

ON PHTHALIDES AND INDANDIONES. I.*

DETERMINATION OF C-METHYL AND O-METHYL DERIVATIVES FORMED ON METHYLATION OF 2-(1-HALO-2-NAPHTHYL)-1,3-INDANDIONES AND 2-(2-HALOPHENYL)-1,3-INDANDIONES

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The results of the methylations of anions of 2-(1-X-2-naphthyl)-1,3-indandiones and 2-(2-X-phenyl)-1,3-indandiones (X = Cl, Br) in dimethyl sulfoxide, dimethylformamide, acetonitrile, acetone, and methyl isobutyl ketone are compared. It was found that the ratio C/O of methyl derivatives is affected in addition to the character of the solvent mainly by the substitution of chlorine by bromine, which led to an increase in the yields of O-derivatives. The C/O ratio of methyl derivatives was determined by IR spectroscopy and gravimetry.

When the anion of 2-phenyl-1,3-indandione and 2-(2-naphthyl)-1,3-indandione reacts with primary haloalkanes in various solvents, C-alkyl derivatives are formed exclusively. However, when a substituent is present in these indandiones in the *ortho*-position, in addition to C-derivatives, O-derivatives are also formed. Thus, for example, it was observed that on methylation of the 2-(2-X-phenyl)-1,3-indandione anion (X = Cl, Br, J) in methanol O-methyl derivative is formed in addition to the C-methyl derivative; the amount of the O-methyl derivative increases with the size of the halogen¹. When the anion of 2-(1-X-2-naphthyl)-1,3-indandiones² (X = Cl, Br, NO₂) is alkylated a different C/O ratio of alkyl derivatives was observed, depending not solely on the character of X, but also on whether alkylation was carried out in dimethylformamide or in ethanol.

In this paper we carried out the methylations with 2-(1-chloro-2-naphthyl)- (*I*), 2-(1-bromo-2-naphthyl)- (*II*), 2-(2-chlorophenyl)- (*III*), 2-(2-bromophenyl)-1,3-indandiones (*IV*). In addition to the study of the effect of the solvent on the C/O ratio we also compared the results when a phenyl group was substituted by a 2-naphthyl group in the position 2 of the indandione ring, and when chlorine in the *ortho* position was substituted by bromine. The methylations were carried out in the following aprotic solvents: dimethyl sulfoxide, dimethylformamide, acetonitrile, acetone, isobutyl methyl ketone. Methylations in protic solvents were not investigated because we found in our preceding papers¹⁻³ that in these solvents only low yields were

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achieved. As our earlier results indicated that the polarity of the solvent affects the C/O ratio in 2-aryl-1,3-indandiones in a manner different than in the case of alkylations of acetylacetone and ethyl acetoacetate, we effected the C/O ratio determination both gravimetrically, after previous separation of isomers, and by IR spectroscopy in order to avoid possible inaccuracies in the case of substances I—III.

EXPERIMENTAL

The starting 2-(2-X-phenyl)-1,3-indandiones were prepared according to ref.⁶ and 2-(1-X-2-naphthyl)-1,3-indandiones according to⁷. Before use the substances were recrystallised twice from 96% ethanol. Their m.p. were identical with^{4,5}. Potassium carbonate was sieved and dried at 150°C. The particle size used was 0.315—0.500 mm.

Methylation of 2-(1-X-2-Naphthyl)-1,3-indandiones and 2-(2-X-Phenyl)-1,3-indandiones (X = Cl, Br)

A mixture of 0.0025 mol of the corresponding indandione, 0.64 g (0.005 mol) of potassium carbonate, and 40 ml of the solvent was stirred at 35°C for 10 minutes and then added with 1.42 g (0.01 mol) of methyl iodide and stirred for another 3 hours. The filtrate was evaporated and 100 ml of chloroform were added to the residue and refluxed for 10—15 minutes. The solution was filtered and concentrated to 30 ml. For spectrophotometric determination the solution was chromatographed on a 2 × 10 cm column of alumina (act. II according to Brockmann, neutral; Reanal, Budapest) with chloroform. The eluate was collected from the moment when the yellow zone was 4 cm from the bottom of the column. The unreacted starting indandione does not move on the column. The eluate was filtered and the solvent distilled off. The residue was dried at 60—80°C *in vacuo*. When C-methyl and O-methyl derivatives were separated a 20 cm high column was used. The colourless C-methyl derivative was eluted first, followed by the yellow O-methyl derivative. The eluates were evaporated, dried at 60—80°C in a vacuum and weighed.

Determination of the C-Methyl and the O-Methyl Derivatives by Infrared Spectroscopy

We made use of the method based on a system of equations overdetermined by the number of frequencies and calibration mixtures according to⁶⁻⁹. For a two-component mixture we chose for each component 3 analytical bands (Table I) and we carried out the calibration with six to eight mixtures. As in papers^{6,7} we also included into our calculation the measurement of pure components. Pure C-methyl and O-methyl derivatives were prepared according to^{1,2}. The spectra were measured in chloroform solution, using a Zeiss UR-20 double-beam prism spectrophotometer. Deviations from linearity were less than 0.5% *T* in the 20—100% *T* region. The matrices of absorbances *A* are formed by absorbancies $a_{gi} = \log T_{g0}/T_{gi}$, where T_{g0} is the transmittance of the solvent, and T_{gi} the transmittance of the solution of the *i*-th mixture at the analytical frequency ν_g . Further, if **C** is the matrix of concentrations c_{ji} of the *j*-th component in the *i*-th mixture, then

$$\mathbf{A} = \mathbf{K}\mathbf{C}, \quad (1)$$

where **K** is the matrix of absorption coefficients. From the calibration mixtures this matrix is calculated from the known **A** and **C** by solving the predetermined system (1), in the sense of least squares

$$\mathbf{K} = \mathbf{A}\mathbf{C}^T(\mathbf{C}\mathbf{C}^T)^{-1}. \quad (2)$$

The obtained matrix \mathbf{K} is used for the calculation of the concentrations of the components in unknown mixtures, again by solving the system (I):

$$\mathbf{C} = (\mathbf{K}^T \mathbf{K})^{-1} \mathbf{K}^T \mathbf{A}. \quad (3)$$

The method enables the calculation of the standard deviation of the i -th sample, s_{v_i} , and the calculation of the estimation of absorbance of the standard deviation of the concentration of the j -th component in the i -th sample, $s_{x_{vj}}$. The results of the calibration were worked up by a digital computer Gier (Regnezentralen, Denmark), using a program in Algol (modification Gier Algol 4) Matrices \mathbf{K} for all three analysed systems are in Table I. The results of the analyses of samples are in Table III. There the content of the components is given in weight percents, calculated from the concentrations.

TABLE I

Matrix \bar{K}_{kn} of Absorption Coefficients k_{gj} of O-Derivatives $j = 1$ and C-Derivatives $j = 2$
 k_{gj} is absorbance of the component j at wavelength g for $c = 0.1$ g/ml and $d = 0.14$ mm.

$\frac{v_g}{\text{cm}^{-1}}$	g	$j = 1$	$j = 2$	$\frac{v_g}{\text{cm}^{-1}}$	g	$j = 1$	$j = 2$
Compound I							
891	1	0.378	0.020	1 750	4	0.040	0.819
978	2	0.158	0.705	1 079	5	0.434	0.023
962	3	0.771	0.097	1 282	6	0.124	0.767
1 284	4	0.185	0.918	Compound III			
1 630	5	1.482	0.050	1 629	1	1.835	0.046
1 750	6	0.071	0.915	987	2	0.090	1.035
Compound II				963	3	1.035	0.076
1 627	1	1.402	0.031	1 750	4	0.122	1.091
991	2	0.057	1.009	897	5	0.652	0.010
978	3	0.856	0.054	1 067	6	0.105	0.838

RESULTS AND DISCUSSION

The determination of C/O ratio in single solvents was carried out both on the basis of the chromatographic separation of the isomers formed, and in the case of substances I–III, on the basis of the quantitative evaluation of the IR spectra. In the majority of cases the results of these determinations are in good accord. A striking difference is observed for substance II in acetonitrile, where a larger amount of the C-methyl derivative was obtained by chromatographic separation. Considering that the spectrophotometric determination is the result of two to four measurements, these results may be considered as more reliable.

TABLE II
The Results of Spectroscopic Analysis of the Reaction Products Formed During the Methylation of Compounds I-III

Solvent	I			II			III					
	n^a %	C-deriv. % (s'x)	O-deriv. % (s'x)	yield %	n^a %	C-deriv. % (s'x)	O-deriv. % (s'x)	yield %	n^a %	C-deriv. % (s'x)	O-deriv. % (s'x)	yield %
Dimethyl sulfoxide	3	68.4 (3.2)	31.5 (2.7)	68.4	0	—	—	—	2	71.4 (2.5)	28.6 (2.0)	72.8
Dimethylformamide	4	55.7 (1.4)	44.3 (1.2)	83.0	2	35.9 (1.5)	64.1 (1.3)	73.5	2	57.7 (0.7)	42.3 (0.5)	81.4
Acetonitrile	2	46.9 (4.0)	53.1 (3.5)	43.5	3	27.9 (2.1)	72.1 (1.9)	33.3	0	—	—	—
Acetone	2	56.3 (2.1)	43.8 (1.8)	57.7	2	39.8 (2.2)	60.2 (1.9)	40.2	2	57.7 (0.5)	42.3 (0.4)	62.8
Isobutyl methyl ketone	2	62.9 (5.3)	37.3 (4.5)	29.9	3	40.8 (2.5)	59.2 (2.2)	22.6	2	56.2 (1.7)	43.8 (1.3)	36.3

^aNumber of determinations; s'x — evaluation of the standard deviation of the concentration.

TABLE III
Yields (%) and the Percentages of the C-Methyl Derivatives Determined by Gravimetric Analysis of the Methylation Products

Solvent	I		II		III		IV	
	yield (% C-)	yield (% C-)	yield (% C-)	yield (% C-)	yield (% C-)	yield (% C-)	yield (% C-)	yield (% C-)
Dimethyl sulfoxide	60.1 (67.3)	46.2 (63.2)	49.1 (62.6)	46.5 (57.5)				
Dimethylformamide	85.6 (58.1)	71.0 (43.5)	65.4 (45.1)	59.6 (54.0)				
Acetonitrile	39.2 (43.6)	28.1 (42.4)	32.0 (28.6)	26.0 (33.2)				
Acetone	61.7 (52.8)	56.2 (38.8)	60.3 (28.8)	50.3 (41.7)				
Isobutyl methyl ketone	31.6 (54.4)	25.3 (36.4)	21.6 (42.3)	16.5 (43.5)				

As may be seen from the results of the methylations listed in Tables II and III the anions of substances *I–IV* afford both possible position isomers in all solvents used. As the anion of the unsubstituted 2-phenyl-1,3-indandione, 2-(2-naphthyl)-1,3-indandione, as well as the anions of 2-(*p*-halophenyl)-1,3-indandiones afford C-methyl derivatives^{1,2} exclusively, the formation of O-methyl derivatives *I–IV* may be ascribed to sterical factors. The presence of the halogen in the position 2 of the phenyl and in the position 1- of the 2-naphthyl group causes a sterical hindrance during the attacking of the ambient anion by the carbon nucleophilic center. In the case of chloro derivatives *I, III* a larger amount of C-methyl derivatives is formed in every solvent than in the case of bromo derivatives *II, IV*. The substitution of phenyl for 2-naphthyl has no substantial effect on the C/O ratio, nor on the total yields. This is in agreement with paper¹⁰ where it was ascertained that the activation energy of the methylation of the 2-(2-naphthyl)-1,3-indandione anion in dimethylformamide is only by 2.0 kcal/mol higher than the activation energy of the methylation of the 2-phenyl-1,3-indandione anion. The C/O ratio of methyl derivatives is not equal in all solvents. The greatest amount of the C-derivative is formed in all instances in dimethyl sulfoxide, *i.e.* in a solvent with a greatest dielectric constant. These results corroborated our previous findings^{1,2} that during the reactions of anions of 2-aryl-1,3-indandiones, in which C- and O-alkyl derivatives are formed in reactions with primary halohydrocarbons, the relationships concerning the effect of the solvent polarity on the C/O ratio obtained by Kurc and coworkers¹¹ in the case of ethyl acetoacetate and acetylacetonate alkylations, are not valid. The mentioned authors found that the largest amount of C-derivatives is formed during the ethylation of ethyl acetoacetate with ethyl bromide in weakly polar aprotic solvents. However, the results of alkylation of ethyl acetoacetate in dimethyl sulfoxide and in hexamethylphosphoric triamide have shown that O-alkyl derivatives are formed in a higher percentual yield in the second than in the first case¹² in spite of the fact that dimethyl sulfoxide has a higher dielectric constant. As is shown by the results of methylations carried out in dimethylformamide and in acetonitrile, *i.e.* in solvents with approximately equal dielectric constant but different structure, the C/O ratio in these solvents is not equal. In dimethylformamide, *i.e.* in a more basic solvent, a larger percentage of C-methyl derivative is formed than in acetonitrile. When comparing the results achieved in acetone and isobutyl methyl ketone, *i.e.* in solvents with approximately equal dielectric constant and structure, it may be seen that the C/O ratio for these solvents is approximately equal. Steffer and Dierichs¹³ methylated the anion of cyclohexandione with methyl iodide in alcohols of different dielectric constant and obtained equal C/O ratios in these alcohols. The difference in total yields is also striking. In acetonitrile and in methyl isobutyl ketone the yields were lowest. These low yields undoubtedly depend on low solvation properties of these solvents. Lower yields in dimethyl sulfoxide than in dimethylformamide may be explained by a competitive reaction of dimethyl sulfoxide with methyl iodide¹⁴.

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