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THE REGIOSPECIFIC SYNTHESIS OF VICINALLY DIALKYLATED CYCLOPENTADIENES AND ITS APPLICATION TO A SYNTHESIS OF ALLETHROLONE

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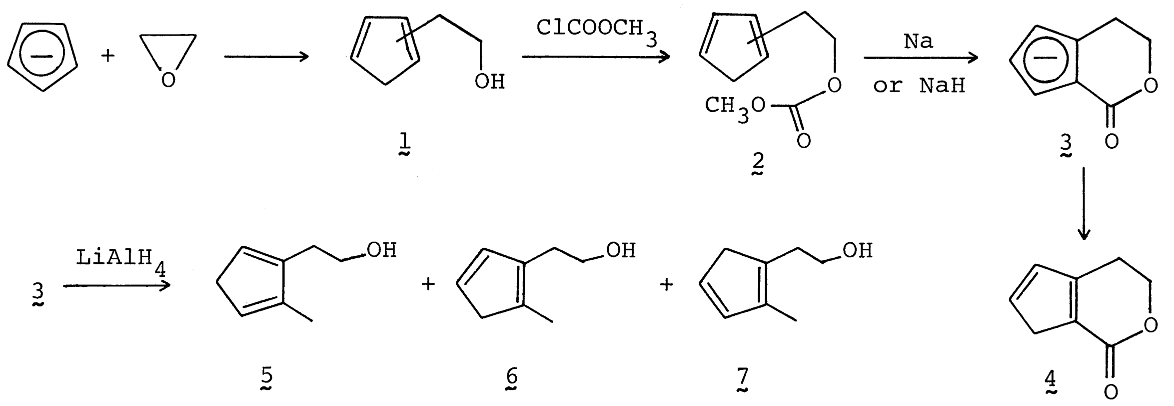
A method for the selective introduction of two alkyl groups into the vicinal positions of cyclopentadiene was investigated by treating esters of cyclopentadienylethanols, prepared from sodium cyclopentadienide and epoxide, with a base, followed by reduction with lithium aluminum hydride. 2-(2-Methylcyclopentadienyl)ethanol thus obtained was transformed to allethrolone via several steps.

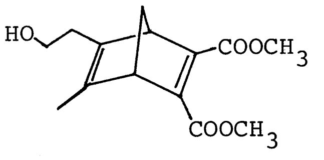
Several five-membered carbocyclic compounds having two alkyl chains at the vicinal positions are known as physiologically active natural products; e. g. prostaglandins,[1)] pyrethroids,[2)] brefeldin A,[3)] jasmonoids,[4)] and so on. Although the most simple and reactive five membered carbocyclic compound is cyclopentadiene, there is no report on the selective method for the introduction of two alkyl chains into the vicinal positions of the diene. On the other hand, an intramolecular cyclization of a carbonate ester of cyclopentadienylethanols was recently reported[5)] from our laboratory to give cyclopentadienolactones in good yields, and the method was applied to the synthesis of C_9-terpene lactones. We now report here a novel method for the regiospecific introduction of two alkyl chains into the vicinal positions of cyclopentadiene by the intramolecular cyclization and reduction.

Treatment of carbonate ester(**2**) of cyclopentadienylethanol(**1**), which was derived from sodium cyclopentadienide and ethylene oxide, with metallic sodium or sodium hydride at 45°C in dimethoxyethane gave the anion(**3**) of cyclopentadienolactone by an intramolecular cyclization.[5)] Addition of the anion **3** into the suspension of lithium aluminum hydride in dimethoxyethane gave an oily product: MS, m/e 124 (M^+); ν_{max} 3340, 1380, and 1040 cm^{-1}; $\delta(CCl_4)$ 1.9(broad s, 3H), 2.5(broad s, 3H), 2.9(broad s, 2H), 3.7(q, 2H), and 6.2(m, 2H). The signal at δ1.9 was assigned to an allylic methyl proton and no peak attributable to carbonyl group was observed in the ir



spectrum. The spectral data show that the product is 2-(2-methylcyclopentadienyl)-ethanol obtained by reducing the carboxylate group of the lactone 3 to the methyl group (95% yield from 2). The similar type of the reduction with lithium aluminum hydride has been already reported on the reduction of fulvene-aldehyde in which a formyl group was converted to a methyl group.6) While methyl group was introduced at a vicinal position of the hydroxy group on the cyclopentadiene ring as shown by the fact that the anion 3 gave cyclopentadienolactone(4),5) it consists of a mixture of three types of isomers for the double bonds in the ring 5, 6 and 7 as suggested by the existence of two protons for the olefinic signal at δ6.2.

The ratio of the isomers was examined by the Diels-Alder reaction and by the 1,4-addition reaction with singlet oxygen. The reaction of the mixture of the isomers with dimethyl acetylenedicarboxylate at room temperature gave the adducts 8, 9 and 10.7) The ratio of the isomer 5, 6 and 7 was calculated as ca 2:1:1 from the integral ratio for bridge head methyl, allylic methyl and olefinic protons in the nmr spectrum of the adducts. On the other hand, the oxygen transfer reaction was carried out by the sequence of protection of the primary hydroxy group with methyl chloroformate, photosensitized oxygenation in the presence of rose bengal at -20～-30°C, reduction with thiourea8) and acetylation of the diol formed.



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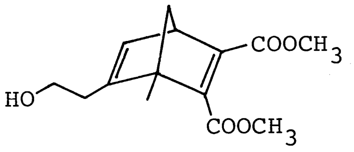

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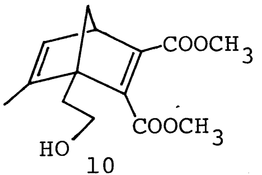

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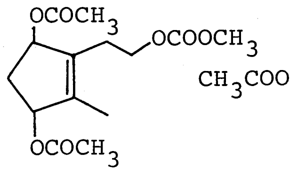

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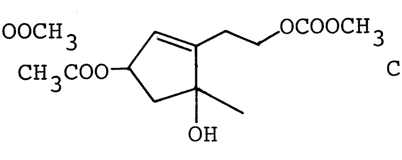

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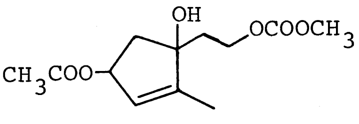

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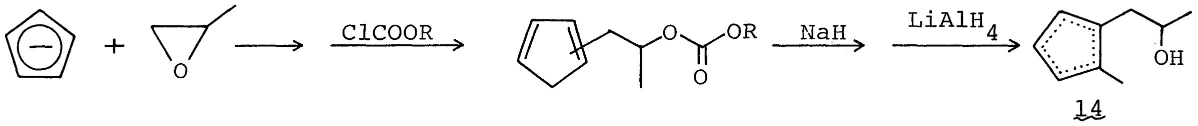
Products 11, 12 and 13[9] were separated by a column chromatography to show the ratio of 5, 6 and 7 to 1:1:1. Although the result is different from that obtained by the reaction with dimethyl acetylenedicarboxylate, it has been already reported that the isomer ratio of cyclopentadiene derivatives can change by the reaction conditions of the 1,4-cycloadditions.

Similarly, 1-(2-methylcyclopentadienyl)propan-2-ol(14)[9] was obtained in a high yield from cyclopentadiene and propylene oxide.



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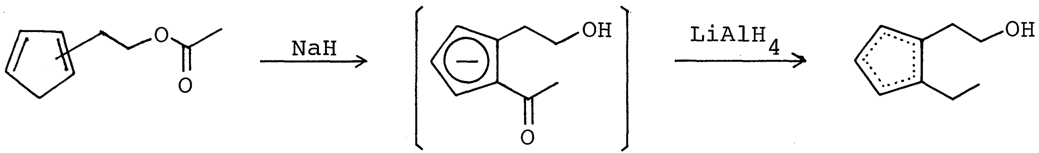
The selective introduction of the methyl group into a vicinal position of hydroxyethyl group in the cyclopentadiene ring by the intramolecular cyclization and reduction was developed to the selective introduction of an arbitrary alkyl group to cyclopentadienylethanol derivatives. Acetic acid ester of cyclopentadienylethanol(15) gave initially 2-(2-acetylcyclopentadienyl)ethanol(16), which was transformed to 2-(2-ethylcyclopentadienyl)ethanol(17)[9] in 89% yield. Thus the method



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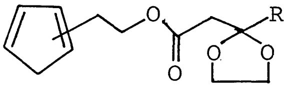
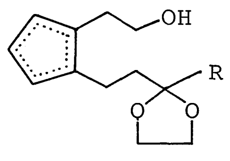
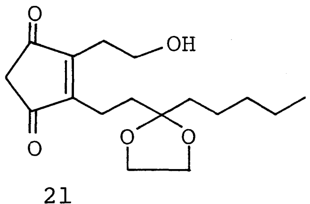
is general for the introduction of two alkyl groups to cyclopentadiene ring at the vicinal positions and can be used widely when functional groups in the alkyl chains are inert to the reaction conditions. The corresponding ester of 3,3-ethylenedioxybutanoic acid(18) gave 2-(2-(3,3-ethylenedioxybutyl)cyclopentadienyl)ethanol(19)[9] in 98% yield. Furthermore, from 3,3-ethylenedioxyoctanoic acid, cyclopentadienylethanol derivative with an eight-carbon chain(20) was obtained in a quantitative yield, whose structure was confirmed by the photosensitized oxygenation and successive oxidation to give cyclopentenedione derivative(21).[9]



18, R=CH_3



19, R=CH_3
20, R=n-C_5H_{11}



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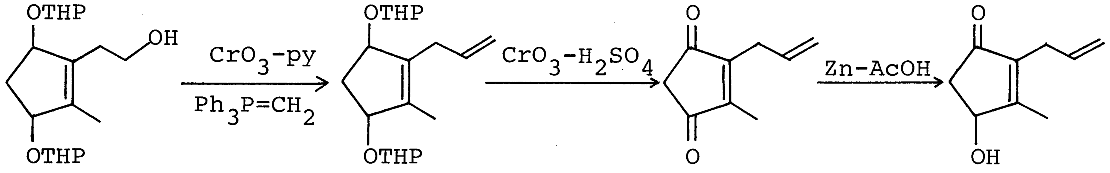
As an application of the method for preparing dialkylated cyclopentadienes, allethrolone(25),11) which is a component of an insecticidal pyrethroid, was synthesized. Tetrahydropyranylated triol(22),12) which was derived from 5, was converted into allylic derivative 23 by the Collins oxidation (92% yield) and the Wittig reaction13) (70% yield). Since the detetrahydropyranylated diol derivative of 23 was unstable under an acidic condition, the dione derivative 24 was directly obtained from 23 by simultaneous deprotection and oxidation under the Jones oxidation conditions (70% yield). The structure of 24 was confirmed by the spectral comparison with the reported data.14) The dione 24 was already reported to transform to allethrolone (25) by the reduction with zinc-acetic acid.14)



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This method thus appears to be of rather general applicability to the synthesis of vicinally dialkylated cyclopentadienes, which has potentiality to prepare the biologically active five-membered carbocycles.

References and Notes

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