prepared by recrystallization from methanol was obtained as colorless prisms, m.p. 231–232°; λ_{max} (log ϵ), 219* (4.33), 225 (4.40), 242 (4.33), 272 (4.38), 278* (4.35), 308* (3.76), 323 (3.83), 338 (4.11), 354 mμ (4.26).

Anal. Calcd. for $C_{14}H_{12}ClNO_4$: C, 57.25; H, 4.12; N, 4.77. Found: C, 57.49; H, 4.43; N, 4.87.

The **picrate** crystallized from methanol as yellow needles, m.p. 177–178.5°.

Anal. Calcd. for $C_{20}H_{14}N_4O_7$: C, 56.87; H, 3.34; N, 13.27. Found: C, 56.60; H, 3.21; N, 13.38.

10(?)-Methylbenzo[*a*]quinolizinium Perchlorate (II, R_2 = CH_3).—This was prepared in a similar manner to its isomer (II) from 2 g. of 2-(3-tolyl)pyridine and 2 g. of chloroacetaldoxime. The perchlorate was crystallized from methanol (charcoal); yield 2 g. (61%), m.p. 221–224°. Recrystallization three times from methanol gave the analytical sample as colorless prisms, m.p. 231–232°; λ_{max} (log ϵ) 218* (4.25), 224 (4.32), 236* (4.36), 240 (4.37), 264 (4.17), 276* (4.20), 284 (4.30), 330 (3.63), 344 (3.94), 360 mμ (4.09).

Anal. Calcd. for $C_{14}H_{12}ClNO_4$: C, 57.25; H, 4.12; N, 4.77. Found: C, 56.85; H, 4.12; N, 4.76.

The **picrate** crystallized from methanol as yellow needles, m.p. 210–215°, with previous softening.

Anal. Calcd. for $C_{20}H_{14}N_4O_7$: C, 56.87; H, 3.34; N, 13.27. Found: C, 56.26; H, 3.71; N, 13.02.

11-Methylbenzo[*a*]quinolizinium Perchlorate (II, R_3 = CH_3).—Treatment of 1 g. of 2-(2-tolyl)pyridine with 1 g. of chloroacetaldoxime by the usual procedure over 12 days and heating the quaternization product under reflux for 65 hr. in 20 ml. of hydrobromic acid afforded 0.20 g. (12%) of tan colored crystals, isolated as the perchlorate. Recrystallization from methanol–ethyl acetate gave the product as light tan prisms, m.p. 209–210°; λ_{max} (log ϵ) 220 (4.62), 274 (4.69), 330 (3.77), 344 (3.97), 360 mμ (4.06).

Anal. Calcd. for $C_{14}H_{12}ClNO_4$: C, 57.25; H, 4.12; N, 4.77. Found: C, 57.61; H, 4.35; N, 4.99.

The **picrate** crystallized from methanol as yellow needles, m.p. 184–185°.

Anal. Calcd. for $C_{20}H_{14}N_4O_7$: C, 56.87; H, 3.34; N, 13.27. Found: C, 56.87; H, 3.16; N, 13.36.

1-(2-Oximidoethyl)-2-benzylpyridinium Chloride (III).—A solution containing 2 g. (0.012 mole) of 2-benzylpyridine and 1.8 g. (0.019 mole) of chloroacetaldoxime in 3 ml. of dry tetramethylene sulfone was allowed to stand in a stoppered flask at room temperature. Quaternization proceeded rapidly and after 2 days the crystalline product was collected and recrystallized from methanol–ethyl acetate; yield, 2.2 g. (71%); m.p. 204–206°. Further recrystallization from methanol–ethyl acetate gave the pure compound as colorless prisms, m.p. 205–207°; λ_{max} (log ϵ) 204 (4.17), 264* (3.73), 268 (3.75), 274* mμ (3.70).

Anal. Calcd. for $C_{14}H_{15}ClN_2O$: C, 63.99; H, 5.75; N, 10.65. Found: C, 64.18; H, 5.76; N, 10.95.

Morphanthridizinium Perchlorate (IV).—A solution of 2 g. (0.0074 mole) of the quaternary salt (III) in 20 ml. of 48% hydrobromic acid was heated under reflux for 40 hr. The acid was removed in the usual manner and the red-brown residue taken up in a small volume of water. Addition of perchloric acid gave the perchlorate which separated on cooling as a pale yellow microcrystalline material. Recrystallization from methanol–ethyl acetate afforded the pure product as colorless leaflets; yield, 1.6 g. (81%); m.p. 182–183°; λ_{max} (log ϵ), 225* (4.12), 282 (3.69), 318 mμ (3.83).

Anal. Calcd. for $C_{14}H_{12}ClNO_4$: C, 57.25; H, 4.12; N, 4.77. Found: C, 57.04; H, 4.21; N, 5.06.

5-Methyl-1-(oximidoethyl)-2-(3-methoxyphenoxy)pyridinium Chloride (V).—Quaternization of 1 g. of 5-methyl-2-(3-methoxyphenoxy)pyridine[8] with chloroacetaldoxime followed the usual procedure, and the mixture was allowed to react for 17 days. The solid obtained by trituration with ethyl acetate crystallized from methanol–ethyl acetate as colorless plates; yield, 0.77 g. (66%); m.p. 158–160°; λ_{max} (log ϵ), 222 (3.97), 253* (2.30), 275* (3.53), 281 (3.60), 303 (3.71), 315 * mμ (3.66).

Anal. Calcd. for $C_{15}H_{17}ClN_2O_3$: C, 58.34; H, 5.55; N, 9.07. Found: C, 57.84; H, 5.53; N, 9.38.

The **perchlorate** crystallized from methanol–ethyl acetate as colorless prisms, m.p. 156–157°.

Anal. Calcd. for $C_{15}H_{17}ClN_2O_7$: C, 48.33; H, 4.60; N, 7.52. Found: C, 48.62; H, 4.48; N, 7.67.

3-Methoxy-8-methylpyrido[2,1-*b*]benz[*f*][1,3]oxazepinium Chloride (VI).—The quaternary salt (V) (0.5 g.) was cyclized by heating under reflux in concentrated hydrochloric acid for 24 hr. The acid was removed as usual and the residue recrystallized with difficulty from methanol–ethyl acetate to give a tan powder; yield, 0.25 g. (61%); m.p. 265° dec.; λ_{max} (log ϵ), 289 (3.70), 314 mμ (3.71).

Anal. Calcd. for $C_{15}H_{14}ClNO_2 \cdot 0.5\ H_2O$: C, 63.26; H, 5.23; N, 4.92. Found: C, 63.17; H, 5.58; N, 5.39.

Acknowledgment.—The authors wish to thank Dr. Charles K. Bradsher for his helpful suggestions and continued encouragement.

The Hoesch Condensation of Dihydro-β-tubanol with Benzyl Cyanides

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Several dimethylpyranoisoflavones, *e.g.*, jamaicin,[1] toxicarolisoflavone,[2] osajin,[3] and pomiferin,[3] have been isolated in recent years. However, the syntheses of these compounds have not been reported. This paper presents the Hoesch condensation of dihydro-β-tubanol with benzyl cyanides and the syntheses of 2,2-dimethyl-3,4-dihydropyranoisoflavones.

The Hoesch condensation of dihydro-β-tubanol (I)[4] with benzyl cyanide (II) afforded isomeric phenylacetyldihydro-β-tubanols, having m.p. 145–147 and 81–83°, respectively. On the basis of qualitative tests and spectral data, which are summarized in Table I, the former was found to be 8-phenylacetyldihydro-β-tubanol (III) and the latter to be the 6-phenylacetyl isomer IV. 6-Phenylacetyldihydro-β-tubanol thus obtained was converted into 2,2-dimethyl-3,4-dihydropyrano[5,6–7,8]isoflavone (V), m.p. 162–164°, according to the Späth–Venkataraman method.

2,4-Dimethoxybenzyl cyanide (VI) similarly reacted with I as described, affording 8-(2,4-dimethoxyphenylacetyl)dihydro-β-tubanol (VII), m.p. 117–118°, and 6-(2,4-dimethoxyphenylacetyl)dihydro-β-tubanol (VIII), m.p. 102–104°. According to the procedure mentioned previously the deoxybenzoin VIII was transformed into 2′,4′-dimethoxy-(2,2-dimethyl-3,4-dihydropyrano)[5,6–7,8]isoflavone (IX), m.p. 191–193°.

3,4-Methylenedioxybenzyl cyanide (X) and I gave 6-(3,4-methylenedioxyphenylacetyl)dihydro-β-tubanol (XI), m.p. 95–97°, and an unidentified compound $C_{18}H_{16}O_8$, m.p. 125–127°, under the Hoesch reaction conditions.

It is of interest to note that two 8-substituted dihydro-β-tubanols III and VII are soluble in aqueous alkali, whereas 6-substituted compounds IV, VIII, and XI are insoluble, in agreement with the general property of 2-hydroxydeoxybenzoins. In contrast to the 8-substituted dihydro-β-tubanols III and VII, the 6-substituted compounds IV, VIII, and XI showed an intense color

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[1] O. A. Stamm, H. Schmid, and J. Büchi, *Helv. Chim. Acta*, **41**, 2006 (1958).

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[3] M. L. Wolfrom, W. D. Harris, G. F. Johnson, J. E. Mahan, S. M. Moffett, and B. Wildi, *J. Am. Chem. Soc.*, **68**, 406 (1946).

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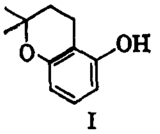
TABLE I

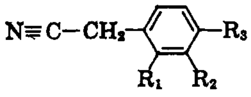
Compound no.	M.p., °C.	Reaction with 2,4-DNP	Solubility in 2 *N* NaOH	Color reaction with $FeCl_3$	$\nu_{C=O}$ in $CHCl_3$, cm.$^{-1}$	λ_{max} (ϵ) in EtOH, mμ
III	145–147	+	Soluble	Negative	1650	235 (12,800) 281 (13,600) 305 (9,600)
IV	81–83	+	Insoluble	Deep violet	1620	234 (13,600) 241 (11,600) s[a] 291 (18,200) 314 (10,700) s
V	162–164				1635	247 (33,100) 302 (24,800) 308 (24,200) s
VII	117–118	+	Soluble	Negative	1660[b]	278 (15,400) 305 (9,400) s
VIII	102–104	+	Insoluble	Deep violet	1615	285 (17,700) 314 (9,000) s
IX	191–193				1635	264 (27,100) 289 (24,100) 308 (21,200) s
XI	95–97	+	Insoluble	Deep violet	1620	289 (19,800) 315 (10,000) s

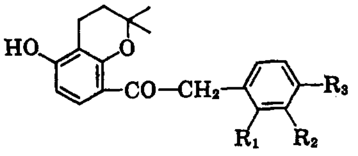
[a] Shoulder. [b] In Nujol.

reaction with ferric chloride, indicating the influence of chelation. This is confirmed by the spectral data; *i.e.*, not only the carbonyl bands in the infrared but also the absorption maxima in the ultraviolet[5] of IV and VIII were shifted toward longer wave lengths than those observed for III and VII, respectively.

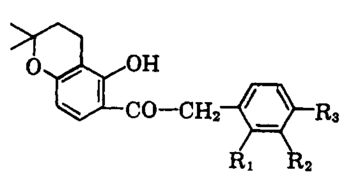


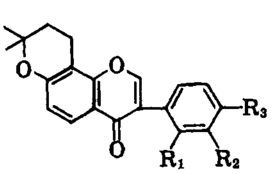
I





II, $R_1 = R_2 = R_3 = H$ III, $R_1 = R_2 = R_3 = H$
VI, $R_1 = R_3 = OMe$; $R_2 = H$ VII, $R_1 = R_3 = OMe$; $R_2 = H$
X, $R_1 = H$; R_2, R_3 = $-OCH_2O-$





IV, $R_1 = R_2 = R_3 = H$ V, $R_1 = R_2 = R_3 = H$
VIII, $R_1 = R_3 = OMe$; $R_2 = H$ IX, $R_1 = R_3 = OMe$; $R_2 = H$
XI, $R_1 = H$; R_2, R_3 = $-OCH_2O-$

Experimental

The Hoesch Reaction of Dihydro-β-tubanol with Benzyl Cyanide.—Into a solution of dihydro-β-tubanol (I) (0.8 g.) and benzyl cyanide (II) (0.8 g.) in a mixture of anhydrous ether (28 ml.) and chloroform (3 ml.) containing anhydrous zinc chloride (2.5 g.) was passed dry hydrogen chloride for 10 min. under ice-cooling, and the mixture was then allowed to stand at room temperature overnight. After removal of the upper ethereal layer by decantation and addition of water to the oily residue, the aqueous solution was heated on a water bath for 2 hr. An oily substance thus formed was extracted with ether, the ethereal solution was washed with 5% aqueous sodium hydroxide, and then the ether was evaporated. Upon crystallizing the residue from ether–pentane (1:1), 6-phenylacetyldihydro-β-tubanol (IV) (0.33 g.), m.p. 81–83°, was obtained.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.75; H, 6.93.

The sodium hydroxide solution described in the preceding preparation was acidified and extracted with ether. After removal of the ether, 8-phenylacetyldihydro-β-tubanol (III) was obtained as colorless prisms (0.28 g.), m.p. 145–147°, upon recrystallization from methanol.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.82; H, 6.82.

2,2-Dimethyl-3,4-dihydropyrano[5,6-7,8]isoflavone (V).—A solution of the deoxybenzoin (IV) (0.377 g.) in ethyl formate (20 ml.) was added dropwise to sodium powder (0.3 g.) under ice-cooling, and the mixture was kept in a refrigerator for 3 days. The reaction mixture was poured into ice-water and the excess ethyl formate was removed under reduced pressure. The product was extracted with chloroform, chromatographed with aluminum oxide (acid washed), eluted with benzene, and distilled *in vacuo* [b.p. 165–171° (0.02–0.012 mm.)]. The distillate was crystallized from 80% ethanol and colorless needles, m.p. 162–164°, were obtained.

Anal. Calcd. for $C_{20}H_{18}O_3$: C, 78.43; H, 5.92. Found: C, 78.52; H, 5.95.

The Hoesch Reaction of Dihydro-β-tubanol with 2,4-Dimethoxybenzyl Cyanide.—The Hoesch reaction of dihydro-β-tubanol (I) (0.8 g.) with 2,4-dimethoxybenzyl cyanide (VI) (1.2 g.) was carried out as described previously and isomeric deoxybenzoin derivatives were yielded. 6-(2,4-Dimethoxyphenylacetyl)dihydro-β-tubanol (VIII) (0.151 g.) showed m.p. 102–104° on recrystallization from 70% ethanol, and the 8-isomer (VII) (0.13 g.), m.p. 117–118°, from aqueous ethanol.

Anal. of VIII. Calcd. for $C_{21}H_{24}O_5$: C, 70.76; H, 6.79. Found: C, 70.98; H, 7.11.

Anal. of VII. Calcd. for $C_{21}H_{24}O_5$: C, 70.76; H, 6.79. Fooound: C, 70.63; H, 6.92.

2′,4′-Dimethoxy-(2,2-dimethyl-3,4-dihydroyrano)[5,6-7,8]isoflavone (IX).—Cyclization of the deoxybenzoin (VIII) (0.15 g.) in ethyl formate (10 ml.) with sodium (1.15 g.) was carried out as mentioned, giving a solid substance. The product was refluxed in acetic acid (2 ml.) for 30 min.[6] After cooling, water was added dropwise until no more solid was formed. The solid was collected by filtration and was crystallized from ethanol, m.p. 191–193°.

Anal. Calcd. for $C_{22}H_{22}O_5$: C, 72.11; H, 6.05. Found: C, 71.88; H, 6.22.

The Hoesch Reaction of Dihydro-β-tubanol with 3,4-Methylenedioxybenzyl Cyanide.—The Hoesch reaction of dihydro-β-tubanol (I) (0.8 g.) with 3,4-methylenedioxybenzyl cyanide (X) (1.2 g.) was carried out by the usual method and yielded 6-(3,4-methylenedioxyphenylacetyl)dihydro-β-tubanol (XI) (0.23 g.)

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(5) D. J. Cram and F. W. Cranz, *J. Am. Chem. Soc.*, **72**, 595 (1950).

(6) W. B. Whalley, *ibid.*, **75**, 1059 (1953).

from the alkali-insoluble part. It gave m.p. 95–97° on recrystallization from aqueous ethanol.

Anal. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.66; H, 5.83.

A compound, m.p. 125–127°, was isolated from the alkali-soluble part.

Anal. Calcd. for $C_{18}H_{16}O_8$: C, 60.00; H, 4.48. Found: C, 60.09; H, 4.45.

The Mechanism of Dehydration of β,β-Diphenyl-β-hydroxypropiophenone[1]

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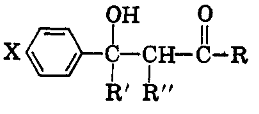
It previously has been demonstrated[3] that, depending on structure, two different mechanisms are available for the dehydration of β-hydroxy ketones. Thus, 4-phenyl-4-hydroxy-2-butanone (I),[3] 4-(*p*-nitrophenyl)-4-hydroxy-2-butanone (II)[3] and β-phenyl-β-hydroxypropiophenone (V)[4] undergo dehydration *via* a mechanism involving a rate-determining enolization step, while 4-(*p*-methoxyphenyl)-4-hydroxy-2-butanone (III)[3] and 4-(*p*-methoxyphenyl)-4-hydroxy-3-methyl-2-butanone (IV)[5] dehydrate *via* a carbonium ion mechanism. The change in mechanism is manifested by a different dependence of the rate on the acidity function H_0 (the carbonium ion mechanism is characterized by linear correlation with H_0 with slope greater than unity) and by different entropies of activation (the carbonium ion mechanism has a less negative entropy by a magnitude corresponding to the absence of involvement of water in the transition state).



I, R = CH_3 R' = H; R'' = H; X = H
II, R = CH_3 R' = H; R'' = H; X = NO_2
III, R = CH_3 R' = H; R'' = H; X = OCH_3
IV, R = CH; R' = H; R'' = CH_3; X = OCH_3
V, R = C_6H_5; R' = H; R'' = H; X = H
VI, R = C_6H_5; R' = C_6H_5; R'' = H; X = H

It was of interest to study the effect that the introduction of a phenyl substituent on the β-position of V would have on the mechanism of the dehydration reaction. The stability of the 1,1-diphenylethyl cation is quite similar to that of the (*p*-methoxyphenyl)ethyl carbonium ion, as estimated from solvolytic data.[6] From the published results of Deno and co-workers[7–9] on arylcarbonium ion equilibria, it is evident that the two carbonium ions are formed, to the extent of 50% from their corresponding alcohols, at 72% and 65% sulfuric acid, respectively. On the basis of these stability estimates for the carbonium ions derived from III and VI, it was expected that the dehydration mechanism would change from the enolization mechanism found in V to a carbonium ion mechanism for β,β-diphenyl-β-hydroxypropiophenone (VI). We have, in fact, found this to be the case.

Rates of dehydration for VI were measured under conditions similar to those used previously. In order to facilitate solubility of VI in the reaction medium, we used a 5% dioxane–95% aqueous sulfuric acid medium. This solvent system has been shown[10] to be useful for H_0 comparisons, and the H_0 scale established in it. Even so it was necessary to carry out measurements with extremely dilute solutions of VI (about 10^{-6} *M*) using 10-cm. cells.

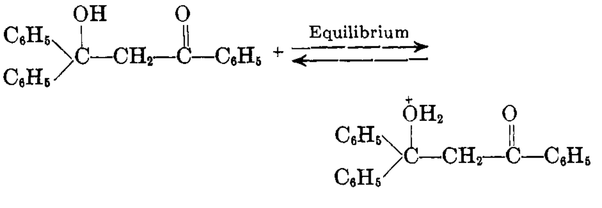
TABLE I

RATE OF DEHYDRATION OF β,β-DIPHENYL-β-HYDROXYPROPIOPHENONE in 5% DIOXANE–95% AQUEOUS SULFURIC ACID

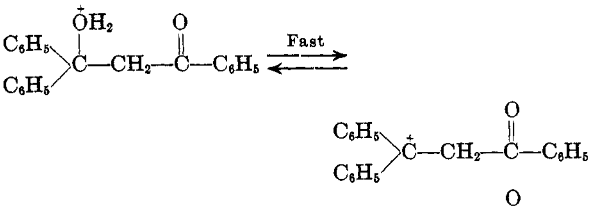
H_2SO_4, *M*	H_0	*k*, sec.$^{-1}$	log *k* + H
		(T = 25.00°)	
1.42	−0.45	1.54×10^{-1}	−5.26
2.56	−1.04	6.20×10^{-1}	−5.25
2.87[a]	−1.15	$8.50 \pm 0.10 \times 10^{-2b}$	−5.22
3.35	−1.42	1.80×10^{-4}	−5.17
3.94	−1.71	4.12×10^{-4}	−5.10
4.26	−1.87	7.0×10^{-4}	−5.03
4.84	−2.13	1.05×10^{-3}	−5.11
		(T = 45.00°)	
2.87[a]	−1.15	8.60×10^{-4}	

[a] $\Delta H^* = 21.2$ kcal.; $\Delta S^* = -10.9$ e.u. [b] Average of two runs.

The measured rates (Table I) show smooth correlation with the acidity function, the slope of log *k* *vs.* H_0 being 1.15. From the temperature coefficient of the rate the entropy of activation (at H_0 = 0) was determined. The value, −11, is similar to that obtained for other dehydration reactions proceeding *via* a carbonium ion mechanism.[3,11] These two facts provide a sound basis for suggesting that β,β-diphenyl-β-hydroxypropiophenone undergoes dehydration *via* the carbonium ion mechanism, namely, equations 1–3.



(1)



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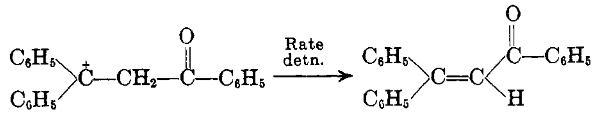

(3)

Further support for the conclusion that dehydration of VI is proceeding *via* the carbonium ion mechanism

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