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A SIMPLE SYNTHESIS OF DIHYDROJASMONE BY A NOVEL CYCLIZATION OF β,γ-ENONE

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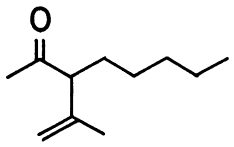
Dihydrojasmone was easily synthesized by bromination of 4-methyl-3-pentyl-4-penten-2-one, which was obtained by the alkylation of mesityl oxide, followed by the treatment with a base.

Recently much attention has been devoted into cyclopentenone synthesis,[2] because of biologically active properties of the derivatives. Most of the synthetic routes presently available are based on the preliminary preparation of 1,4-diketones,[3] which are subsequently cyclized under basic conditions into cyclopentenones so as to form a bond between the 2 and 3 positions in the ring. On the other hand, an example of the cyclization by making a bond between the 1 and 2 positions in the ring is available in the case of the treatment of γ-lactone with phosphorus pentoxide.[4] We wish to report here a simple method for the synthesis of dihydrojasmone by a novel cyclization by forming a bond between the 4 and 5 positions in the ring.

The key step for the jasmone synthesis is the cyclization of 4,5-dibromopentan-2-one with a base. Although 5-chloropentan-2-one[5] and 5-bromo-3,3-dimethylpentan-2-one[6] are known to cyclize under the basic conditions into acetylcyclopropane and a cyclic enol ether, respectively, the cyclization of 4,5-dibromopentan-2-one was found to give cyclopentenone. As an important starting enone, 4-methyl-3-pentyl-4-penten-2-one (**1**) was easily prepared by the alkylation of mesityl oxide using sodium amide in refluxing liq. ammonia.[7] The bromination of the enone with bromine in methylene chloride was performed at -15 °C. After evaporation of the solvent, the residue was treated with 2N sodium hydroxide solution at 55 °C for 16 h to give dihydrojasmone (**2**) in a yield of 61%. As by-products, furan derivative (**3**), 3-pentylmesityl oxide (**4**) and the starting enone **1** were obtained simultaneously. Among several bases examined for the cyclization, sodium amide in liq. ammonia gave also the jasmone in a yield of 62%. The yield of the furan derivative was increased, when an organic solvent was used.

An attempt was made to characterize the intermediate of the process. The addition of sodium hydrogen carbonate after the bromination of the enone gave a comparative stable liquid dibromide **5**, but it could not be purified by the distillation,



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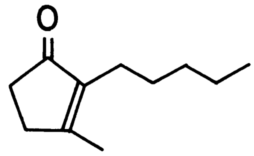

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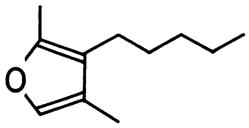

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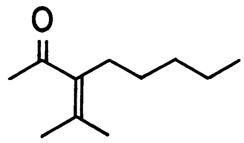

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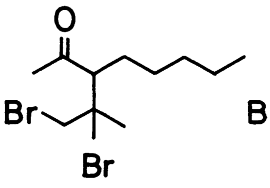
because it decomposed even at room temperature after ca. 10 min. The dibromide **5** showed carbonyl peak at 1720 cm^{-1} in the IR spectrum and the NMR spectrum was consistent with the structure [CCl$_4$, δ 3.87 and 3.80 (each s, 2H for the two peaks), 3.17 (m, 1H), 2.27 (s, 3H), 1.86 (s, 3H), 1.3 (broad s, 8H), and 0.95 (t, 3H)]. The MS spectrum, however, gave only a pattern of the corresponding monodebrominated structure (m/e 249 and 247) and did not show the parent peak. On the other hand, the dibromide obtained by the careful bromination with pyridinium hydrobromide perbromide in pyridine could be purified by the distillation at 80 °C (bath)/0.1 mmHg, and gave correct elementary analysis (Calcd. C. 40.36%, H, 6.21%. Found, C, 40.26%, H, 6.21%).

The cyclization route is uncertain, but it may be speculated from the evidences for the cyclization of 5-halopentan-2-ones.[5,6] An enolate anion of methine side **6** may give an acetylcyclopropane derivative **7** as in the case of the cyclization of 5-chloropentanone.[5] It is considered to be one of the favorable intermediates for the cyclopentenone **2** *via* a ring expansion. An alternative intermediate, γ-bromo-α,β-enone **8**, may also be derived from the anion **6**, and may give **2** in the presence of a base. On the other hand, an enolate anion of methyl side **9** may give the furan derivative **3** as speculated from the cyclization of 5-bromo-3,3-dimethylpentanone.[6]



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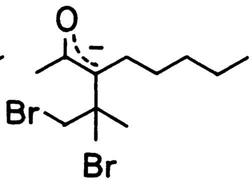

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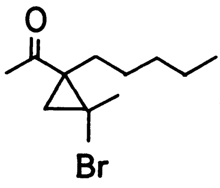

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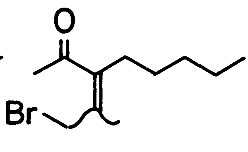

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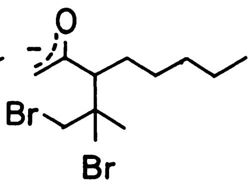

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The analogous β,γ-enones with similar alkyl substituents gave also cyclopentenone derivatives, and one with longer alkyl substituent resulted in lower yield of cyclopentenone and increased the formation of the corresponding furan derivative.

Thus, the cyclization of β,γ-enones, which are easily obtained from mesityl oxide, offers a convenient and general synthetic method for various cyclopentenones.

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References

1. Chemistry Department of Resources, Mie University, Tsu, Mie 514.
2. R. A. Ellison, *Synthesis*, **1973**, 397; T.-L. Ho, *Synth. Commun.*, **4**, 265 (1974).
3. G. Rio and M. A. Lecas-Nawrocka, *Bull. Soc. Chim. France*, **1976**, 317.
4. R. L. Frank, P. G. Arran, J. W. Richter, and C. R. Vanneman, *J. Am. Chem. Soc.*, **66**, 4 (1944).
5. R. A. Bartsch and D. M. Cook, *J. Org. Chem.*, **35**, 1714 (1970).
6. H. O. House, W. V. Phillips, T. S. B. Sayer, and C.-C. Yau, *J. Org. Chem.*, **43**, 700 (1978).
7. M. Matsui, T. Yoshida, and H. Mori, *Agr. Biol. Chem.*, **28**, 94 (1964); G. Büchi and H. Wüest, *J. Am. Chem. Soc.*, **96**, 7573 (1974).

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