lower than that found in wheat germ oil (2.00%) by Frankforter and Harding.[10]

The deep golden-brown color of this oil suggests the presence of the carotinoid pigments. In view of the fact that vitamin A potency is now generally associated with carotene, and since the antimony chloride reaction[11] is presumed to indicate its presence, application of this test bid fair to lead to affirmative results.

When the oil itself was added to a chloroform solution of this salt, a strong blue coloration appeared. The unsaponifiable matter which had been extracted with ethyl ether gave a stronger reaction than did that recovered by treatment with petroleum ether, a condition which is probably due to the fact that the latter removes less coloring matter from the oil than does the former.

Summary

The more important physical and chemical characteristics and the approximate percentage composition of rye germ oil have been determined. It is a semi-drying oil which is characterized by the quantity of heavily pigmented unsaponifiable matter which it contains. Correlation of its constants with those obtained by others, with perhaps one exception,[1g] cannot satisfactorily be made because of the diversity of products which have been included under the name rye oil.

The percentage composition of this oil was found to be as follows: myristin, 2.33; palmitin, 8.11; stearin, 0.18; olein, 31.92; linolein, 44.05; linolenein, 4.99; unsaponifiable matter, 7.28; undetermined, 1.14.

[10] Frankforter and Harding, THIS JOURNAL, **21**, 758 (1899).

[11] Carr and Price, *Biochem. J.*, **20**, 497 (1926).

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[CONTRIBUTION FROM THE EXPERIMENTAL RESEARCH LABORATORIES, BURROUGHS WELLCOME AND COMPANY]

MIXED BENZOINS. VIII. FURTHER DETERMINATIONS OF STRUCTURES. QUESTION OF ISOMERS

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The present paper deals mainly with the determination of the structure of a number of mixed benzoins, most of them new, in continuation of the authors' purpose to characterize a sufficiently large number of mixed benzoins to enable worth-while deductions to be made regarding the reactivity of aldehydes. The method used depends on the Beckmann transformation of the second type, previously used and described in Part IV.[1] The reaction appears to be trustworthy, as no results so far obtained contradict

[1] Buck and Ide, THIS JOURNAL, **53**, 1912 (1931).

structures established in other ways. The transformation is considered as taking place in the Beckmann sense, between vicinal groups, and not in the Meisenheimer sense between *anti* groups. The method also enables the structure of the oximes of the benzoins to be deduced. The structures of the corresponding desoxy compounds have been determined by a method also previously described[2] (Beckmann transformation of the first type). In the present paper, the benzoins and their oximes together with the derived desoxybenzoins and their oximes and transformation products are described.

A point of considerable importance in the study of mixed benzoins is whether both of the possible isomers are formed by the condensation of two different aldehydes in the presence of potassium cyanide, or whether only one is formed. In an earlier paper[3] the present authors reported that they had isolated two such isomers, using benzaldehyde and piperonal. The evidence was chiefly analytical. Tiffeneau and Lévy[4] have failed to isolate the two isomers. The present authors, after many attempts, have also failed to repeat the isolation of the two isomers. It now seems probable that the compound melting at 110° was a side-product such as benzyl piperonylate or piperonyl benzoate, of the same synoptic formula, isolated by chance. Unfortunately, none of the compound is now available to settle the point.

Tiffeneau and Lévy[4] believe that they have in two cases obtained evidence for the existence of pairs of isomeric benzoins. In work which was probably carried out simultaneously with Tiffeneau and Lévy's work, the present authors[5] have twice commented upon the ability of benzoins to form addition compounds, and it seems to them that Tiffeneau and Lévy's results could be readily explained on the basis of addition compound formation rather than on the basis of the formation of isomers. Thus in the condensation of piperonal and anisaldehyde, Tiffeneau and Lévy obtain two substances, melting at 75 and at 110°. The first is admittedly a mixture and gives on potash fission a mixture of piperonylic and anisic acids. In the hands of the present authors this substance, on oxidation with Fehling's solution, gave a mixture of about equal amounts of piperil and methoxymethylenedioxybenzil, showing the presence of considerable amounts of piperoin in the preparation. The substance melting at 110° similarly gave on oxidation, piperil, methoxymethylenedioxybenzil and anisil in the ratio 20:4:1 and is hence chiefly piperoin.

The other case is the condensation of benzaldehyde and *m*-methoxybenzaldehyde. The two products described by Tiffeneau and Lévy were

[2] Buck and Ide, THIS JOURNAL, **53**, 1536 (1931).

[3] Buck and Ide, *ibid.*, **52**, 220 (1930).

[4] Tiffeneau and Lévy, *Bull. soc. chim.*, [4] **49**, 725 (1931).

[5] Buck and Ide, THIS JOURNAL, **53**, 2350, 2784 (1931).

regenerated from a semicarbazone preparation. Both on potash fission gave benzoic and *m*-methoxybenzoic acids and so are not entities. No analyses are given, and the main product, m. p. 80°, is admittedly not pure.

It is evident that, by potash fission, the same acids would be obtained either from a mixture or addition compound of two simple benzoins, or from a mixture or addition compound of the corresponding pair of isomeric mixed benzoins.

In view of the above considerations, it would appear that the claim to have obtained evidence of two pairs of isomeric mixed benzoins requires further substantiation. It seems to the present authors that the evidence is strongly in favor of addition compounds. Benzoin reactions are, however, very susceptible to variations in experimental conditions, and unless these are exactly specified, it is not at all certain that two different workers will always reproduce each other's results.

The present authors therefore consider that no case of the formation of a pair of isomeric mixed benzoins has been conclusively demonstrated, and they are inclined to the belief that only one isomer is formed. Experimental proof, for or against, will be difficult on account of the possible complexity of the reaction mixtures (*cf.* Lachman[6]) and the probability that, if both isomers are formed, one will be present only in small amount.

It is intended to investigate the question of isomeric mixed benzoins from another angle, by regenerating the benzoins from the corresponding benzils, where isomerism and addition compound formation are not involved.

Note on Nomenclature.—The system earlier suggested by Buck and Ide[3] (depending on the termination -oin) is inadequate for the more highly substituted benzoins and derivatives. The authors therefore suggest using primes for the numbered substituents on the benzene ring next to the CO group (or in the case of oximes, the C=NOH group). This method has been followed in the present paper, using the full systematic name, however. In future, *o*-chlorobenzveratroin (old name) will be written 2-chloro-3′,4′-dimethoxybenzoin, and so on.

Experimental

Benzoins.—The benzoins not previously described were prepared by dissolving 0.2 mole of each aldehyde in 100 cc. of alcohol; 10 g. of potassium cyanide, dissolved in 20 cc. of water, was then added and the solution refluxed on the steam-bath for one to one and one-half hours. The crystalline products are obtained from the reaction mixtures by treatment with solvents and exposure to cold (refrigerator). Steam distillation to remove unchanged aldehydes was not resorted to, on account of the pos-

[6] Lachman, THIS JOURNAL, **46**, 708 (1924).

TABLE I

BENZOINS

	Benzoin	Aldehydes used	
I	2-Chloro-α-hydroxybenzyl-3',4'-diethoxyphenyl ketone	2-Chlorobenz-	3,4-Diethoxybenz-[a]
J	2-Chloro-α-hydroxybenzyl-3'-ethoxy-4'-methoxyphenyl ketone	2-Chlorobenz-	3-Ethoxy-4-methoxybenz-[b]
K	2-Chloro-α-hydroxybenzyl-3'-methoxy-4'-ethoxyphenyl ketone	2-Chlorobenz-	3-Methoxy-4-ethoxybenz-[c]
L	3-Chloro-α-hydroxybenzyl-4'-dimethylaminophenyl ketone[7]	3-Chlorobenz-	4-Dimethylaminobenz-
M	4-Chloro-α-hydroxybenzyl-3',4'-methylenedioxyphenyl ketone[7]	4-Chlorobenz-	Piperonal
N	3,4-Methylenedioxy-α-hydroxybenzyl-4'-dimethylaminophenyl ketone[8]	Piperonal	4-Dimethylaminobenz-

	Formula	M. p., °C.	Yield, %	Appearance	Analyses, % Calcd.		Found	
I	$ClC_6H_4CHOHCOC_6H_3(OC_2H_5)_2$	106	63	Stout prisms	C, 64.55	H, 5.72	C, 64.42	H, 5.65
J	$ClC_6H_4CHOHCOC_6H_3(OC_2H_5)OCH_3$	103	81	Fine needles	C, 63.63	H, 5.34	C, 63.71	H, 5.60
K	$ClC_6H_4CHOHCOC_6H_3(OCH_3)OC_2H_5$	120	60	Rhombs	C, 63.63	H, 5.34	C, 63.91	H, 5.49
L	$ClC_6H_4CHOHCOC_6H_4N(CH_3)_2$	140	45	Rhombs	Cl, 12.24		Cl, 11.98	
M	$ClC_6H_4CHOHCOC_6H_3O_2CH_2$	110	40	Needles	C, 61.95	H, 3.79	C, 61.81	H, 3.68
N	$CH_2O_2C_6H_3CHOHCOC_6H_4N(CH_3)_2$	136	40	Fern-like crystals	C, 68.19	H, 5.73	C, 68.47	H, 5.92
					N, 4.68		N, 4.77	

[a] Prepared by ethylating 3-ethoxy-4-hydroxybenzaldehyde with ethyl sulfate and sodium hydroxide. Described and prepared in another way by Gattermann, *Ann.*, **357**, 368 (1907).

[b] Prepared by methylating 3-ethoxy-4-hydroxybenzaldehyde with methyl sulfate and sodium hydroxide. Described and prepared in another way by Schorigin and co-workers, *Ber.*, **64**, 274 (1931).

[c] Prepared by ethylating vanillin with ethyl sulfate and sodium hydroxide. Described and prepared in another way by Tiemann, *Ber.*, **8**, 1127 (1875).

[7] Buck and Ide, THIS JOURNAL, **52**, 4107 (1930).

[8] Buck and Ide, *ibid.*, **53**, 2350 (1931).

sibilities of change in the reaction mixtures during the process. The benzoins, when crystallized from alcohol, are persistently yellow. Crystallization from acetic acid gives the benzoin in a pure white form. The results are given in Table I. Derived compounds, such as oximes, have the same letter as the parent benzoin.

Benzils.—The benzils were all prepared by dissolving the appropriate mixed benzoin in alcohol (usually 2.0 g. was taken) and oxidizing with a slight excess of Fehling's solution. The crude product was recrystallized from alcohol until pure.

TABLE II

BENZILS

	Benzil	M. p., °C.	Yield, %	Appearance	Analyses, % Calcd. C	Calcd. H	Found C	Found H
I	2-Chloro-3′,4′-diethoxy-	110	70	Yellow rhombs	64.94	5.15	64.92	5.07
J	2-Chloro-3′-ethoxy-4′-methoxy-	150	84	Yellow hexagons	64.03	4.74	64.20	5.01
K	2-Chloro-3′-methoxy-4′-ethoxy-	132	80	Yellow needles	64.03	4.74	64.36	5.08
L	3-Chloro-4′-dimethylamino-[7]	130	90	Amber plates	66.77	4.91	66.53	5.21
M	4-Chloro-3′,4′-methylenedioxy-[7]	132	78	Yellow needles	62.38	3.12	62.24	2.99
N	3,4-Methylenedioxy-4′-dimethylamino-	174	60	Yellow hexagons	68.65	5.08	68.84	5.21

Desoxy Compounds.—The desoxy compounds were prepared by the method previously described.[7] Alcohol is usually the best solvent for recrystallization. All the desoxy compounds are white. It will be seen that, with all the desoxy compounds below, the structure corresponds to that of the parent benzoin, the CHOH group being reduced to CH_2. This is not invariably the case.[1]

TABLE III

DESOXY COMPOUNDS

	Phenyl ketone	M. p., °C.	Yield, %	Appearance	Analyses, % Calcd. C	Calcd. H	Found C	Found H
I	2-Chlorobenzyl-3′,4′-diethoxy-	95	58	Long needles	67.79	6.01	67.63	6.21
J	2-Chlorobenzyl-3′-ethoxy-4′-methoxy-	98	57	Long needles	66.97	5.61	67.16	5.79
K	2-Chlorobenzyl-3′-methoxy-4′-ethoxy-	121	55	Long needles	66.97	5.62	67.28	5.83
L	3-Chlorobenzyl-4′-dimethylamino-[7]	125	80	Needles	70.18	5.89	69.90	5.99
M	4-Chlorobenzyl-3′,4′-methylenedioxy-[7]	113	80	Needles	65.56	4.01	65.72	4.09
N	3,4-Methylenedioxybenzyl-4′-dimethylamino-	140	44	Glittering plates	72.05	6.05	72.17	6.27

Oximes of Desoxy Compounds.—The oximes were prepared by one of the methods given in Part IV[1] for the benzoin oximes. The figure in the last column of the table refers to the preparation. All the oximes are white, well-crystallized compounds. They have, in every case, the *anti*-benzyl configuration.

The amides were identified either by hydrolysis and the identification of the acid so produced (the basic fragment is always decomposed) or by synthesis. The amides are very stable and require many hours' refluxing with concentrated hydrochloric acid in order to hydrolyze them. Amides I, J and K gave on hydrolysis *o*-chlorophenylacetic acid, identified by comparison and mixed melting point determinations with an authentic specimen. Amide L on hydrolysis gave *m*-chlorophenylacetic acid, identical

TABLE IV

OXIMES OF DESOXY COMPOUNDS

	Phenyl ketoxime	M. p., °C.	Yield, %	Appearance	Analyses, % Calcd. C	Calcd. H	Found C	Found H	Method of prepn.
I	*Anti*-2-chlorobenzyl-3′,4′-diethoxy-	105	70	Slender needles	64.74	6.04	64.81	6.08	1
J	*Anti*-2-chlorobenzyl-3′-ethoxy-4′-methoxy-	130	63	Fine needles	63.82	5.67	63.98	5.89	1
K	*Anti*-2-chlorobenzyl-3′-methoxy-4′-ethoxy-	167	94	Needles	63.82	5.67	63.89	5.76	3
L	*Anti*-3-chlorobenzyl-4′-dimethylamino-	146	70	Slender prisms	66.52	5.93	66.79	6.03	1
M	*Anti*-4-chlorobenzyl-3′,4′-methylenedioxy-	119	55	Tiny hexagons	62.16	4.17	62.30	4.30	1
N	*Anti*-3,4-methylenedioxy-	152	70	Fine needles	68.42	6.08	68.67	6.20	3

TABLE V

AMIDES

	Anilide	M. p., °C.	Yield, %	Appearance	Analyses, % Calcd. C	Calcd. H	Found C	Found H
I	2-Chlorophenylacet-3′,4′-diethoxy-	178	50	Fine needles	64.74	6.04	65.13	6.21
J	2-Chlorophenylacet-3′-ethoxy-4′-methoxy-	165	60	Long needles	63.82	5.67	63.71	5.43
K	2-Chlorophenylacet-3′-methoxy-4′-ethoxy-	166	60	Slender prisms	63.82	5.67	63.97	6.00
L	3-Chlorophenylacet-4′-dimethylamino-	178	50	Tiny needles	66.52	5.93	66.82	6.10
M	4-Chlorophenylacet-3′,4′-methylenedioxy-	195	80	Tiny needles	62.16	4.17	62.40	4.49
N	3,4-Methylenedioxyphenylacet-4′-dimethylamino-	170	40	Tiny needles	68.42	6.08	68.58	6.13

with a specimen prepared as described below. Amide M on hydrolysis gave *p*-chlorophenylacetic acid, identical with a specimen prepared by the method of Petrenko-Kritschenko, *Ber.*, **25**, 2239 (1892). Amide N was identified with a synthetic specimen prepared from homopiperonoyl chloride and dimethyl-*p*-phenylenediamine hydrochloride, by the Schotten–Baumann method.

***m*-Chlorophenylacetic Acid. Azlactone.**[9]—One-tenth mole of *m*-chlorobenzaldehyde, 0.1 mole of hippuric acid and 0.1 mole of freshly-fused, powdered, anhydrous sodium acetate are mixed with 0.3 mole of acetic anhydride and the mixture heated on a hot-plate, with constant stirring, until liquid. The flask is then at once transferred to a water-bath and heated for 105 minutes. After cooling, the magma is stirred with an equal volume of alcohol and left overnight. The crystals are then filtered off and washed with a little cold alcohol and then with hot water. The azlactone forms a mass of canary-yellow crystals. The yield is 63%. After recrystallization from alcohol the compound melts at 164°.

Anal. Calcd. for $C_{16}H_{10}O_2NCl$: C, 67.71; H, 3.55. Found: C, 67.93; H, 3.93.

***m*-Chlorophenylpyruvic Acid.**—Fifteen grams of azlactone is refluxed (oil-bath) with 100 cc. of 10% sodium hydroxide solution for four hours. The mixture, after cooling, is saturated with sulfur dioxide (temperature below 40°), and the benzoic acid filtered off and washed with a little water. The filtrate and washings are then heated nearly to boiling and concentrated hydrochloric acid added cautiously, in small

[9] *Cf.* Kropp and Decker, *Ber.*, **42**, 1188 (1909).

portions, until excess is present. The mixture is gently boiled for a short time, then cooled and the *m*-chlorophenylpyruvic acid filtered off and washed with water. The yield is 8.1 g. (77%). Recrystallized from acetic acid, the compound forms white, tiny, felted needles, melting at 145°.

Anal. Calcd. for $C_9H_7O_3Cl$: C, 54.43; H, 3.55. Found: C, 54.60; H, 3.79.

***m*-Chlorophenylacetic Acid.**[10]—Six grams of the pyruvic acid, dissolved in a solution of 8.0 g. of sodium hydroxide in 25 cc. of water, together with 10 g. of ice, is treated with a solution of 7.5 g. of superoxol (30% H_2O_2) in 15 cc. of water. The addition is carried out slowly, with cooling and shaking. After standing for five hours the solution

TABLE VI

BENZOIN OXIMES

The oximes were prepared by the methods given in Part IV.[1] The numbers refer to these preparations. All the oximes are of the α (*anti* phenyl) form.

	Ketoxime	M. p., °C.	Yield, %	Appearance	Analyses, % Calcd. C	Calcd. H	Found C	Found H	Method of prepn.
I	2-Chloro-α-hydroxybenzyl-3′,4′-diethoxyphenyl-	*ca.* 61	59	Obscure	61.78	5.76	61.90	5.72	1
J	2-Chloro-α-hydroxybenzyl-3′-ethoxy-4′-methoxyphenyl-	113	80	Irreg. plates	60.78	5.40	60.68	5.38	2
K	2-Chloro-α-hydroxybenzyl-3′-methoxy-4′-ethoxyphenyl-	114	71	Hexagons	60.78	5.40	60.97	5.66	2
L	3-Chloro-α-hydroxybenzyl-4′-dimethylamino-	148	57	Tiny needles	63.03	5.62	63.30	5.75	2
M	4-Chloro-α-hydroxybenzyl-3′,4′-methylenedioxyphenyl-	178	40	Fine needles	58.91	3.95	59.21	4.08	2
N	3,4-Methylenedioxy-α-hydroxybenzyl-4′-dimethylamino-	145	71	Fine prisms	64.93	5.77	65.10	5.81	2

TABLE VII

BECKMANN REACTION

The reaction was carried out as previously described, using benzene sulfone chloride and alkali.[1] The residues from oximes I and N were very small. In all the other cases a considerable residue remained after fractionation. The reaction mixtures were fairly clean, except in the cases of oximes L and M, where considerable tarry matter was formed. In no case was there more than a trace of isonitrile odor.

		1st Fraction			2d Fraction		
Oxime	Taken, g.	Name, aldehyde	Yield g.	Yield %	Name, nitrile	Yield g.	Yield %
I	17	*o*-Chlorobenz-[a]	6.0	88	3,4-Diethoxybenzo-[c]	8.0	87
J	12	*o*-Chlorobenz-[a]	3.7	73	3-Ethoxy-4-methoxybenzo-[c]	2.8	44
K	12	*o*-Chlorobenz-[a]	3.3	65	3-Methoxy-4-ethoxybenzo-[d]	3.8	60
L	6.7	*m*-Chlorobenz-[a]	1.6	52	*p*-Dimethylaminobenzo-[e]	2.0	62
M	6.0	*p*-Chlorobenz-[a]	1.4	38	Pipero-[e]	1.8	47
N	8.0	Piperonal[b]	3.1	77	*p*-Dimethylaminobenzo-[e]	2.5	63

[a] Converted into the acid and identified by mixed melting point determinations with an authentic specimen. [b] Identified by mixed melting point determinations with the authentic aldehyde. [c] Identified by mixed melting point determinations with a specimen of nitrile prepared as described below. [d] Identified by mixed melting point determinations with a specimen of authentic nitrile prepared by the action of acetic anhydride on the corresponding oxime. Previously obtained by Keffler, *J. Chem. Soc.*, **119**, 1476 (1921). [e] Identified by comparison with the authentic nitrile prepared as in Part IV.[1]

[10] *Cf.* Mauthner, *Ann.*, **370**, 375 (1909).

is cautiously acidified with hydrochloric acid, and, while still warm, extracted with benzene. The extract is dried and the benzene evaporated. After recrystallization from aqueous alcohol, the acid forms large, pearly leaflets, melting at 74°. The yield is 3.0 g. (57%).

Anal. Calcd. for $C_8H_7O_2Cl$: C, 56.29; H, 4.13. Found: C, 56.00; H, 4.26.

3,4-Diethoxybenzaldoxime was prepared by the action of hydroxylamine acetate on the aldehyde. The oxime forms tiny needles melting at 98°.

Anal. Calcd. for $C_{11}H_{15}O_3N$: C, 63.12; H, 7.23. Found: C, 63.55; H, 7.33.

3,4-Diethoxybenzonitrile was prepared by refluxing the above oxime with acetic anhydride for two hours, and pouring the mixture into water. When recrystallized from aqueous alcohol, the nitrile forms long, flat prisms, melting at 68°.

Anal. Calcd. for $C_{11}H_{13}O_2N$: C, 69.07; H, 6.85. Found: C, 69.25; H, 7.00.

3-Ethoxy-4-methoxybenzaldoxime, prepared by means of hydroxylamine acetate, forms fine needles, melting at 98°.

Anal. Calcd. for $C_{10}H_{13}O_3N$: C, 61.50; H, 6.71. Found: C, 61.85; H, 6.86.

3-Ethoxy-4-methoxybenzonitrile was prepared from the above oxime by refluxing with acetic anhydride for two hours and pouring the reaction mixture into water. Recrystallized from aqueous alcohol it forms a mass of tiny needles melting at 70°.

Anal. Calcd. for $C_{10}H_{11}O_2N$: C, 67.76; H, 6.26. Found: C, 68.00; H, 6.30.

3-Methoxy-4-ethoxybenzaldoxime, prepared in the usual way by means of hydroxylamine acetate, forms tiny needles, melting at 100°.

Anal. Calcd. for $C_{10}H_{13}O_3N$: C, 61.50; H, 6.71. Found: C, 61.63; H, 6.65.

Summary

The structures of six mixed benzoins and their oximes, together with the corresponding desoxy compounds and their oximes, have been determined. The benzils and Beckmann transformation products are also described.

The question of the formation of pairs of isomeric mixed benzoins (by the potassium cyanide condensation) is discussed. It is considered that reported cases of the occurrence of such pairs of isomers require further substantiation.

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