[CONTRIBUTION FROM THE LABORATORY FOR PURE RESEARCH OF MERCK & CO., INC.]

The Identity of Narceine with Pseudonarceine, its Dehydration and Structure

BY C. R. ADDINALL AND RANDOLPH T. MAJOR

The accepted formulation of narceine as a substituted phenyl benzyl ketone, $C_{23}H_{27}NO_8 \cdot 3H_2O$, and the establishment of its identity with the pseudonarceine of Roser,[1] are due to the continued investigations of Freund and his collaborators.[2] The misleading differences in physical properties and physiological effect between opium narceine and that made from narcotine were shown[3] to be due to impurities which were only eliminated after long and careful purification. The formula, $C_{23}H_{29}NO_9 \cdot 2H_2O$, advanced by Anderson[4] for narceine had been confirmed by the analyses of later workers[5] but Roser demonstrated that pseudonarceine, which he considered identical with natural narceine, had the formula $C_{23}H_{27}NO_8 \cdot 3H_2O$. The establishment of the identity of pseudonarceine and naturally occurring narceine by Freund and Frankforter through the analysis of their salts with alkali metals proved the latter to be derived from a substance having the formula $C_{23}H_{27}NO_8$. Determination of the water of crystallization content of natural narceine showed the presence of three molecules of water, two of which were lost with ease, the third only with great difficulty. On account of this and the extremely hygroscopic nature of the dried material the composition of the fully dried narceine is in doubt From his work on the color reaction of sodium nitroprusside[6] with narceine, Zwikker[7] came to the conclusion that the $—CH_2CO$ grouping of desoxybenzoin is not present in narceine, but that a ring closure between the $—CH_2$ and a neighboring $—NMe_2$ has occurred whereby the —CO group is attached directly to two rings and is therefore no longer reactive. Narceine would then have the same ring structure as the parent substance Narcotine. The fluorescence of narceine under ultraviolet irradiation and the conclusion of Moir[8] that fluorescence may occur in all cases where two rings are joined at two places by two groups of almost any sort, offers some support for this assumption. Failure on our part to reduce narceine to hydronarceine[9] by catalytic hydrogenation, to carry out a benzylidene condensation[10] and to isolate the alkyl narceines, together with lack of success in the

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(1) Roser, *Ann.*, **247**, 187 (1888).

(2) Freund and Frankforter, *ibid.*, **277**, 20 (1893); Freund and Michaels, *ibid.*, **286**, 248 (1895); Freund, *Ber.*, **40**, 194 (1907); Freund and Oppenheim, *ibid.*, **42**, 1084 (1909).

(3) Schroeder, *Arch. exptl. Path. Pharmakol.*, **17**, 138 (1883).

(4) Anderson, *Ann.*, **86**, 179 (1853).

(5) Hesse, *ibid.*, **129**, 250 (1864); Beckett and Wright, *J. Chem. Soc.*, **28**, 699 (1875); Claus and Meixner, *J. prakt. Chem.*, [2] **37**, 1 (1888).

(6) Bela von Bitto, *Ann.*, **269**, 377 (1892).

(7) Zwikker, *Pharm. Weekblad.*, **66**, 461 (1929).

(8) Moir, *Trans. Roy. Soc. S. Africa*, **12**, Pt. 2, 45 (1924).

(9) Max and Michel Polonovski, *Bull. soc. chim.*, **49**, 541 (1931).

(10) Knoevenagel and Weissgerber, *Ber.*, **26**, 442 (1893).

repetition of Freund's narcindonine preparations[11] so vital to the conception of narceine as a highly substituted desoxybenzoin, coupled with the uncertain nature of dried narceine and the recent doubts as to its structure, led to the undertaking of the preparation of pure narceines from opium and narcotine sources, their dehydration and the investigation of the possibility of a modified formula for narceine.

Narceine was prepared from narcotine by the methods of Roser and of Hope and Robinson.[12] After careful purification these narceines and that from opium were converted into their sodium salts, hydrochlorides, chloroplatinates and picrates and the identity of these derivatives was established by melting point determinations. Further evidence as to absolute identity was afforded by examination of the carefully purified narceines by ultraviolet radiation. Polarimetric measurements showed all three narceines alike to be optically inactive.

Previous attempts to dehydrate narceine and to analyze the water-free material had always failed. Not only is the dried material extremely hygroscopic but some decomposition takes place, causing the resulting dried narceine to be variable in composition. By combining the drying process and the analysis a satisfactory series of analyses for the dried material was obtained.[13] These results, in conjunction with the water of crystallization determinations made by a macro method, gave a completely satisfactory analysis of narceine for carbon, hydrogen and water of crystallization. These analytical results give further support to the proof of the absolute identity of narceine prepared from narcotine with that found among the products extracted by the established trade procedures from the gum of the opium poppy along with morphine and narcotine.

It would therefore seem that air-dried narceine has the constitution $C_{23}H_{27}NO_8 \cdot 3H_2O$ and that, always provided that the drying temperature does not exceed 110° and is not prolonged more than two hours, the sample not being exposed to oxidation during this period, the water of crystallization can be removed quantitatively without the decomposition of the dry material, which has then the empirical formula $C_{23}H_{27}NO_8$ (I) precluding the possibility of the structure of narceine being represented by any structural formulation involving the empirical formula $C_{23}H_{29}NO_9$. Since all of the substituent groups, *i. e.*, 3(OMe), COOH, CH_2O_2, C_2H_4-NMe_2 are well established, only the validity of the supposed —$COCH_2$— grouping remains doubtful in the present recognized structural formulation.

Narceonic acid (II) prepared by a modification of the method of Freund[14] was converted into dihydronarceonic acid by catalytic hydrogenation. Treatment of the methyl ester of this saturated acid with MeMgI in an

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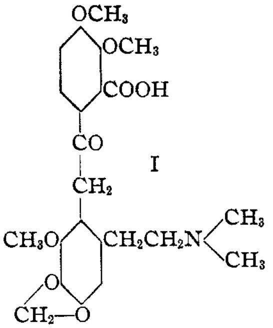
[11] Freund and Oppenheim, *Ber.*, **42**, 1084 (1909).

[12] Hope and Robinson, *J. Chem. Soc.*, **105**, 2100 (1914).

[13] Hayman, *Ind. Eng. Chem., Anal. Ed.*, **4**, 256 (1932).

[14] Freund, *Ann.*, **277**, 55 (1893).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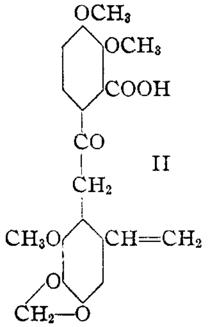
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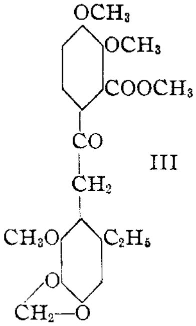
III

apparatus for determining both the quantity of gas evolved and the amount of reagent consumed[15] showed that it contained no active hydrogen and so afforded evidence against the assumption of OH groups in the narceine molecule. This evidence was confirmed by the failure of many attempts to methoxylate narceine and its derivatives. The formulation of narceine as a highly substituted desoxybenzoin and the erroneous claims of early workers[16] led to many fruitless efforts to isolate alkyl narceines and its derivatives. The bromination of this methyl ester with bromine in chloroform gave an interesting monobromide $C_{22}H_{23}O_8Br$ which may contain a bromine atom in the only unoccupied position of the cotarnine half of the molecule. The ease of substitution in this position has already been noted.[17]

Through ring formation with the COOH group the addition of $HONH_2$ and $PhNHNH_2$ to narceine yields oxime and phenylhydrazone anhydrides. The condensation of $MeONH_2$ with narceine to give the simple addition compound $C_{24}H_{30}N_2O_8$ without further internal rearrangement affords further evidence for the accepted —$COCH_2$— formulation.

We wish to thank Mr. Douglas F. Hayman of this Laboratory for the microanalyses recorded in this paper and also Professor E. P. Kohler for his kindness in carrying out the active hydrogen determination.

Experimental Part

Preparation of Pure Narceine from Opium and Synthetic Material

Opium Narceine.—Commercial narceine recovered from the mother liquors from the preparation of morphine hydrochloride usually contains small amounts of acid and other impurities from which it is freed with difficulty.[18] The impure factory narceine was dissolved in dilute hydrochloric acid and then made slightly alkaline with ammonia. The alkaline solution was digested on the steam-bath and then allowed to cool. After crystallization the filtered material was dissolved in a minimum of hot 95% alcohol and after dilution to 50% with distilled water the solution was cooled. The resulting fine prismatic needles were recrystallized from hot water.

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[15] Kohler and Richtmyer, THIS JOURNAL, **52**, 3736 (1930).

[16] Claus and Ritzefeld, *Ber.*, **18**, 1569 (1888); Tambach and Jaeger, *Ann.*, **349**, 185 (1906); Knoll and Co., *Friedländer*, VIII, 1164, 1166.

[17] Freund and Fleischer, *Ber.*, **45**, 1171 (1912).

[18] Merck, *Chem.-Ztg.*, **13**, 525 (1889).

Narceine (Roser).—Narcotine, recrystallized from acetone, was digested with an excess of methyl iodide for four hours. The crude gum was freed from methyl iodide by heating *in vacuo* and the resulting dry amorphous yellow powder was digested with freshly prepared silver chloride in water. The addition product gradually went into solution and the quaternary ammonium chloride was filtered free from the silver iodide formed. On treatment with potassium hydroxide and heating on a steam-bath crude narceine separated out.

Narceine (Hope and Robinson).—To 60 g. of recrystallized narcotine was added 21 g. of redistilled dimethyl sulfate in the cold. The mixture was shaken, warmed on steam-bath and stood overnight in a stoppered 250-cc. Erlenmeyer flask. Benzene was added to ensure contact, and after refluxing for a time, was removed. Water was added and the flask was warmed until solution was effected. On adding potassium hydroxide to slight alkalinity and heating, crude narceine was formed.

The crude synthetic narceines were dissolved in dilute hydrochloric acid and precipitated with ammonia. They were then recrystallized from 50% alcohol until yellowness was absent from the mother liquors. The coloration present was due to a brown water-soluble oil which was soluble also in alcohol and alkali and which could be removed from neutral solutions by boiling with norite. The colorless material was recrystallized from boiling water and the filtered cakes were dried by exposure to the air in a dust proof box.

All three materials melted between 171–173°. The opium and Roser samples were unchanged under ultraviolet radiation whereas all Hope and Robinson samples showed a green fluorescence. Analyses for the two former corresponded to $C_{23}H_{27}NO_8 \cdot 2H_2O$ and to $C_{23}H_{27}NO_8 \cdot 2.5H_2O$ for the latter material. The narceines were treated with freshly prepared 33% sodium hydroxide, heated on the steam-bath and the hard lumps formed were broken up with a glass rod. After digestion and filtration through a sintered glass funnel the residue was ground up to a fine paste which was returned to fresh 33% sodium hydroxide and was redigested. In this way a clear solution was obtained which gave a crystalline material on cooling. After filtration and washing with cold ethanol the solid was dissolved in hot ethyl alcohol and on cooling ether was added. Large white crystals were formed which were redissolved in hot ethyl alcohol and recrystallized.

In some of the preparations a red color appeared on dissolving the crude sodium salt in ethyl alcohol with heating. This color formation was accelerated by the addition of norite. By converting the crude sodium salt into narceine with dilute acetic acid, recrystallizing the narceine from water and treating with 33% sodium hydroxide, a sodium salt was formed which gave a colorless alcoholic solution.

The sodium salts, all melting at 162–163°, melting point unchanged on mixing, were dissolved in hot distilled water and carbon dioxide was passed through the dilute solution. The cold solution containing a semi-solid crystalline network was filtered, the narceine was shaken up in cold water and washed three times by decantation. The narceines so formed were recrystallized from water. The samples were then placed in an air-drier consisting of a box with a sliding front and a back covered with good grade fine-meshed cheese cloth. The material was dried for forty-eight hours and after being finely ground was dried again for twenty-four hours. Samples were then bottled in vials with screw caps, the inner cork lining being covered with waxed paper. All samples had m. p. 176–178°.

ANALYSES OF AIR-DRIED NARCEINES

		C		H	
Calculated for $C_{23}H_{27}NO_8 \cdot 3H_2O$		55.31		6.61	
Found:	Opium narceine	55.75	55.72	6.28	6.30
	Roser narceine	55.42	55.57	6.52	6.57
	Hope–Robinson narceine	55.19	55.26	6.71	6.69

Quantitative Determination of the Water of Crystallization.—Nitrogen freed from oxygen and moisture by passage through concd. sulfuric acid, over hot copper shavings and through a U-tube packed with dehydrite was passed slowly over a weighed sample of narceine contained in a U-tube placed in a drying oven for two hours at 103–105°. The moisture absorbed by the nitrogen was removed by passage through a weighed U-tube containing dehydrite which was guarded from the air by a second similar tube. The whole train terminated in a U-tube of concd. sulfuric acid acting as a bubble counter and included a deep sulfuric acid T-safety valve between the supply tank and the first sulfuric acid wash bottle.

Narceine	Sample, g.	Water lost, g.	Water recovered, g.	% H_2O (Calcd. for $3H_2O$, 10.82)
Opium	1.9043	0.2021	0.2025	10.61
	1.6147	.1730	.1737	10.73
Roser	2.8440	.3036	.3038	10.68
Hope–Robinson	1.2016	.1292	.1296	10.77

In the case of the Hope–Robinson material advantage was taken of the previous results and the sample was purified still further by reconversion into the sodium salt and back again to narceine—both materials being recrystallized from water. The heating was continued for three and one-half hours at 101–102°.

Analysis of Narceine Freed from Water of Crystallization.—Although excellent results for $3H_2O$ were obtained by the above macro-analysis, the satisfactory analysis of the dried material was found to be impossible by the usual procedure. Dehydration of the air-dried material weighed out in a platinum boat placed in a combustion tube in the same manner as for a regular carbon and hydrogen determination was carried out by the passage of preheated dry nitrogen over the sample heated to 100–105° by a Pregl heating block. The absorption tubes were then attached and the combustion was completed in the usual manner. The results of the analysis of the dried material were excellent and these in conjunction with the determinations of the water of crystallization by the macro method give a completely satisfactory and definite determination of narceine for carbon, hydrogen and water of crystallization. The Hope–Robinson material (calcd. for $C_{23}H_{27}NO_8 \cdot 3H_2O$: C, 55.31; H, 5.61; H_2O, 10.82; N, 2.80. Found: C, 55.26; H, 6.69; H_2O, 10.77; N, 2.85) was used throughout the analyses.

Anal. Calcd. for $C_{23}H_{27}NO_8$: C, 62.02; H, 6.07. Found: C, 62.09, 62.26; H, 5.73, 5.75.

The Melting Points of Narceines and their Derivatives.—Narceine dissolves in a solution of hydrochloric acid in methanol. The solution deposits crystals with a composition $C_{22}H_{27}NO_8 \cdot HCl \cdot CH_3OH$. On heating for a short time at 100° the methanol is totally eliminated with the formation of $C_{23}H_{27}NO_8 \cdot HCl$. This hydrochloride when dissolved in 16% hydrochloric acid and warmed at 70–80° with chloroplatinic acid yields a chloroplatinate. Narceine forms a distinctive picrate[19] by mixing aqueous solutions of picric acid and narceine. The opium, Roser and Hope–Robinson narceines and their derivatives prepared according to the above procedures have the following melting points: narceine, $C_{23}H_{27}NO_8 \cdot 3H_2O$, m. p. 176–177°, liquefying to an almost colorless melt, decomposing with evolution of gas between 176 and 178°. Sodium narceinate, $C_{23}H_{26}NO_8Na$, m. p. 162–163°. Narceine hydrochloride, $C_{23}H_{27}NO_8 \cdot HCl$, m. p. 192–193°. Narceine chloroplatinate $(C_{22}H_{27}NO_8 \cdot HCl)_2PtCl_4$, m. p. 195–196° (decompn.). Narceine picrate, m. p. 195°. Mixed melting point determinations showed no depression.

The Melting Point of Water-Free Narceine, $C_{23}H_{27}NO_8$.—In view of the difficulties

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[19] Maplethorpe and Evers, *Pharm. J.*, **115**, 137 (1925).

found in completely drying narceine and preventing the extremely hygroscopic material from changing its composition by absorption of water from the air, a current of pure dry nitrogen was passed through capillary tubes containing narceine. The samples were introduced into the middle of the capillary tubes and were enclosed by the regenerating block of the Pregl outfit. They were submitted to two hours of drying in the current of dry nitrogen at 105–110°. The capillary tubes were then sealed by a point flame and after cooling the samples were shaken down to one end. Opium, Roser and Hope–Robinson narceine samples were used. Samples previous to drying, $C_{23}H_{27}NO_8 \cdot 3H_2O$, m. p. 176–178°; samples after drying, $C_{23}H_{27}NO_8$, m. p. 137–138° (to a water white melt). Merck[18] gives 170–171° for the melting point of the hydrated base while Hesse stated that the anhydrous material melted at 140.5°.[20]

Fluorescence Phenomena.—The identity of the various samples of narceine was investigated by examination of the carefully purified samples by means of ultraviolet radiation provided by a Hanovia Universal quartz-mercury arc lamp provided with a filter screen. The filter is of special composition glass which absorbs the visible light and permits the passage of the invisible—consisting largely of the long wave ultraviolet—*but including a narrow band in the extreme violet, just within the border of visibility.* With this extreme violet visible light in mind comparison of various samples was made with the results recorded by Boyle and Fabre[21] who used a ray 365.0 Hg provided by a mercury arc lamp with a thick nickel oxide screen. Most glasses fluoresce and since paper "fluoresces beautifully" under the Hanovia lamp, the air-dried powdered samples were viewed on strips of densely black dull matte paper (from a Bausch and Lomb catalog) which showed no fluorescence whatsoever. Boyle and Fabre had found narcotine and narceine to fluoresce with a clear violet tinge. Examination of narcotine and the three narceines showed them to act alike and to exhibit a very faint purplish tinge. Whatever may be the interpretation of the variation in the tints observed by us as compared with those reported by Boyle and Fabre, it was established that no difference in fluorescence phenomena exists between the various samples of narceine. When insufficiently purified samples are observed such differences are apparent but the green fluorescence previously exhibited by an impure Hope–Robinson preparation was evidently not due to traces of narcotine. The discrepancy in the descriptions of different workers of the appearance of fluorescence, the misty violet tinge of the mercury light as seen through a Wood's glass filter and the disturbing effects of traces of impurities have recently been the subject of comment by Grant.[22]

Optical Activity.—The three narceines were identical in their behavior, showing no optical activity in either acid or alkaline solution. These findings are contrary to those of Bouchardat and Bondet,[23] who were probably using slightly impure material, and in agreement with those of Hesse.[24]

Narceonic Acid, $C_{21}H_{20}O_8$ (II).—Fifty grams of narceine was heated to a clear solution with 100 cc. of 4% sodium hydroxide, and 12.5 g. of dimethyl sulfate was weighed into a cold solution. The mixture was gently heated in a glass-stoppered flask for two hours on the steam-bath. An excess of concentrated hydrochloric acid was added and the digestion continued as long as the solution deposited crystalline material. After the mixture had cooled and stood overnight, the crude solid was filtered; yield 50 g. of a white crystalline narceine methochloride, m. p. 243°. A suspension of 20 g. of this crude methochloride in 150 cc. of absolute alcohol was refluxed in the hood and 40 cc. of 33% potassium hydroxide was added. The refluxing was continued for one

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[20] Hesse, *Ann.*, **129**, 250 (1864).

[21] Boyle and Fabre, *Compt. rend.*, **178**, 2181–3 (1924).

[22] Julius Grant, *Chemist and Druggist*, **116**, 421 (1932).

[23] Bouchardat and Bondet, *J. pharm. chim.*, [3] **23**, 292 (1853).

[24] Hesse, *Ann.*, **176**, 199 (1875).

and one-half hours until the emission of trimethylamine ceased. The clear orange solution was filtered and diluted with water. This dilute alkaline solution was added slowly with efficient stirring to about 1.5 liters of dilute hydrochloric acid. The pure white precipitate was filtered and washed. After air-drying the crude material weighed 16 g. and melted at 217°; recrystallized from butanol, m. p. 217°.

Dihydronarceonic Acid, $C_{21}H_{22}O_8$.—Ten grams of narceonic acid (0.025 mole) was heated to a clear solution with 150 cc. of methanol and 15 cc. of dioxane. To this clear warm solution in a magnesium citrate bottle was added 0.2 g. of platinum catalyst. On hydrogenation 0.025 mole of hydrogen were absorbed in about two minutes. After filtration through a sintered glass funnel, the clear solution was added to a large excess of cold distilled water. The white precipitate was recrystallized from hot methanol, m. p. 197–198°; yield 10 g.

Anal. Calcd. for $C_{21}H_{22}O_8$: C, 62.69; H, 5.47. Found: C, 62.53; H, 5.28.

Esters of Narceonic Acid.—Though attempts to esterify narceonic acid by refluxing alcoholic solutions with dry hydrochloric acid failed, the esters were formed by refluxing the silver salt, $C_{21}H_9O_8Ag$, with methyl and ethyl iodides. The resulting products when recrystallized from their respective alcohols yielded methyl narceonate, m. p. 155°, and ethyl narceonate, m. p. 139–140°.

Anal. Calcd. for $C_{22}H_{22}O_8$: C, 63.77; H, 5.31. Found: C, 63.48; H, 5.14.

Anal. Calcd. for $C_{23}H_{24}O_8$: C, 64.48; H, 5.61. Found: C, 64.50; H, 5.80.

Methyl Dihydronarceonate (III).—By refluxing dihydronarceonic acid dissolved in methanol containing about 4% of hydrochloric acid esterification took place readily. The ester was insoluble and crystallized out during the operation. The material held tenaciously a yellow coloration but gave a snow-white product on recrystallization from benzene, m. p. 155°.

Anal. Calcd. for $C_{22}H_{24}O_8$: C, 63.46; H, 5.77. Found: C, 63.25; H, 5.70.

When 0.3 millimole of III was added to 6 cc. of a solution of MeMgI in isoamyl ether,[25] about half of the material dissolved in the cold without giving off a trace of gas. The substance, therefore, contained no active hydrogen. More dissolved on heating but efforts to get a complete solution were unsuccessful. It was estimated that one mole of the substance reacted with three moles of the reagent without giving off any gas.

Bromination of III.—Treatment of a chloroform solution of III with bromine in chloroform, removal of the chloroform and recrystallization of the product from methanol gave $C_{22}H_{23}O_8Br$ containing methanol of crystallization which was removed with difficulty, it being necessary to dry at 80° for one and one-half hours and then at 120° for two hours to yield *methyl dihydronarceonate monobromide*, m. p. 189°.

Anal. Calcd. for $C_{23}H_{23}O_8Br$: C, 53.33; H, 4.65; Br, 16.2. Found: C, 53.37; H, 4.54; Br, 16.6.

Narceine Methoxime.—To a solution of 1 g. of narceine in 50 cc of methanol was added 0.2 g. of $MeONH_2$. The mixture was heated in a bomb tube for 70–80 hours at 118° and then concentrated by evaporation on a steam-bath. The product crystallized out in good yields. It was crystallized from methanol and washed with ether, the crystals disintegrating to a fine crystalline powder which was dried at 100° for three hours, m. p. 190°.

Anal. Calcd. for $C_{24}H_{30}N_2O_8$: C, 60.76; H, 6.33. Found: C, 60.54; H, 6.29.

Summary

1. The identity of opium narceine with that obtained by the conversion of narcotine methyl iodide, chloride and methosulfate has been con-

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[25] Kohler, Stone and Fuson, THIS JOURNAL, **49**, 3181 (1927).

firmed by comparison of the physical properties of carefully purified material.

2. The formulation of narceine as $C_{23}H_{27}NO_8 \cdot 3H_2O$ has been definitely established by quantitative determination of the water of crystallization content and analyses of the dehydrated material.

3. Dihydronarceonic acid, its methyl ester and the methyl and ethyl esters of narceonic acid have been prepared.

4. Although attempts to alkylate the methylene group and to effect the reduction of the CO group by catalytic hydrogenation were unsuccessful, the lack of active hydrogen in methyl dihydronarceonate, its behavior on bromination and the formation of narceine methoxime confirm the formulation of narceine as a highly substituted desoxybenzoin.

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The Reaction between Acid Chlorides and Ethers in the Presence of Zinc Chloride

BY L. P. KYRIDES

Descudé[1] reported that on mixing acetyl chloride and anhydrous ethyl ether with a sufficiently large amount of zinc chloride a violent reaction took place immediately which needed to be kept under control by means of external cooling. On working up the reaction mixture he obtained ethyl acetate and ethyl chloride in yields approximating 90 and 67%, respectively, on acetyl chloride, based on the equation

$$CH_3COCl + (C_2H_5)_2O \longrightarrow CH_3CO_2C_2H_5 + C_2H_5Cl$$

The author, furthermore, makes the statement that "the yields are almost theoretical."

Wedekind and Hauessermann[2] obtained a 50% yield of ethyl benzoate from benzoyl chloride and excess of ether in presence of large amounts of sublimed ferric chloride.

Recently H. W. Underwood, Jr., has extended the study of this reaction, stressing the catalytic action of zinc chloride. He and Wakeman[3] have refluxed the acid chlorides mixed with a slight excess of anhydrous ethers in presence of relatively substantial amounts of zinc chloride and isolated the corresponding esters in some instances in as high as 79% of the theoretical yield.

The amount of alkyl chlorides isolated by Underwood and Toone[4] was far from that which is required by Descudé's equation. The authors, in

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(1) Descudé, *Compt. rend.*, **132**, 1129 (1901).

(2) Wedekind and Haussermann, *Ber.*, **34**, 2081 (1901).

(3) Underwood and Wakeman, THIS JOURNAL, **52**, 387 (1930).

(4) Underwood and Toone, *ibid.*, **52**, 391 (1930).