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Abstract

Full Text

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On the Problem of Intramolecular Donor-Acceptor Interaction

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At one time, one of us (1) obtained 2-benzyl-α-phenacylindandione-1,3 (I a),

(I) (II)

where X: a) H; b) Br; c) Cl; d) I; e) OCH_3; f) OC_2H_5; g) OC_3H_7-n

where X: a) H; b) Br; c) I

which proved to be an active blood anticoagulant. It is characteristic that 2-benzylindandione-1,3 (II a) does not possess such activity (2).

It had previously been suggested that the anticoagulant activity of derivatives of indandione-1,3 depends on their tendency to give up the hydrogen atom of the indane ring, which is evidently connected with the stability of the indandionyl radical (3,4).

If this is so, then the physiological activity of I a and the inactivity of II a should be sought in the more pronounced tendency of the former compound to enter into reactions of homolytic abstraction of a hydrogen atom, which, in turn, should be explained by intramolecular activation of the hydrogen atom of the indane ring by the benzoyl group according to the mechanism of donor-acceptor interaction (an intramolecular complex with charge transfer). We studied the unquestionably heterolytic (5) alcoholysis reaction of the halogen derivatives I (b, d) and II (b, c) and found a sharp difference in the reactivity of the halides.

Whereas the halogen derivatives I (b, d) readily undergo alcoholysis, the corresponding II (b, c) remain inert to the action of alcohols. This once again suggests that the carbonyl group, separated from the indandionyl hydrogen atom by two methylene units, exerts a strong influence on the hydrogen atom of the indane ring through space, analogous to the ortho effect in the aromatic series. In the present case we have an example of intramolecular catalysis by the mechanism of donor-acceptor interaction. A similar alcoholysis reaction in a series of indandione derivatives has been observed for the first time.

In addition, in the present work conditions are reported for the first time for the preparation of 2-iodo-substituted indandione-1,3, using I a as an example, by the direct action of a halide (^{6}). II a is incapable of direct iodination, and the corresponding 2-iodo derivative (II c) was therefore obtained by an exchange reaction of the bromide (II b) with potassium iodide in an alcoholic medium. This, again, can be explained only by the activating influence of the benzoyl group.

Since 2-monosubstituted alkyl-, aryl-, or alkarylindandiones readily dissolve in alkalis with an intense red or orange coloration, while 2,2-substituted compounds, in particular 2-alkyl-2-alkoxy derivatives, lose this ability because of the absence of a mobile hydrogen atom, the structure of the products obtained follows unambiguously from their complete insolubility in aq-

ous or aqueous-alcoholic alkalis, in contrast to I a, which dissolves readily with a red coloration.

It must be assumed that the phenomenon of intramolecular donor–acceptor interaction is of great importance in the reactivity of many substances and often determines the bioreactivity of organic compounds.

Experimental Part

2-Bromo-2-benzyl-α-phenacylindandione-1,3 (I b). 4 g of (I a) were dissolved, with heating on a water bath, in 25 ml of carbon tetrachloride; then 1.8 g of bromine in 20 ml of the same solvent was gradually added to the warm solution. After boiling on a water bath with a reflux condenser, the solution was left overnight. On rubbing with a glass rod, a crystalline precipitate separated. Weight 2.9 g, m.p. 148°. After recrystallization from alcohol—a white crystalline powder with m.p. 151-152°.

Found %:	C 66.86; H 4.34; Br 18.44
$C_{24}H_{17}O_3Br$. Calculated %:	C 66.52; H 3.92; Br 18.46

1 g of the bromine derivative obtained (I b) was dissolved in 20 ml of acetic acid, after which 0.39 g of potassium iodide was added. The solution was heated for 15 min on a water bath; the liberated iodine was titrated with 0.1 N hyposulfite solution. Quantitative liberation of free iodine was established (7). On dilution with water, a precipitate of I a with m.p. 128° separated (after recrystallization from alcohol), which gave no depression of the melting point with authentic I a.

On heating on a water bath with a solution of sodium methylate in methanol, I b again replaces the halogen by hydrogen, forming I a.

2-Chloro-2-benzyl-α-phenacylindandione-1,3 (I c). Chlorine was passed into a heated solution of 1 g of I a in 20 ml of carbon tetrachloride. After cooling, a product with m.p. 140–144° separated in good yield. It crystallizes from acetic acid in the form of elongated prisms with m.p. 146–147°.

Found %: C 74.15; H 4.73; Cl 9.12
$C_{24}H_{17}O_3Cl$. Calculated %: C 74.13; H 4.38; Cl 9.13

2-Iodo-2-benzyl-α-phenacylindandione-1,3 (I d). a) 0.5 g of I b was dissolved in 15 ml of methyl alcohol; 0.2 g of potassium iodide was added, and the mixture was heated on a water bath for 15 min. The solution turns red; a light-yellow precipitate separates with m.p. 129–130°. Recrystallized from alcohol, m.p. 132° with decomposition.

Found %: C 59.63; H 3.93; I 26.23
$C_{24}H_{17}O_3I$. Calculated %: C 59.26; H 3.54; I 26.43

b) 1.06 g of I a and 0.76 g of iodine were dissolved in alcohol. After 15 min of heating on a water bath and subsequent cooling, the precipitate that separated was filtered off, washed with alcohol, and recrystallized from the same solvent. M.p. 132°; with the previously obtained compound it melts without depression. Yield 1 g, or 69% of theory.

2-Bromo-2-benzylindandione-1,3 (II b). 2.26 g of II a were dissolved in 10 ml of acetic acid. On heating on a water bath, 1.6 g of bromine in 10 ml of acetic acid was added. White precipitate. Weight 2.8 g, m.p. 152–153°. Yield 88% of theory.

Found %: C 60.86; H 3.92; Br 25.08
$C_{16}H_{11}O_2Br$. Calculated %: C 60.95; H 3.49; Br 25.35

2-Iodo-2-benzylindandione-1,3 (II c). 0.75 g of II b was dissolved in 25 ml of methyl alcohol with heating on a water bath, and then 0.42 g of potassium iodide was added. Yellow precipitate. Weight 1 g, m.p. 184–186° with decomposition. Recrystallization from alcohol does not change the melting point.

Found %: C 53.29; H 3.28; I 35.14
$C_{16}H_{11}O_2I$. Calculated %: C 53.01; H 3.04; I 35.04

Interaction of halogen derivatives of 2-benzyl-α-phenacylindandione-1,3 (I , I) with alcohols. a) 1 g of the bromo derivative I was boiled for 5 h in ethanol on a water bath. On cooling, a crystalline precipitate formed. Recrystallization from alcohol gave slightly yellowish crystals containing no halogen. M.p. 151–152°.

$C_{26}H_{22}O_4$. Found, %: C 78.49; H 5.77
Calculated, %: C 78.39; H 5.53

b) 1 g of the same substance I , upon heating for eight hours in methanol on a water bath, gave a substance with m.p. 132°.

$C_{25}H_{20}O_4$.	Found, %:	C 77.59;	H 5.63
	Calculated, %:	C 78.12;	H 5.21

c) Heating I under the same conditions in propyl alcohol gave a substance with m.p. 116–117° (from alcohol, benzene, or ethyl acetate). In all three cases the iodo derivative I can be used with equal success.

The bromo and iodo derivatives of 2-benzylindandione (I , II) remain unchanged under these conditions.

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