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CYCLOADDITIONS OF 4-SUBSTITUTED 3,5-DIMETHYL-5,6-DIHYDROANISOLES WITH METHYL ACRYLATE

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The title reactions proceeded smoothly and gave mixtures of four stereoisomeric cycloadducts differing in the configurations at C-8 and C-2, whose relative amounts varied depending on bulkiness of the 4-substituents and reaction temperature used.

The bicyclo[2.2.2]octene system has been employed effectively in natural product synthesis.1) The most straightforward approach to the system uses the Diels-Alder reaction between the title dienes and suitable dienophiles. A recent paper2) on the cycloaddition prompts us to report our result concerning the title reactions, which is described in this communication.

Our results, including those of the reactions with 2-chloro-2-propenenitrile as a dienophile for comparison, are summarized in Table 1. The data indicate that the cycloadditions proceeded in satisfactory practical yields (60-80%) except in two convincible instances and gave a variety of ratios of four stereoisomeric cycloadducts differing in the configurations of C-8 (*syn*- and *anti*-8-CH_3 to the C-2-C-3 bond) and C-2 (*endo*- and *exo*-2-$COOCH_3$). It is emphasized that (i) in contrast to exclusive production of adducts with an *anti*-8-methyl group (*anti*-isomers) in the reactions with 4-unsubstituted1b) and 4-methyl dienes1c) (runs 1 and 2), introduction of ethyl and substituted ethyl groups into C-4 of the starting diene led to formation of *syn*-isomers, and (ii) ratios of the *syn*-isomers to the corresponding *anti*-isomers in the latter reactions increased with lowering temperature. The results are interpreted well by assuming that relative amounts of two transition states leading to the *syn*- and *anti*-isomers parallel nearly those of two extreme conformers in the ground state, whether the cyclohexadiene ring takes a half-chair or a coplanar conformation (Fig. 1).3) There seem not to be any precedents for such temperature dependency of the configuration of cycloadducts.

Fig. 1.

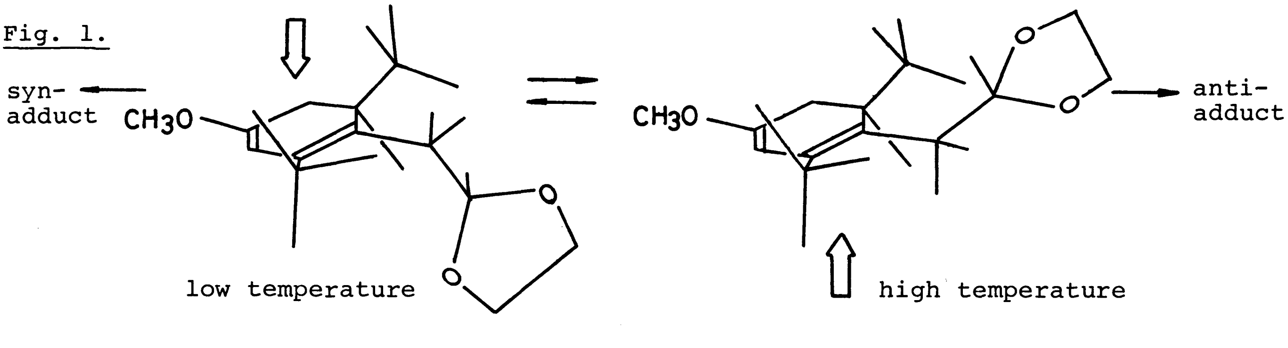
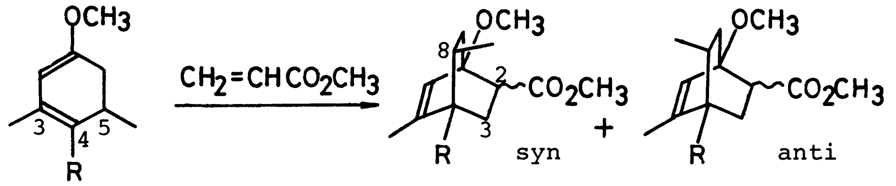


Table 1. Cycloadditions between 4-substituted 5,6-dihydro-3,5-dimethylanisoles and methyl acrylate (runs 1 ∿ 12) and 2-chloro-2-propenenitrile (runs 13 and 14)[a]



Run	Diene[b]	Conditions		Adducts		
	R	temp (°C)[c]	time	yield[d]	syn:anti[e]	endo:exo[e]
1	H[f] ($\Delta^{1,4}$)	155[g]	40 h	24 (31)[f]	0:1	3:1
2	CH_3[h] ($\Delta^{1,4}$)	90[i]	16 h	58 (87)[h]	0:1	---
3	C_2H_5 ($\Delta^{1,4}$)	90[i,j]	8 d	25 (45)	1:1	4:1
4	$CH_2CH_2OCH_3$ ($\Delta^{1,4}$)	80[i]	12 d	22 (71)	2:1	7:1
5	$CH_2CH_2OCOCH_3$ ($\Delta^{1,3}$)	25[k,m]	2 d	46 (66)	3.4:1	1:0
6	($\Delta^{1,3}$)	170[g]	3 d	34 (70)	1.8:1	5:1
7	$CH_2CH(OC_2H_4O)$[l] ($\Delta^{1,3}$)	25[k,m]	2 d	65 (88)	3.2:1	10:1
8	($\Delta^{1,4}$)	90[i,j]	14 d	61 (77)	2.0:1	6.6:1
9	($\Delta^{1,3}$)	150[g]	3 d	60 (78)	1.5:1	5.9:1
10	($\Delta^{1,3}$)	190[g]	4 d	58 (75)	0.9:1	3.2:1
11	$CH_2CH(OC_5H_{10}O)$[l] ($\Delta^{1,4}$)	90[i,j]	16 d	41 (62)	1.5:1	20:1
12	($\Delta^{1,4}$)	180[g,i]	3 d	50 (90)	1.3:1	14:1
13	$CH_2CH_2OCH_3$ ($\Delta^{1,4}$)	120[n]	1 d	45 (67)	1.7:1	exo-CN ?
14	$CH_2CH(OC_2H_4O)$[l] ($\Delta^{1,4}$)	90[i,j]	2 d	57 (72)	2.0:1	exo-CN ?

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a) All reactions were carried out with excess of the dienophiles in neat state at atmospheric pressure, unless otherwise stated. b) Most of the 3,6-dihydroanisoles were prepared by the Birch reduction of the corresponding anisoles and converted into the 5,6-dihydro derivatives by heating or by treatment with dichloromaleic anhydride (DCMA) before or during the cycloadditions. c) Bath temperature. d) The figures in parentheses denote yields based on the recovered dienes. e) Estimated by the NMR spectra. f) Ref. 1b. The ene reaction took place (24%). g) Performed in a sealed tube. h) Ref. 1c. i) Performed in the presence of DCMA (1%). j) Performed in benzene. k) Performed at 15 kbar pressure. l) The formulas "OC_2H_4O and $OC_5H_{10}O$" denote "ethylenedioxy and 2,2-dimethyl-1,3-propylenedioxy groups," respectively. m) Performed in ether. n) Performed in toluene.

References and Notes

1) a) S. A. Monti and Shen-Chu Chen, J. Org. Chem., 44, 1170 (1979), and references cited therein. b) A. Murai, H. Taketsuru, and T. Masamune, Bull. Chem. Soc. Jpn., 53, 1049 (1980). c) K. P. Dastur, J. Am. Chem. Soc., 96, 2605 (1974).

2) N. C. Madge and A. B. Holmes, J. Chem. Soc., Chem. Commun., 1980, 956.

3) Chemical shifts of the 5-methyl protons (J = 6.5 Hz) of a diene with a substituted ethyl group [R = $CH_2CH(OC_2H_4O)$] at C-4 increased (in δ-value) from δ 0.85 to 0.91 (in DMSO-d_6) with elevating temperature (25 to 150 °C), while those of the 4-unsubstituted diene (R = H) remained unchanged (δ 0.95 to 0.96).

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