{array}$	Colorless needles	70	$C_{23}H_{20}O_2$	C, 84.14 H, 6.1	84.30 5.9
$C_{\mathfrak{s}} C_{\mathfrak{s}} CH = CC_{\mathfrak{s}} H_{\mathfrak{s}} OCOCH_{\mathfrak{s}}(p)^{\mathfrak{s}}$	Colorless needles	109	C <sub>18</sub> H <sub>16</sub> O <sub>4</sub>	C, 72.97 H, 5.4	$72.83 \\ 5.6$
(p) CH <sub>3</sub> COOC <sub>6</sub> H <sub>4</sub> CH=CC <sub>6</sub> H <sub>5</sub> <sup>e</sup> $\downarrow$ OCOCH <sub>3</sub>	Cream col- ored nee- dles	119	C <sub>18</sub> H <sub>16</sub> O <sub>4</sub>	C, 72.97 H, 5.4	73.54 5.8
$(C_{\delta}H_{\delta})_{2}C = CC_{\delta}H_{\delta}^{\delta}$	Colorless needles	104	$C_{22}H_{18}O_2$	C, 84.07 H, 5.7	84.08 5.9
Mes-CH=C-Mes <sup>d</sup>   OCOCH <sub>3</sub>	Colorless needles	106	$C_{22}H_{26}O_2$	C, 81.98 H, 8.1	81.83 8.3
$C_{\delta}H_{\delta}CH = C_{\delta}H_{4}OCH_{\delta}(p)^{d}$ $ $ $OCOCH_{\delta}$	Colorless needles	88	C17H16O3	C, 76.12 H, 6.0	76.3 $6.2$
(p)CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH=CC <sub>6</sub> H <sub>5</sub> °   OCOCH <sub>3</sub>	Yellow needles	86	C <sub>17</sub> H <sub>16</sub> O <sub>3</sub>	OCH3, 11.6	11.8
(p)CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH=CC <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub> $(p)$ <sup>b</sup>   OCOCH <sub>3</sub>	Colorless needles	90	$C_{18}H_{18}O_{4}$	OCH3, 20.8	21.0
$(p) O_2 N C_6 H_4 CH \longrightarrow CC_6 H_5 \circ$ $  OCOCH_3$	Yellow needles	107	C <sub>16</sub> H <sub>13</sub> NO <sub>4</sub>	C, 67.84 H, 4.6	67.87 5.0
$(p) HNC_{6}H_{4}CH = CC_{6}H_{5} \circ     COCH_{5} OCOCH_{6}$	Cream colored needles	137	C18H17NO3	C, 73.22 H, 5.8	73.66 6.1

TABLE I Desoxybenzoin Acetates<sup>4</sup>

<sup>a</sup> All of these acetates hydrolyze smoothly in alcoholic hydrochloric acid to the parent desoxybenzoins; the p'-amino acetate goes to the p'-aminodesoxybenzoin hydrochloride. <sup>b</sup> Refluxed for one hour.

<sup>o</sup> Refluxed for six hours.

Renuxed for six hours.

<sup>d</sup> Refluxed for four hours.

• Refluxed for one-half hour. The desoxymesitoin was graciously supplied by Professor Reynold C. Fuson.

potassium acetate. The ease with which the different reactions took place is indicated by the length of time of refluxing required. At the end of the heating period the solution was cooled and poured into a large volume of water to decompose the acetic anhydride. Invariably an oil was thrown down, which upon extraction with ether, and washing with sodium bicarbonate, was dried and evaporated. The residual oil was crystallized from methanol.

Methyldesoxymesitoin was recovered unchanged after a period of thirty-seven hours of refluxing.

### SUMMARY

1. The preparation and characterization of p'-methoxydesoxybenzoin is given.

2. Eleven acetates of enolic modifications of desoxybenzoins are reported.

3. A mechanism presented for the benzoin rearrangement is applied to the acetylation of desoxybenzoins.

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