Anal. Calcd. for $C_{18}H_{12}O_2$: C, 83.0; H, 4.65. Found: C, 82.8; H, 4.71.

The same compound (0.35 g.) (mixed melting point and infrared spectrum) was obtained when 0.5 g. of 4-methoxy-1-phenyl-2-naphthoic acid[8] was boiled for 15 min. with thionyl chloride, and the resulting oily acid chloride was treated with 0.4 g. of aluminum chloride in 5 ml. of benzene.

Chalcone and aluminum chloride in benzene. When a suspension of 70 g. of aluminum chloride in 300 ml. of benzene was treated with 100 g. of chalcone, a smooth exothermic reaction took place during 15 min., forming a bright yellow solid complex. Boiling for 15 min. more gave an orange-red solution, and this was hydrolyzed with iced hydrochloric acid. Most of the benzene was then distilled and replaced with 60–70° ligroin, giving 97 g. of nearly pure β,β-diphenylpropiophenone. The mother liquor was concentrated and treated again with ligroin, giving 21 g. more of the same ketone. The material (17.4 g.) remaining in the second mother liquor was separated by fractional distillation and chromatography into 6.4 g. of β,β-diphenylpropiophenone, 2 g. of diphenylmethane, and 0.29 g. of 3-phenylhydrindone, m.p. 76–77° alone or mixed with an authentic sample.

α-Methylchalcone. A mixture of 5.5 g. α-methylchalcone, 4 g. of aluminum chloride, and 20 ml. of benzene gave an orange-red solution when it was boiled 15 min. Decomposition with iced hydrochloric acid, etc., furnished 5.1 g. of *2-methyl-3-phenylhydrindone*, a colorless oil b.p. 195–198° at 16 mm.

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.4; H, 6.35. Found: C, 86.5; H, 6.30.

Treatment with the calculated amount of bromine in acetic acid, followed by potassium hydroxide in methanol gave a nearly quantitative yield of 2-methyl-3-phenylindone, yellow prisms m.p. 83–84° alone or mixed with an authentic sample.[3]

α-Phenylchalcone. A mixture of 1.5 g. of aluminum chloride and 2.8 g. of α-phenylchalcone in 15 ml. of benzene gave a clear yellow-brown solution after it had been boiled 2 min. There was obtained 2.8 g. of solid product, separated by fractional crystallization from alcohol into 0.9 g. of 2,3-diphenylhydrindone, m.p. 98–100° alone or mixed with an authentic sample,[9] and 1.3 g. of colorless needles m.p. 135–153°. The latter substance was probably largely a stereoisomeric form of 2,3-diphenylhydrindone, since both products gave 2,3-diphenylindone on treatment with oronine and then potassium hydroxide.

α-Bromochalcone. Crystalline α-bromochalcone (1.5 g.) in 10 ml. of benzene containing 1.5 g. of aluminum chloride gave a green-brown solution after 10-min. boiling. There was obtained 1.5 g. of 2-bromo-3-phenylhydrindone which had m.p. 84–87° after crystallization from alcohol.

Anal. Calcd. for $C_{15}H_{11}BrO$: C, 62.7; H, 3.84. Found: C, 62.6; H, 3.92.

This product was a stereoisomer of the compound m.p. 88–90°, obtained by brominating 3-phenylhydrindone.[10] A mixture of the two had m.p. 78–83°; infrared spectra were identical except that the 87° isomer absorbed at 765, 745, and 703 cm.$^{-1}$, whereas in the 90° isomer these bands occurred at 760, 742, and 700 cm.$^{-1}$ Each of the compounds gave 3-phenylindone-semicarbazone, m.p. 205° dec. (reported[11] 212° dec.), characterized by infrared spectra.

α-Carbethoxychalcone. This substance (1.5 g.) reacted rapidly with 2 g. of aluminum chloride in 10 ml. of benzene to form a yellow oily complex which dissolved after the mixture had been boiled for 15 min. There was obtained 1.45 g. of pale yellow product that crystallized completely when it was rubbed with ether. Recrystallization from alcohol gave *2-carbethoxy-3-phenylhydrindone*, faintly pink needles, m.p. 86–88° that gave a blue-violet color with ferric chloride.

Anal. Calcd. for $C_{18}H_{17}O_3$: C, 76.9; H, 6.05. Found: C, 77.1; H, 5.90.

The product was identical (mixed melting point and infrared spectrum) with the one obtained from 2-carbethoxy-3-phenylindone by (a) catalytic reduction[12] or (b) reduction with zinc and acetic acid. Condensation of 3-phenylhydrindone with ethyl carbonate[13] in this laboratory also gave the same substance and not the form m.p. 103–104° reported by the British investigators. The latter form is more likely an allotropic modification than a stereoisomer, for it is difficult to believe configuration would be preserved in a substance so easily enolized. The instability reported by Yost and Burger is not simply steric inversion, as suggested by Baker, and is really not very pronounced. A sample kept in this laboratory for two years had become brown and sticky in spots, but still contained over 50% unchanged material.

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The Stevens Rearrangement in the Benzomorphan Synthesis

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Synthesis of analgesics of the benzomorphan type has been accomplished either by means of the Grewe synthesis[1] as in diagram A, or through a β-tetralone.[2] This note concerns a synthesis based on the Stevens rearrangement of the *N*-benzyl quaternary salt (III) and is diagrammed in B.

The action of basic reagents on quaternary ammonium salts may yield a variety of products depending on the nature of the reactants.[3] A recent example related to this work is that of benzylmethylpiperidinium iodide which with sodium amide in liquid ammonia gave three rearrangement products as a result of aryl- and alkyl-migrations.[4] One of these was 2-benzyl-1-methylpiperidine, obtained in 23% yield. It was felt that in the tetrahydro system (III) the most readily formed ylid would be that conjugated with the double bond and that substitution at the desired site (2- position) might thereby be favored. At present it is not possible to say what percentage of the total re-

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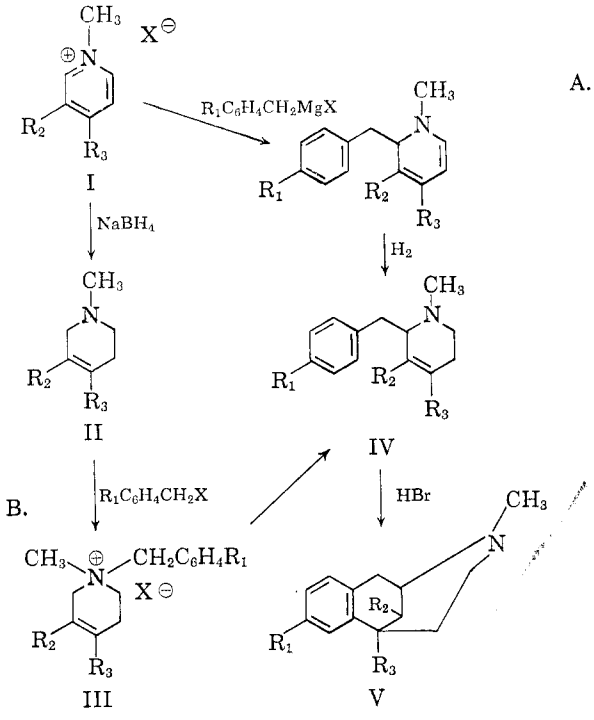

I and II

b. R_2 = H, R_3 = CH_3
c. R_2 = R_3 = CH_3
d. R_2 = R_3 = C_2H_5

III and IV

a. R_1 = H, R_2 = R_3 = CH_3
b. R_1 = OCH_3, R_2 = H, R_3 = CH_3
c. R_1 = OCH_3, R_2 = R_3 = CH_3
d. R_1 = OCH_3, R_2 = R_3 = C_2H_5

V

a. R_1 = H, R_2 = R_3 = CH_3
b. R_1 = OH, R_2 = H, R_3 = CH_3
c. R_1 = OH, R_2 = R_3 = CH_3
d. R_1 = OH, R_2 = R_3 = C_2H_5

arrangement is directed to the 2- position for only the Stevens product IV has as yet been identified.

The tetrahydropyridine bases were easily obtained by sodium borohydride reduction of the *N*-methyl quaternary pyridine salts[5] and then converted to the quaternary salts III. The NMR spectrum of IIIb showed a line at 5.33 p.p.m. due to vinylic hydrogen. No corresponding line was present in the spectra of IIIa and IIIc. Furthermore the line at 1.78 p.p.m. (CH_3—C=C—) was half that of IIIa and IIIc (CH_3—C=C—CH_3) in this region. Thus the correct position of the double bond is assured and its position is also consistent with the results of other work on the hydride reduction of 3-substituted pyridine quaternary salts.[5] Rearrangements with phenyllithium gave in part the desired compounds (IV). Whether a base IV was isolated or was part of a mixture, its structural identification rests on that of the known benzomorphan resulting from ring closure. In one case (IVa) NMR showed no vinylic hydrogen and hence no bond migration.

Although the rearrangement step has not been carefully investigated, yields thus far indicate that the method has no advantage over the older one except that possibly use of the rearranging base is preferable to that of the Grignard reagent utilized in the Grewe synthesis. Yield comparisons are given in the experimental section.

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EXPERIMENTAL

Melting points are uncorrected. Microanalyses are by Paula Parisius of the Analytical Services Unit of this Laboratory, Harold McCann, director. NMR spectra, 60 Mc, are with tetramethylsilane as internal reference standard and deuterchloroform as solvent.

The *N-methyltetrahydropyridines* (II) were prepared in *N* sodium hydroxide solution using a molar equivalent of sodium borohydride. The ratio of solution to the weight of hydride was approximately 50 to 1. If the reduction did not start spontaneously the solution was warmed to *ca.* 50°. The exothermic reaction was gentle and the end was marked by disappearance of yellow color and cessation of effervescence. The bases were recovered with ether and converted to the quaternary salts (III) by addition of the benzyl halide to either an acetone or ether solution of the base.

1-p-Methoxybenzyl-1,4-dimethyl-1,2,5,6-tetrahydropyridinium (IIIb) *chloride*. A mixture of 12 g. (0.05 mole) of γ-picoline methiodide, 100 ml. of *N* sodium hydroxide, and 2 g. of sodium borohydride was stirred (temperature rose to 54° during 15 min.) for 3 hr. Sodium chloride was added and the mixture was extracted thrice with ether. Drying (sodium sulfate) and distillation of the ether at atmospheric pressure gave a quantitative yield of apparently stable IIb which, in 25–30 ml. of acetone, was treated with 9 g. (slight excess) of *p*-methoxybenzyl chloride. After 1 hr. at room temperature and 2–3 hr. at −5° the crystalline chloride IIIb was obtained in a yield of 11 g. (82% from Ib) and was purified from absolute ethanol-ether. Hygroscopic, it was dried at 60°/50 mm. prior to analysis; m.p. 181–182°.

Anal. Calcd. for $C_{15}H_{22}ClNO$: C, 67.27; H, 8.28. Found: C, 67.36; H, 8.37.

1-Benzyl-1,3,4-trimethyl-1,2,5,6-tetrahydropyridinium bromide (IIIa), obtained in 73% yield from Ic was purified from acetone-alcohol, m.p. 206–208°.

Anal. Calcd. for $C_{15}H_{22}BrN$: C, 60.81; H, 7.49. Found: 60.61; H, 7.43.

1-p-Methoxybenzyl-1,3,4-trimethyl-1,2,5,6-tetrahydropyridinium chloride (IIIc) was obtained from Ic in 61% yield. It crystallized from acetone containing a little absolute alcohol in rods of m.p. 169–171°. The somewhat hygroscopic material was dried at 60°/40 mm. for analysis.

Anal. Calcd. for $C_{16}H_{24}ClNO$: C, 68.20; H, 8.58. Found: C, 68.09; H, 8.86.

The iodide was obtained by adding KI to an aqueous solution of the chloride. Purified from alcohol it melted at 175–178°.

Anal. Calcd. for $C_{16}H_{24}INO$: C, 51.48; H, 6.48. Found: C, 51.28; H, 6.47.

1-p-Methoxybenzyl-1-methyl-3,4-diethyl-1,2,5,6-tetrahydropyridinium chloride (IIId), obtained in 39% yield from Id, was purified from acetone and melted at 157–160°. The hygroscopic crystals were dried at 78°, high vacuum, prior to analysis.

Anal. Calcd. for $C_{18}H_{28}ClNO \cdot 1/2\ H_2O$: C, 67.77; H, 9.16. Found: C, 68.06; H, 9.40.

After drying at 135° in high vacuum the weight loss was 2.94% (calcd. for 1/2 H_2O, 2.82%).

Anal. Calcd. for $C_{18}H_{28}ClNO$: C, 69.76; H, 9.11. Found: C, 70.04; H, 9.38.

The 2-benzyl-1,2,5,6-tetrahydropyridines (IV) were prepared by the addition of excess 0.9*N* phenyllithium in ether to the quaternary salts (III). The reaction was exothermic and at its completion (2–4 hr., stirring) the mixture was decomposed with ice and the product recovered by drying and evaporation of the ethereal layer.

2-Benzyl-1,3,4-trimethyl-1,2,5,6-tetrahydropyridine (IVa) is an oil. Its picrate was isolated in 13% yield (9.5% from Ic) and was purified from alcohol. It proved identical with the compound (45% from Ic) isolated in the Grewe synthesis (not characterized in previous publication[2]), m.p. 127–129°.

Anal. Calcd. for $C_{21}H_{24}N_4O_7$: C, 56.75; H, 5.44. Found: C, 56.88; H, 5.45.

2-p-Methoxybenzyl-1,3,4-trimethyl-1,2,5,6-tetrahydropyridine (IVc) is an oil. Its picrate was obtained in 38% yield (23% from Ic). Purified from alcohol it melted at 168–174°.

Anal. Calcd. for $C_{22}H_{26}N_4O_8$: C, 55.69; H, 5.52. Found: C, 55.92; H, 5.40.

2-p-Methoxybenzyl-1,4-dimethyl-1,2,5,6-tetrahydropyridine (IVb) was a constituent of an oil obtained from 9 g. of the chloride IIIb. The base was distilled at 95–105°/0.1 mm., weighed 7.4 g., and was subjected to ring closure.

2-p-Methoxybenzyl-1-methyl-3,4-diethyl-1,2,5,6-tetrahydropyridine (IVd) was part of a mixture. Six grams of chloride IIId yielded after rearrangement 5.4 g. of evaporatively distilled oil (0.07 mm., bath at 150–175°) which was used in the ring closure.

The benzomorphans were prepared by ring closure of IV with 48% hydrobromic acid using the published procedure[2,6] and were identified by melting points, mixed melting points, and infrared spectrograms.

2,5,9-Trimethyl-6,7-benzomorphan (Va) *hydrochloride.* Yield from Ic, this work, 6.5%; yield from Grewe synthesis.[2] 20%.

2′-Hydroxy-2,5,9-trimethyl-6,7-benzomorphan (Vc). Yield from Ic, this work, 18%; yield from Grewe synthesis, 25%.[6]

2′-Hydroxy-2,5-dimethyl-6,7-benzomorphan (Vb). Yield from Ib, this work, 25%; yield from Grewe synthesis, 5%.[7]

2′-Hydroxy-2-methyl-5,9-diethyl-6,7-benzomorphan (Vd). Yield from Id, this work, 11%; yield from Grewe synthesis, 12%.[8]

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Reaction of Propene-1-C^{14} with Maleic Anhydride

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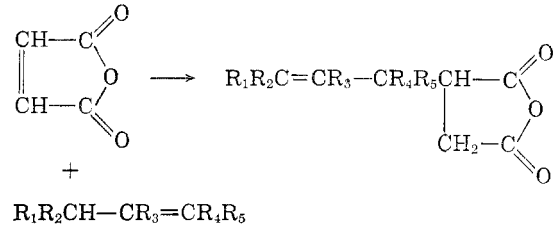
In conjunction with a study involving labeled propene, propene-1-C^{14} was condensed with maleic anhydride. Reactions of this nature between mono-olefins and dienophiles have been known for some time.[2–4] The similarity between these reactions and the familiar Diels-Alder condensation involving a diene is obvious. However, it is likewise apparent that it is impossible to draw a rigid analogy between the reaction mechanism of mono-olefins and those postulated for dienes.[5] The localization of the double bond, the lack of secondary bonding electrons, and the transfer of hydrogen during the course of the reactions are significant differences which must be considered in the case of mono-olefins.

Although the first investigators assumed these reactions were examples of addition of an acidic hydrogen across a double bond,[2,3] it has later been shown that for many unsymmetrical mono-olefins of the type $R_1R_2CH{-}CR_3{=}CR_4R_5$, the reaction proceeds with migration of the double bond as illustrated below.



$R_1R_2CH{-}CR_3{=}CR_4R_5$

This bond migration has been variously attributed to an initial formation of a rearranging ionic or free radical intermediate of the olefin which then reacts in its more stable form,[2] and to a cyclic six-membered transition state involving a concerted mechanism.[6–8]

For those symmetrical olefins which have been studied (*e.g.*, propene, isobutylene, 2-pentene, cyclopentene, and cyclohexene), the product which would be obtained by the "direct" mechanism[6] without migration of the bond, and that obtained by the "indirect" mechanism with migration are identical. Consequently studies of the structure of the product do not aid in elucidating the mechanistic route of the reaction.

When propene-1-C^{14} was condensed with maleic anhydride and the adduct (I) saponified, allylsuccinic acid (II) was obtained with an activity of 5.48 ± 0.01 mc./mole. Ozonolysis of this product followed by oxidation yielded 3-carboxyglutaric acid (III) of activity 5.45 ± 0.01 mc./mole.

These results confirm the migration of the double bond. The lack of scrambling in the adduct is in

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