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Study of the Separation of Dianin's Compound Formed in the Bisphenol-A Synthesis

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Abstract. A method of separating Dianin's compound from a complex mixture of by-products obtained from the bisphenol-A industrial process is described using compounds which form crystalline clathrate structures with Dianin's compound. Under the conditions used the clathrate structure obtained could be crystallized with high purity (above 99.5%). The described statistical model of mixture design shows that the highest yield of crystallization was found by using a single solvent (ethyl alcohol) for separation of Dianin's compound.

Key words: Dianin's compound, clathrate, mixture design separation

1. Introduction

The synthesis processes and/or applications of 2H-1-benzopyran derivatives attract more and more interest recently. These derivatives show biological activity and hence the number of their uses quickly increases [1, 2]. They can be employed e.g. in pharmacology where they are utilized to treat diseases resulting from the activity of smooth muscles [3].

Dianin's compound [4-(3,4-dihydro-2,2,4-trimethyl-2H-1-benzopyrane-4-yl)-phenol or usually referred to as 4-*p*-hydroxyphenyl-2,2,4-trimethylchroman] is one of the compounds which contain the 2H-1-benzopyran structure. There are numerous publications and patents reporting on the capability of Dianin's compound of yielding clathrate structures with a number of organic compounds. The structure of the host consists of six molecules of Dianin's compound arranged around a ring and bound one to another by hydrogen bonding of the hydroxyl groups. Such an arrangement makes it possible for two molecules of Dianin's compound to yield the final structure that resembles a cage. Numerous organic compounds can be trapped in such a 'cage'. [4]

Goldup and Smith [5] provided detailed information on the structure of Dianin's compound (X-ray data) and supplied a number of examples of mixtures which can be easily separated by 'clathrating' one of the components. The sorption of some organic compounds (acids, bases and alcohols) by Dianin's compound was

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studied by Harrington [6] who also described its clathrates with other compounds. He suggested making use of Dianin's compound and/or its clathrates to separate selectively some chemical compounds from mixtures. He also tried to separate selectively secondary alcohols from mixed aliphatic alcohols [7]. Some further investigations by Harrington suggested that the clathrates of Dianin's compounds act under some conditions like zeolites and the clathrate structures can be formed with the compounds having some specific size and shape only [8].

In this publication we use the reverse concept whereby formation of crystalline clathrate structures with Dianin's compound can be used to separate it from a very complex mixture of by-products obtained from the industrial synthesis of bisphenol-A by reaction of phenol with acetone.

2. Experimental

2.1. RAW MATERIALS AND REAGENTS

The following raw materials and reagents were used in the study:

1. The byproducts from the industrial synthesis of bisphenol-A from the ion-exchanger-catalyzed process. Solid, yellow-to-brown, with a melting point of ~60°C. This is an industrial product obtained at the 'Blachownia' Chemical Works (in Kędzierzyn-Koźle, Poland) with the following qualitative and quantitative composition (determined by means of gas chromatography employing 2-hydroxybiphenyl as an internal standard, Table I).
2. *Ethyl alcohol*, 96% (w/w) [ZPS 'Polmos' at Kutno (Poland).]
3. *Isopropyl alcohol*, [POCh Gliwice (Poland).]
4. *n-Hexyl alcohol*, [MERCK (Darmstadt, Germany).]
5. *Ethyl acetate*, [POCh Gliwice (Poland).]
6. Dianin's compound obtained by heating the ethyl acetate clathrate in air at 180°C for 30 minutes [9].

2.2. EQUIPMENT AND GENERAL METHOD USED FOR THE SEPARATION OF DIANIN'S COMPOUND

Standard laboratory equipment was employed. A typical set, which was used to dissolve the by-product, was composed of a three-neck flask (volume of 250, 500, 750 or 1,000 mL) provided with a mechanical stirrer, dropping funnel and reflux condenser. The residue from the bisphenol-A process was charged to the flask together with a suitable volume of a solvent (or mixture of solvents) and heated to the boiling point of the solvent(s) used. If the by-product did not dissolve, further volumes of solvent(s) were introduced from the graduated dropping funnel. When the by-product was completely dissolved, the solution was refluxed for 15 minutes and allowed to crystallize at ambient temperature for 48–72 hours. The crystals precipitated were vacuum-filtered with the use of a sintered-glass filter and washed

Table I. Qualitative and quantitative composition of the by-product of the bisphenol A reaction

Item No.	Component	Amount [wt.%]
1	Phenol	Traces
2	x	0.31
3	*p-tert*-butylphenol	0.26
4	*p*-isopropenylphenol	1.93
5	9,9-dimethylxanthene	0.43
6	Dimethylhydroxybiphenyl	5.30
7	*o,p*-bisphenol-A	1.99
8	x	0.94
9	4-(3,4-dihydro-2,2,4-trimethyl-2H-1-benzopyrane-4-yl)-phenol (Dianin's compound)	30.61
10	Bisphenol-A	2.63
11	3-(4-hydroxyphenyl)-2,3-dihydro-1,1,3-trimethyl-1H-indene-5-ol (cyclic dimer)	17.24
12	Linear dimer of isopropenylphenol	2.97
13	Linear dimer of isopropenylphenol	4.05
14	x	3.08
15	Σ x, higher-boiling	28.25

with a volume of cold solvent(s). They were then re-crystallized from the same solvent(s), filtered off, dried in air and weighed.

High-volume tests were run in a 10-litre glass reactor equipped with a mechanical stirrer and reflux condenser.

2.3. ANALYTICAL METHODS USED IN QUALITATIVE AND QUANTITATIVE EVALUATIONS

2.3.1. *Chromatography*

Gas chromatography was employed to analyze the by-product used as well as the separated and synthesized chemical compounds. The instrument (Carlo-Erba Instruments) was equipped with a flame-ionization detector and capillary column (25×0.32 mm) with the stationary phase (50% *Phenyl-Silicone*) 0.25 μm thick. Helium was used as carrier gas, flow rate of 2.5-ml min^{-1}. The column temperature profile was programmed within 60 to 280°C. The samples were injected with the use of the on-column procedure, by means of a Hamilton syringe, and equal volumes of 1 μl of 1% solution were introduced. 2-Hydroxybiphenyl was employed as the internal standard.

2.3.2. ^{1}*HNMR spectroscopy*

This method was utilized to confirm the structures of the products obtained at successive stages of the study. Also, it provided the preliminary evaluation of the purity of the products. The analysis employed a Hitachi Perkin-Elmer 60 MHz instrument. Dioxane-d_6, acetone-d_6, $CDCl_3$ or CCl_4 were used as solvents.

3. Results and Discussion

3.1. SEPARATION OF DIANIN'S COMPOUND; IDENTIFICATION STUDIES

Having the product stream available with the chemical composition as per Table I, derived from the bisphenol-A synthesis, initial attempts were made to separate the clathrate of Dianin's compound with ethyl acetate. The experiments covered the trials of crystallizing the Dianin's compound out of the product mixture with the use of selected esters and alcohols (or mixtures thereof) as solvents. Ethyl acetate was found to be a very efficient solvent of the by-product. Solutions of the by-product were prepared with their concentrations ranging from 10–40% w/w. The solutions with higher concentrations were of very high viscosity which was found to be disadvantageous for crystallization to occur. The solutions prepared were cooled down and allowed to stand at room temperature. However, not a single crystal could be found after 24 hours. The solutions were further cooled down to about 5°C. And again, no crystallization could be noticed after 48 hours.

The by-product concentrations were increased to 50%, 60% and 70% despite the high viscosity of the resulting solutions. Despite the high concentration and high viscosity, crystals appeared after 48 hours. The crystalline material was filtered off, washed with ethyl acetate and dried at about 60°C.

The structure of the separated compound was studied by means of ^{1}H NMR spectroscopy. The shifts are tabulated in Table II.

Signals 4, 5 and 8 arise from the solvent used – ethyl acetate, while the remaining signals come from Dianin's compound.

Gas chromatography was employed to compare the purities for the obtained clathrate of Dianin's compound with ethyl acetate and for the empty clathrate (obtained by heating the ethyl acetate clathrate compound up to 180°C for 30 minutes). The qualitative and quantitative data are presented in Table III.

The findings revealed that the purity of the re-crystallized Dianin's compound with no guest could be above 99.5% (w/w). However, the clathrate of Dianin's compound with ethyl acetate contains 94.8% (w/w) of Dianin's compound and 4.6% (w/w) of ethyl acetate. The findings also confirm that some impurities have been removed in the process of eliminating the guest compound (30 minutes at 180°C).

Table II. Shifts for the separated Dianin's compound (with ethyl acetate)

Pos.	Group of protons	Shift δ
1	—OH—	8.0
2	Ar—	6.9–7.2
3	C—CH_2–C	4.8
4	O—CH_2–C	3.9–4.3
5	CH_3—CO	2.0–2.6
6	—CH_3	1.7
7	—CH_3	1.4
8	—C–CH_3	1.2
9	—CH_3	1.0

Table III. Qualitative and quantitative compositions for "full" (with ethyl acetate) and "empty" clathrate of Dianin's compound, as found by GC

Pos.	Component	Concentration, %(w/w)	
		Empty clathrate	Full clathrate
1	Dianin's compound – both enantiomers (host)	99.62	94.8
2	*ethyl acetate* (*guest*)	–	4.6
3	Phenol	–	–
4	DMHB	–	0.03
5	*o*,*o*-bisphenol-A	0.01	0.03
6	*o*,*p*-bisphenol-A	0.02	0.06
7	*p*,*p*-bisphenol-A	0.01	0.04
8	Cyclic dimer	0.19	0.10
9	Σ x	0.14	0.33

3.2. STUDY ON THE EFFECT OF THE SOLVENT COMPOSITION ON THE YIELD FROM THE CRYSTALLIZATION OF THE DIANIN'S COMPOUND

In order to study the effect of the type and composition of the solvents used on the yield of crude Dianin's compound the SIMPLEX-CENTROID model was used to plan a series of experiments involving a three-component system of solvents. The solvents used and the yields obtained are provided in Table IV. All samples were obtained by crystallization of the by-product with a suitable solvent or solvent mixture.

Table IV. Solvent compositions and yields for a 3-factor plan of experiments as per SIMPLEX-CENTROID

Pos.	Solvent			Amount of Dianin's compound* in g	Yield of Dianin's compound* % (w/w)
	Ethanol wt. parts	Hexanol wt. parts	*i*-Propanol wt. parts		
1	100	0	0	9.64	29.40
2	0	100	0	6.61	20.15
3	0	0	100	7.63	23.27
4	50	50	0	7.17	21.87
5	50	0	50	8.66	26.40
6	0	50	50	6.90	21.01
7	33	33	33	7.30	22.24
8	67	17	17	8.19	24.96
9	17	67	17	6.00	18.32
10	17	17	67	7.23	22.05
11	100	0	0	9.88	30.05
12	0	100	0	6.66	20.30

* Empty clathrate of Dianin's compound.

The following correlation equation resulted from the statistical analysis of the yields of crystallization obtained:

$$Y = 29.78(\pm 0.58) \cdot X_1 + 20.04(\pm 0.58) \cdot X_2 + 23.24(\pm 0.81) \cdot X_3 - 13.22(\pm 3.67) \cdot X_1 \cdot X_2, \quad (1)$$

Y is the yield of Dianin's compound, % w/w; X_1 is the weight of ethanol in the solvent, % w/w; X_2 is the weight of *n*-hexanol in the solvent, % w/w; X_3 is the weight of *i*-propanol in the solvent, % w/w.

The coefficient of determination $R^2 = 0.98$, and the statistical error of estimation was 0.83. The graphical presentation of the equation derived is shown in Figure 1, while Figure 2 provides the error analysis for the function obtained.

The statistical analysis confirmed the essential effect of the solvent composition on the yield of Dianin's compound. The equation derived reveals small contributions from second order factors (there is only one factor $X_1 \cdot X_2$ in the equation). Hence, the solvents themselves can be expected to have a critical influence on the yield of Dianin's compound. No proof was found for mixtures of individual solvents to be useful. The chromatographic analysis confirmed the high purity (over 99.5%) of Dianin's compound obtained.

The study presented above demonstrates that there is a possibility – under specific conditions – of separating a selected chemical individual, e.g. Dianin's

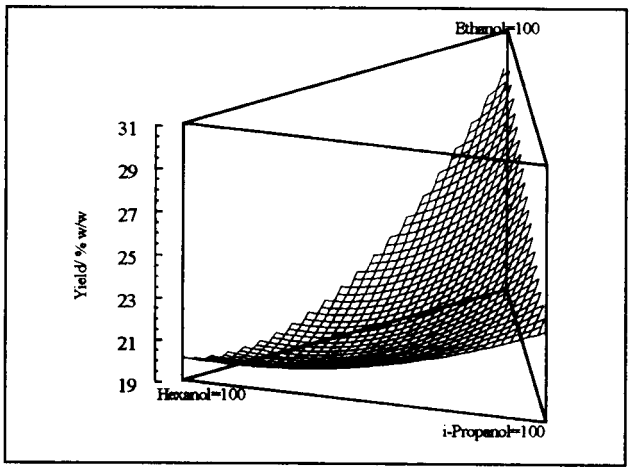

Figure 1. Three-component plan for the yield of crude Dianin's compound versus solvent composition (weight %).

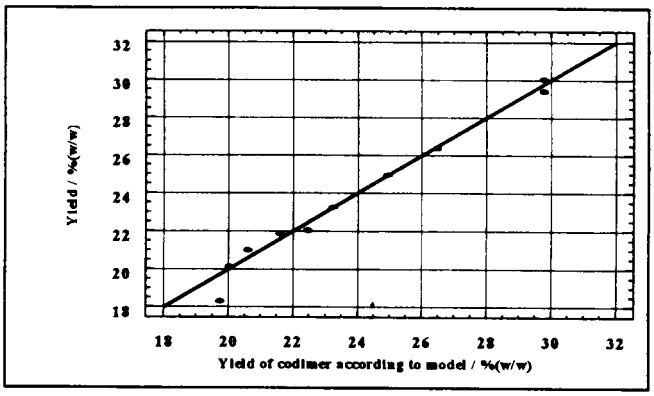

Figure 2. Experimental yield from crystallization versus yield as per mathematical model (error of model).

compound, from a complex mixture of by-products in high purity exceeding 99.5%.

4. Conclusions

1. Taking advantage of the possibility of Dianin's compound to form clathrates and of the fact that such structures crystallize easily, high-purity clathrates of 4-(3,4-dihydro-2,2,4-trimethyl-2H-1-benzopyran-4-yl)-phenol (Dianin's compound) could be separated from a complex mixture of by-products formed in the bisphenol-A synthesis process.

2. The clathrate structures obtained can be crystallized under the applied conditions. The clathrate crystals containing the solvent used in the experiments offered high purity of over 99.5% after just a single crystallization.
3. Statistical modeling of the solvent mixture composition revealed that it was optimum to use a single solvent. Ethyl alcohol was found to be the best solvent within the range of the materials studied.

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