A Novel Synthesis of Dihydrojasmone

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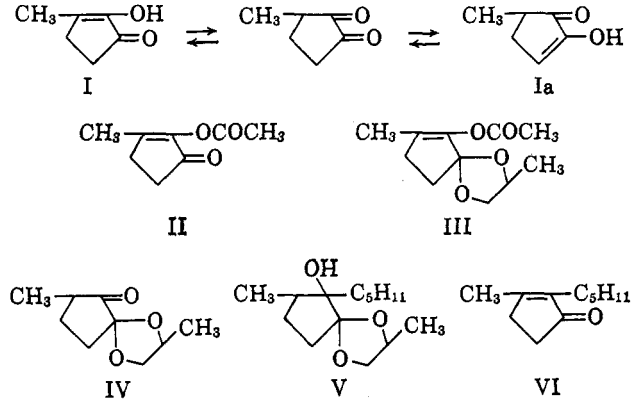
3-Methylcyclopent-2-en-2-ol-1-one (I), a readily available substance of natural occurrence, may be utilized in the preparation of dihydrojasmone. The synthesis is described, and confirms structure I assigned to this enol.

Dihydrojasmone (VI) was first synthesized by Staudinger and Ruzicka[1] by a Dieckmann ring closure of the necessary dicarboxylic ester, and has since been prepared by several general methods. Dihydrojasmone was obtained by the catalytic hydrogenation of the well-known natural product, jasmone,[2,3] and by the reduction of 4-chlorotetrahydropyrethrone,[4-6] a derivative of pyrethrolone obtained from pyrethrin. Various methods have been described[7-14] utilizing γ-hexyl-γ-methylbutyrolactone and also the closely related paraconic acid, which upon dehydration yield dihydrojasmone. Decarboxylation[11,13] of the paraconic acid has been accomplished prior to, or simultaneous with, the dehydration step. VI has also been obtained by the cyclization of 2,5-undecanedione[15-17] or its carbethoxy derivative.[18]

In this investigation it is shown that dihydrojasmone may be synthesized from 3-methylcyclopent-2-en-2-ol-1-one (I), a readily available substance of natural occurrence which was first isolated by the dry distillation of beech wood[19] and later was found in the acetic oil fraction of pyroligneous acid,[20] in tall oil,[21] and in a number of soluble wood tars.[22,23] It was also obtained by the alkaline hydrolysis of spruce wood,[24] and recently has been identified as an important component in the coffee bean.[25] Reported syntheses of this compound include dehydrogenation of divinyl glycol[26] over copper at 280°, hydrolysis of the 5,5-dichloro derivative of 2-methylcyclopentanone,[27] and methylation of the condensation product of ethyl oxalate and ethyl glutarate, followed by decarboxylation.[28]

There has been some controversy with regard to the correct structure of this compound. Early evidence[19,29,30] supported the enolic structure (I). Almost 30 years later, evidence[31] which seemed compelling was presented to show that the enol structure of the diketone was not 3-methylcyclopent-2-en-2-ol-1-one (I) as earlier reported, but the enolic structure (Ia). The question of structure was resolved recently[32] by n.m.r. spectral studies of this substance which demanded the structure, 3-methylcyclopent-2-en-2-ol-1-one (I).

Similarities in the structures of 3-methylcyclopent-2-en-2-ol-1-one (I) and dihydrojasmone (VI) prompted this investigation to determine the feasibility of converting I into VI.



The success of the synthesis depended primarily upon the acquisition of the ketone ketal IV. Attempts to obtain IV directly from 3-methylcyclopent-2-en-2-ol-1-one (I) proved unsuccessful. An investigation of the literature[33] revealed that cyclic ketals had been obtained in low yield, however, by the action of ethylene oxide on ketones in the presence of catalytic amounts of stannic chloride. Higher yields of cyclic ketals were reported[34] by addition of a mixture of epichlorohydrin and ketone, dissolved in carbon tetrachloride, to a dilute solution of stannic chloride in the same solvent at 20 to 30°. Accordingly, 3-methylcyclopent-2-en-2-ol-1-one (I) was acetylated with acetic anhydride to give 2-acetoxy-3-methylcyclopent-2-en-1-one (II), thus removing the enolic hydrogen and leaving the carbonyl group intact for ketal formation. Of the various oxides investigated, propylene oxide

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proved most suitable. Thus, II reacted with propylene oxide in the presence of stannic chloride to give 2-acetoxy-3-methylcyclopent-2-en-1-one propylene ketal (III) in 53% yield. Saponification of III with 10% sodium hydroxide solution gave the unstable vinyl alcohol which reverted to 3-methyl-1,2-cyclopentanedione 1,1-propylene ketal (IV) in 80% yield.

3-Methyl-1,2-cyclopentanedione 1,1-propylene ketal (IV) is a novel and important compound, since it might very well serve as a precursor to the acquisition of many interesting natural and synthetic products, and it exhibits an interesting case of stereoisomerism. The projection formula of IV might indicate the possibility of two structural isomers, depending upon the mode of addition of propylene oxide. This is not the case, however, since the two rings are in perpendicular planes and IV has only the possibility of existing as four sets of optical enantiomorphs. Thus, reversing the mode of addition of propylene oxide leads only to diastereoisomers.

Upon treatment of IV with *n*-amylmagnesium chloride, followed by hydrolysis with ammonium chloride solution, 2-*n*-amyl-3-methylcyclopentan-2-ol-1-one propylene ketal (V) was obtained, and its physical properties were determined. Dehydration and deketalization of V to yield dihydrojasmone (84%) was accomplished by stirring and refluxing V with 25% sulfuric acid solution, followed by steam distillation.

The infrared spectrum of dihydrojasmone was characterized by absorption bands at 5.85 and 6.05 μ, which were attributed to a conjugated carbonyl and a C=C double bond,[7] respectively. It also exhibited λ_{max}^{EtOH} 236 mμ (ϵ 12,000). The purity of dihydrojasmone (97%), obtained directly from very pure IV or V, seems to be limited only by the purity of the *n*-amyl chloride used. There seems to be no doubt regarding the position of the C=C double bond since the acid dehydration of V to form dihydrojasmone no doubt requires carbonium ion formation and ejection of a tertiary rather than a secondary hydrogen ion. This synthesis confirms structure I assigned to this enol.

There are two steps in the reaction sequence that may be bypassed. II may be converted to IV directly, thus avoiding the isolation of III. In doing this, however, it was found that the yield was impaired slightly and the operations involved in the isolation of IV were cumbersome owing to contaminating products accompanying the formation of the ketal. Also, the isolation of V proved entirely unnecessary and higher yields were obtained by converting IV into VI directly.

The over-all yield of dihydrojasmone (VI) from 3-methylcyclopent-2-en-2-ol-1-one (I), based on the recommended sequence of reactions, I → II → III → IV → VI, was 26%. Obviously, the method may be extended to yield other 2-alkyl-3-methylcyclopent-2-en-1-ones.

Experimental[35]

3-Methylcyclopent-2-en-2-ol-1-one (I).[36]—This substance was obtained as a hydrate, m.p. 77–81°. Purification was accomplished by refluxing the crude material dissolved in benzene in a flask fitted with a Dean–Stark trap until the water was removed. The benzene solution was concentrated by distillation until only a small quantity of solvent remained, and the residue was recrystallized from isopropyl alcohol to give a white solid: m.p. 105.5–106.5° [lit.[29] m.p. 105–106°; m.p. 106–107° (sublimed)]; λ_{max}^{EtOH} 258 mμ (ϵ 710); $\lambda_{max}^{CCl_4}$ 2.83, 2.97, 3.42, 5.80, 5.97, 6.93, 7.08, 7.14, 7.34, 7.77, 8.14, 8.33, 9.00, and 9.77 μ.

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.25; H, 7.31.

2-Acetoxy-3-methylcyclopent-2-en-1-one (II).—A mixture of 336 g. (3 moles) of 3-methylcyclopent-2-en-2-ol-1-one (I) and 918 g. (9 moles) of acetic anhydride was refluxed for 1 hr. The acetic acid and excess acetic anhydride were removed by distillation and the residue was fractionated to yield 435 g. (94%) of a liquid, b.p. 105–106° (3 mm.). Upon standing, the product crystallized very slowly to yield a hard, white solid, m.p. 61.5–62.5°, which gave a negative ferric chloride test. Recrystallization from either benzene, methanol, or water gave crystals: m.p. 62–62.5° [lit.[19] m.p. 65° (water); b.p. 129–130° (12 mm.)]; $\lambda_{max}^{CCl_4}$ 3.41, 5.60, 5.77, 5.97, 6.93, 7.09, 7.22, 7.30, 7.52, 8.38, 9.19, 9.61, and 11.43 μ.

Anal. Calcd. for $C_8H_{10}O_3$: C, 62.32; H, 6.54. Found: C, 62.22, 62.20; H, 6.55, 6.60.

2-Acetoxy-3-methylcyclopent-2-en-1-one Propylene Ketal (III).—To 34 g. (0.13 mole) of stannic chloride dissolved in 150 ml. of carbon tetrachloride was added dropwise (2 hr.) with stirring at 20° a mixture of 200 g. (1.3 moles) of 2-acetoxy-3-methylcyclopent-2-en-1-one (II), 93 g. (1.6 moles) of propylene oxide, and 475 ml. of carbon tetrachloride. The mixture was hydrolyzed by addition of 520 ml. of 10% sodium hydroxide solution. The organic layer was separated, washed with 150 ml. of water, and then dried over anhydrous potassium carbonate. The solvent was removed and the residue was distilled to give 5.2 g. of forerun, b.p. 66–102° (3 mm.); 146 g. (53%) of the product, b.p. 102–107° (3 mm.); and 38 g. of a tarry residue. Refractionation through a 10-in., vacuum-jacketed, packed column gave 136 g. of III: b.p. 104–106.5° (3 mm.); $n^{25}D$ 1.4653; d^{25}_4 1.1004; MR 53.24 (calcd. 53.08); and λ_{max} 3.45, 5.65, 5.85, 6.90, 7.30, 7.54, 7.75, 8.20–8.80, 9.10–9.40, 9.60–9.75, 10.17, 10.77, 11.07, 11.38, 11.83, and 12.75–13.25 μ. The product was shown to be 98% pure by vapor phase chromatographic analysis. Acid hydrolysis of III gave I, m.p. 105–106°, m.m.p. 105–106°.

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60; mol. wt., 212.2. Found: C, 61.93; H, 7.81; mol. wt. (benzene), 197, 201.

3-Methyl-1,2-cyclopentanedione 1,1-Propylene Ketal (IV).—To 450 ml. of 10% sodium hydroxide solution at 25° was added 134 g. (0.63 mole) of 2-acetoxy-3-methylcyclopent-2-en-1-one propylene ketal (III) and the resulting suspension was stirred for 0.5 hr. The reaction mixture was extracted with three 75-ml. portions of ether; the combined ethereal extracts were washed with 50 ml. of water and then dried over anhydrous potassium carbonate. The ether was removed by evaporation, and the clear residual oil was distilled through a 10-in., vacuum-jacketed, packed column to give 86 g. (80%) of IV: b.p. 65.5–66° (3 mm.); $n^{25}D$ 1.4485; d^{25}_4 1.0683; MR 42.63 (calcd. 42.66); and λ_{max} 3.40, 5.70, 6.85, 7.27, 7.45, 7.64, 7.80, 8.37, 8.55, 9.25, 9.30, 9.58–9.87, 10.18, 10.60, 11.13, 11.75, 12.87, 13.14, and 13.98 μ. Vapor phase chromatographic analysis gave a single peak.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.15; H, 8.35.

2-*n*-Amyl-3-methylcyclopentan-2-ol-1-one Propylene Ketal (V).—To an ethereal solution of *n*-amylmagnesium chloride, prepared from 76 g. (0.72 mole) of *n*-amyl chloride and 15.6 g. (0.64 g.-atom) of magnesium, was added over a period of 15 min. 68 g. (0.4 mole) of 3-methyl-1,2-cyclopentanedione 1,1-propylene ketal (IV). The mixture was stirred and refluxed for 15 min. and then poured into a mixture of 250 ml. of a saturated ammonium chloride solution containing 250 g. of crushed ice. The ethereal solution was separated, washed successively with 50 ml. of water, 50 ml. of 1% sodium hydroxide solution, and again with 50 ml. of water, and then dried over anhydrous potassium carbonate. The ethereal solution was concentrated and the residue was fractionated through a 10-in., vacuum-jacketed, packed

(35) Melting points are corrected and boiling points are uncorrected. Microanalyses were determined by Mr. R. L. Seab, of this laboratory. Spectra were recorded on a Perkin-Elmer Model 21 infrared spectrophotometer and a Cary Model 14 ultraviolet spectrophotometer. Gas phase chromatographic analyses were performed on a Barber–Colman Model 20 gas chromatograph using a 100-ft. GE 96 capillary column.

(36) Supplied as "Ketonarome" by Givaudan-Delwanna, Inc., New York, N. Y.

column to yield 12 g. of forerun, b.p. 75–110° (2 mm.), and 70 g. (72%) of V: b.p. 110–111° (2 mm.); $n^{25}D$ 1.4590, d^{25}_4 0.9951; MR 66.52 (calcd. 67.27); and λ_{max} 2.80, 3.90, 6.83, 7.27, 7.60–7.70, 8.62, 9.15, 9.65, 10.27, 10.55, 10.72, and 11.42 μ.

Anal. Calcd. for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.65; H, 10.50.

Dihydrojasmone (VI).—To 38 g. (0.157 mole) of 2-*n*-amyl-3-methylcyclopentan-2-ol-1-one propylene ketal (V) was added 100 ml. of 25% sulfuric acid solution, the resulting suspension was stirred and refluxed for 2 hr., and then the reaction mixture was steam distilled. The organic layer was separated and the water layer was saturated with sodium chloride before extraction with 200 ml. of ether. The combined organic layers were dried over anhydrous magnesium sulfate, the ether was removed, and the residue was distilled to give 22 g. (84%) of dihydrojasmone: b.p. 87–88° (2 mm.); $n^{25}D$ 1.4771; d^{25}_4 0.9157; MR 51.31 (calcd.[37] 50.34) [lit.[2] b.p. 101–102° (5 mm.); $n^{15}D$ 1.48107, d^{15} 0.9201; lit.[9] b.p. 117° (9 mm.); $n^{18}D$ 1.4810, d^{18}_4 0.9165]; λ_{max}^{EtOH} 236 mμ (ϵ 12,000); and λ_{max} 3.43, 5.85, 6.05, 6.93, 7.09, 7.23, 7.40, 7.48, 7.72, 7.90, 8.50, 9.33, 9.84, 10.05, 10.62, 10.80, 12.20, and 13.75 μ. The product was shown to be 97% pure by vapor phase chromatographic analysis.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.61; H, 11.38.

3-Methyl-1,2-cyclopentanedione 1,1-propylene ketal (IV) may be converted into VI directly, thus avoiding the isolation of V, and with profit in yield. From the reaction between 61 g. of IV and *n*-amylmagnesium chloride (prepared from 69 g. of *n*-amyl chloride and 13.6 g. of magnesium), a residue was obtained as described in the preparation of V, which, without further purification, was stirred with 120 ml. of 25% sulfuric acid and then steam distilled. This distillate was worked up and gave 39 g. (65%) of VI, b.p. 86–89° (2 mm.). Refractionation of the odorous material through a packed column gave a product which boiled at 86.5–88° (2 mm.), $n^{25}D$ 1.4771, and was identified as VI by its infrared spectrum.

(37) Uncorrected for exaltation.

Ring-Size Effects in the Neophyl Rearrangement. V. The Carbenoid Decomposition of 1-Phenylcycloalkanecarboxaldehyde Tosylhydrazones

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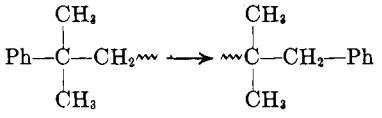
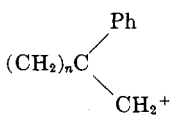
1-Phenylcycloalkylcarbenes (**5**) have been prepared *in situ* by the decomposition of 1-phenylcycloalkanecarboxaldehyde tosylhydrazones with sodium methoxide in N-methyl-2-pyrrolidone at 180° (the aprotic Bamford–Stevens reaction). The ring sizes studied were the three- through six-membered. These reactive intermediates (**5**) rearrange to mixtures of hydrocarbons in good yield, with varying degrees of phenyl migration and alkyl migration (ring expansion). The percentage of phedyl migration (the neophyl rearrangement) was found to increase with increasing ring size, from none in the cyclopropane case to 41% in the cyclohexane case. No evidence of insertion products was found in the hydrocarbon mixtures, although they conceivably could have formed and then rearranged under reaction conditions. The synthesis and properties of the starting aldehydes and tosylhydrazones are discussed, as well as attempted syntheses of possible insertion products. Comparisons are made between the results obtained here and those of related carbenoid systems in the literature.

The neophyl rearrangement is that shown below.

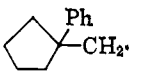


There exist examples of this rearrangement in radical, carbonium ion, and carbene processes. We have been studying the effect of pinning back the *gem*-dimethyl group into rings of various sizes to ascertain the effect such rings have on the ability of phenyl to migrate in all three types of intermediates. These studies show that there are definite differences in the ability of phenyl to migrate in such 1-phenylcycloalkylcarbinyl systems. The past work has involved ring sizes three through seven in the carbonium ion intermediates **1**[2] and ring

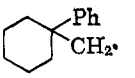


1, $n + 1$ = 3–7 (ring size)

sizes five and six in the radical intermediates **2** and **3**.[3] The ring-size effect in the fused system **2′** (related to **2**) has also been determined.[4] Work has been completed[5]



2



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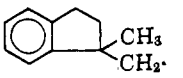
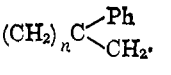


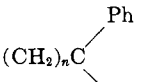
2′

on the radicals shown (**4**) and this will be reported separately at a later date. The present paper presents



4, $n + 1$ = 3, 4, and 7 (ring size)

the results of such ring-size effects in the neophyl carbene rearrangement.[6] Carbene intermediates of structure **5** have been produced and their rearrangement has been studied. The results obtained for ring sizes five



5, $n + 1$ = 3–6 (ring size)

and six in this work substantiate the earlier observations concerning the effect of these rings in neophyl re-

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