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Diels-Alder Reaction of 2-Methyl-2-cyclohexenone and Substituted Butadienes[1]

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Synopsis. Diels-Alder adducts of 2-methyl-2-cyclohexenone and substituted butadienes were obtained in a high yield in the presence of catalytic aluminum chloride.

Eremophilane type sesquiterpenoids possess the basic skeleton (I) and syntheses of these compounds have been reported.[2–5] One of the important problems for elaboration of eremophilane type skeleton is a construction of *cis* fused six-membered rings. Diels-Alder reaction is expected to be a useful method for synthesis of these *cis* fused rings. Although Diels-Alder reactions of 2-methyl-2-cyclohexenone with substituted butadienes have been reported,[6–8] the addition products were generally formed in a low yield. It has been known that some of the Diels-Alder reactions are catalyzed by Lewis acids,[9] but dienes are unstable under these acidic conditions. Now we found that in the presence of catalytic aluminum chloride, Diels-Alder reaction afforded the adducts in a satisfactory yield (Table 1).

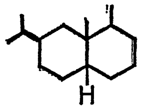
The reaction between 2-methyl-2-cyclohexenone and butadiene proceeded smoothly at room temperature in the presence of one tenth mole of aluminum chloride to dienophile in methylene chloride and adduct (II) was obtained in a good yield (95%). A small amount of hydroquinone was added to prevent polymerization of diene. Under the same reaction condition, however, both reactions of 3-methyl-2-cyclohexenone and 2,3-dimethyl-2-cyclohexenone with butadiene did not give any addition products. On the other hand, the reaction of 2-methyl-2-cyclohexenone with isoprene or piperylene in methylene chloride gave the adducts (III or IV) in a poor yield and a resinous material was obtained. The reason may be due to that the rate of the polymerization of diene is faster than that of the addition of diene to dienophile. In benzene, the adduct, III or IV, was obtained, but the reaction was very slow. When this reaction was carried out in the presence of one forth mole of aluminum chloride to dienophile in benzene, the reaction took place smoothly, and the adducts III and IV were obtained in a high yield. Structures of the adducts described above were determined by NMR.

TABLE 1. DIELS-ALDER ADDITIONS OF 2-METHYL-2-CYCLOHEXENONE AND SUBSTITUTED BUTADIENE IN THE PRESENCE OF $AlCl_3$

Diene	Enone-$AlCl_3$ mol ratio	Solvent	Yield (%)[a]	Product (ratio)
Butadiene	10 : 1	CH_2Cl_2	93	II
	1 : 1	CH_2Cl_2	47	II
			30[b]	II
Isoprene	10 : 1	CH_2Cl_2	20	IIIa
	4 : 1	Benzene	88	IIIa
			64[c]	IIIa(9), IIIb(1)[c][f]
Piperylene	10 : 1	CH_2Cl_2	26	IVa(2.2), IVb(7.8)[e]
	4 : 1	Benzene	76	IVa(2.2), IVb(7.8)
		Toluene	17[d]	IVa(2.7), IVb(7.3)

a) Based on enone. b) Based on diene, quoted from Ref. 5b. c) Based on diene, quoted from Ref. 7. d) Quoted from Ref. 8. e) Ratio was evaluated from integration of tertiary methyl group in NMR data (Varian 60 MHz). f) See Ref. 10.

These results seem to be of considerable utility for building up *cis* fused rings of eremophilane type sesquiterpenoids and several examples of the successful total syntheses have been reported.[9]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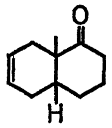
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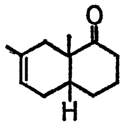
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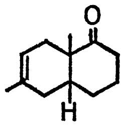
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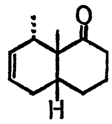
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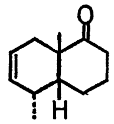
IVb

Experimental

General Procedure. To an ice cooling suspension of $AlCl_3$ in solvent was added dropwise dienophile. $AlCl_3$ was dissolved to give a colored solution, to which hydroquinone was added. The reaction flask was provided with a dry ice condenser, and then butadiene was absorbed in the reaction mixture. After the reaction flask was closed with stoppers, the mixture was stirred at room temperature for several days. The reaction process was traced by gas chromatography. After excess butadiene was recovered, the mixture was extracted with CCl_4. The organic layer was washed with water, dried and concentrated. The residue was distilled to give the adduct.

Reaction of 2-Methyl-2-cyclohexenone and Butadiene. To

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a suspension of 6.5 g (0.048 mol) of powdered anhydrous $AlCl_3$ in 650 ml of CH_2Cl_2 was added 55 g (0.5 mol) of 2-methyl-2-cyclohexenone and then 100 g of butadiene. The mixture was stirred for 4 days. Work-up as described gave 75.5 g (93%) of adduct (II), bp 80—90 °C/5 mmHg (lit,[7b] bp 58—65 °C/0.4 mmHg). IR(neat): 3020, 1725, 1655, 925 cm^{-1}. NMR(CCl_4): 1.08 (s, 3H), 5.58—5.62 ppm (m, 2H).

Reaction of 2-Methyl-2-cyclohexenone and Isoprene. 2-Methyl-2-cyclohexenone (11 g, 0.1 mol) was added to a suspension of 3.3 g (0.025 mol) of $AlCl_3$ in 120 ml of dry benzene. $AlCl_3$ was gradually dissolved to form a paste, to which was added dropwise with ice cooling 20 ml of isoprene. After the mixture was stirred for 2 days, 20 ml of isoprene was added again. Up to the end of the reaction after additional 3 days, a heterogeneous mixture became homogeneous reddish brown. Work-up as described gave 15.6 g (88%) of the adduct (IIIa). IR(neat): 3010, 1705, 995, 920 cm^{-1}, NMR ($CDCl_3$): 1.13 (s, 3H), 1.70 (s, 3H), 5.36 ppm (m, 1H).

Reaction of 2-Methyl-2-cyclohexenone and Piperylene. The adduct (IV) was prepared from 2.2 g (20 mmol) of 2-methyl-2-cyclohexenone, 0.66 g (5 mmol) of $AlCl_3$ and 5 ml of piperylene in 24 ml of benzene. The reaction mixture was stirred for 2 days. After work-up in usual way, the residue was chromatographed on silica gel with CH_2Cl_2 and gave 2.7 g (76%) of IV. The IR and NMR spectra of the mixture of (IVa) and (IVb) matched the published data of that mixture.

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