This product was subjected to preparative HPLC (Waters Associates, ethyl acetate/MeOH (60:40) as eluent) which gave the pure monomer. However, on checking rotations of different runs of cyclizations we found different values for [α]. Using again the HPLC system but now with CH_3OH and 0.5% $(C_2H_5)N$, we were able to separate the optically active pure monomer and the meso compound: yield 153 mg, 0.4 mmol (8% yield); $[\alpha]^{21}_D$ −89° (c 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.73 (m, 4 H), 2.30 (s, 12 H), 2.66 (m, 18 H); ^{13}C NMR ($CDCl_3$) δ 64.15, 40.70, 32.53, 32.34, 32.24, 31.62, 28.17; mass spectrum, exact mass m/e 382.160 (theory 382.160). Purification was also achieved on a reversed-phase column (Rhodorsyl C8) with water/CH_3OH (10–40% water) and 0.5% CF_3COOH as eluent: ^1H NMR of the bis(trifluoroacetate) salt ($CDCl_3$) δ 1.81 (br s, 4 H), 2.74 (m, 4 H), 2.91 (s, 12 H), 2.95 (m, 12 H), 3.72 (m, 2 H).

2,5,9,12-Tetrathiatridecane (25) was prepared on 5-mmol scale analogously to ref 13 from dithianonane-1,9-dithiol and methyl iodide: yield 95%; ^1H NMR ($CDCl_3$) δ 1.90 (m, 2 H, CH_2), 2.10 (s, 6 H, SCH_3), 2.70 (t, 4 H, CH_2CH_2S), 2.75 (s, 8 H, CH_2S).

Cross-Coupling Reactions. The synthesis of the Grignard reagent of 1-phenyl-1-chloroethane was carried out by two different procedures. Method A: In $(C_2H_5)_2O$ (50 mL) was dissolved 1-phenyl-1-chloroethane (8.4 g, 60 mmol) and the resultant mixture added dropwise to a suspension of freshly activated Mg turnings (1.58 g, 65 mmol) in 50 mL of $(C_2H_5)_2O$; the reaction was started with a crystal of I_2 and held at 0–5 ° during addition of the chloride. The entire Grignard solution was decanted from the unreacted turnings into an addition funnel. The Grignard suspension was added to a suspension of $NiCl_2$ (0.4 mmol), ligand (0.4 mmol), and vinyl bromide (5.36 g, 50 mmol) in $(C_2H_5)_2O$ (10 mL). The Grignard suspension was added at such a rate that the temperature did not rise above −40 °C. The entire solution was stirred magnetically and held under constant N_2 pressure. After addition the solution was allowed to come to 0 °C over a period of 16 h and to room temperature for 1 h. The reaction mixture was hydrolyzed at 0 °C with 1 N HCl solution (50 mL). The resulting mixture was poured into a separatory funnel and the flask rinsed with $(C_2H_5)_2O$ (50 mL). The aqueous HCl layer was drawn off, and the ether layer was again washed with 1 N HCl solution (40 mL) and water. The ether layer was dried over $MgSO_4$. After removal of the solvent the crude material was distilled [bp 90–110 °C (30 torr)], and the sample was then analyzed by ^1H NMR spectroscopy and polarimetry; analytically pure product was obtained by preparative GLC.

Method B differs in the preparation of the Grignard reagent, which was now prepared on a 500-mmol scale as described above. The solid materials were allowed to settle, and then the supernatant solution was removed by syringe prior to reaction, which was carried out as described above.

In both methods an aliquot of the Grignard reagent was removed, hydrolyzed with 1 N HCl solution, and then back-titrated with base. The ratio of Grignard to vinyl bromide in method A is 0.8 to 1. In the case of method B a Grignard to vinyl bromide ratio of 2:1 is used.

Registry No. **2**, 672-65-1; **3**, 593-60-2; **4**, 61474-21-3; **5**, 61045-33-8; **5** (diamide), 105206-81-3; **5** (diamine), 105206-82-4; **6**, 90633-68-4; **7**, 105206-80-2; **8**, 105206-84-6; **8** (amide), 105206-83-5; **9**, 105307-25-3; **9** (dithiol), 68170-33-2; **11a**, 105206-90-4; **11e**, 105206-91-5; **11c**, 105206-92-6; **12a**, 90633-69-5; **12b**, 105206-85-7; **12c**, 105206-86-8; **12d**, 105206-87-9; **12e**, 105206-88-0; **12f**, 105206-89-1; **13**, 90633-71-9; **14**, 87338-21-4; **15a**, 3570-55-6; **15b**, 25423-55-6; **15c**, 25676-62-4; **15d**, 60147-09-3; **15e**, 14970-87-7; **16a**, 79130-37-3; **16b**, 56187-04-3; **17a**, 105206-93-7; **17b**, 90633-72-0; **17c**, 105206-94-8; **17d**, 105206-95-9; **17e**, 105229-63-8; **18a**, 87338-20-3; **18b**, 105206-96-0; **19a**, 105206-97-1; **19b**, 95954-69-1; **19c**, 105229-64-9; **20a**, 103747-96-2; **20b**, 103747-98-4; **20c**, 103747-99-5; **21a**, 103747-89-3; **21b**, 105206-99-3; **21c**, 103747-91-7; **21d**, 103747-92-8; **21e**, 103747-93-9; **21f**, 103747-94-0; **22**, 52-90-4; **23a**, 103748-00-1; **23a** (diacid), 105229-65-0; **24**, 103747-95-1; **25**, 105207-00-9; C_2H_5SH, 75-08-1; C_6H_5SH, 108-98-5; CH_3I, 74-88-4; $C_6H_5CH_2SH$, 100-53-8; (L)-$C_6H_5CH_2CH(NH_2)CO_2CH_3$, 2577-90-4; ClCOCOCl, 79-37-8; $ClCO(CH_2)_2COCl$, 543-20-4; $ClCOCH_2OCH_2COCl$, 21062-20-4; $Br(CH_2)_2Br$, 106-93-4; $HS(CH_2)_2SH$, 540-63-6; $HS(CH_2)_4SH$, 1191-08-8; $NiCl_2$, 7718-54-9.

Diels–Alder Reactions of Cycloalkenones. 11. Regioselectivity of 2-Cyclohexenones[1]

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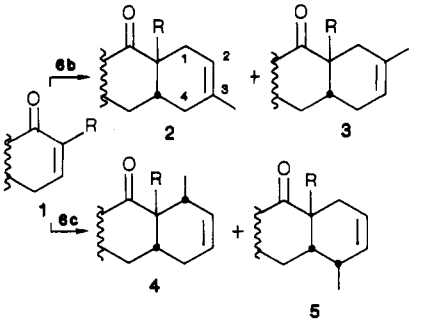
The Diels–Alder reactions of isoprene and 2-methyl-1,3-pentadiene with 2,4-dimethyl-, 4,4-dimethyl-, and 5,5-dimethyl-2-cyclohexenone and 2,4,4-trimethyl-, 2,5,5-trimethyl-, and 2,6,6-trimethyl-2-cyclohexenone under aluminum chloride catalysis are described. Structure analysis of the adducts by NMR spectroscopy is presented. The relationship between the *gem*-dimethyl site and the regioselectivity and diastereoselectivity of the cycloadditions is discussed.

In principle, the Diels–Alder reaction of an unsymmetrical diene and/or dienophile can lead to two regioisomeric adducts, e.g., the reactions of ketone 1 with isoprene (**6b**) or (*E*)-piperylene (**6c**) (Scheme I). The Lewis acid catalyzed cycloadditions of alkylated 2-cyclohexenones and these dienes, however, have shown high regioselectivity in favor of adducts of types **2** and **4**, respectively,[3] in accord with frontier molecular orbital theory.[4] An exception has been the reaction of 4,4-dimethyl-2-cyclohexenone (**7a**)

Scheme I



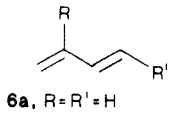
(1) For the previous paper see: Angell, E. C.; Fringuelli, F.; Minuti, L.; Pizzo, F.; Porter, B.; Taticchi, A.; Wenkert, E. *J. Org. Chem.* **1986**, *51*, 2649.

(2) (a) University of California. (b) Università di Perugia.

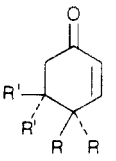
(3) (a) Fringuelli, F.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1982**, *47*, 5056. (b) Angell, E. C.; Fringuelli, F.; Minuti, L.; Pizzo, F.; Porter, B.; Taticchi, A.; Wenkert, E. *Ibid.* **1985**, *50*, 4686. (c) Angell, E. C.; Fringuelli, F.; Halls, T. D. J.; Pizzo, F.; Porter, B.; Taticchi, A.; Tourris, A. P.; Wenkert, E. *Ibid.* **1985**, *50*, 4691.

0022-3263/86/1951-5177$01.50/0

with isoprene (**6b**), which gave a 1:1 mixture of adducts of types **2** and **3**. On the other hand, the introduction of one more double bond into the ketonic ring, i.e., the use



6a, R = R' = H
b, R = Me, R' = H
c, R = H, R' = Me
d, R = R' = Me



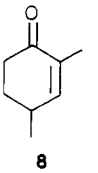
7a, R = Me, R' = H
b, R = H, R' = Me

of 4,4-dimethyl-2,5-cyclohexadienone, leads again to high regioselectivity, albeit unexpectedly with formation of an adduct of structure type **3**.[6] Finally, the 2-carbomethoxy derivative of the dienone interacts with isoprene (**6b**) in such a way as to produce mixtures of adducts of the substitution types **2**[7] and **3**, the **3**/**2** ratio of reactions under the influence of boron trifluoride and stannic chloride being 2.3 and 0.22, respectively.[7] In order to understand these apparently conflicting results and gain more insight into the factors governing Diels–Alder regiochemistry, cycloadditions of several 2-cyclohexenones with the dienes **6** had to be undertaken and the resulting data correlated.

In order to permit the Diels–Alder products to be described in a regiochemically concise and accurate manner, a nomenclature for the adducts is needed. Heretofore the description of the three variously disubstituted benzenes (ortho, meta, and para) was used in the Diels–Alder product field but had encountered difficulties on adducts as simple as those emanating from disubstituted dienes and dienophiles. Thus it now is proposed to change the naming system to one by which the positional relationship of a substituent (derived from a substituted 1,3-butadiene) and the electron-withdrawing group (derived from the dienophile) within the cyclohexene component of the product of a normal Diels–Alder reaction can be recognized easily and identified by a simple number set. The original diene carbons are numbered one through four, the lowest number being closest to the electron-withdrawing group (e.g. the numbering on adduct **2**), and the site of substitution is identified by a number within a bracket in front of the word "adduct". Thus, for example, ketones **2**–**5** are [3], [2], [1], and [4] adducts, the cycloaddition product of cyclopentadiene is a [1,4] adduct, that of 1-vinylcyclohexene a [1,2] adduct and that of 2-methyl-1,3-pentadiene (**6d**) a [1,3] adduct. Finally, to describe the regiochemistry of the products of cycloadditions of dienes with two or more dissimilar substituents may require incorporation of their names in the new notation, e.g., the Lewis acid catalyzed interaction of 2-cyclohexenone with 2-acetoxy-3-(arylthio)-1,3-butadienes having been reported to yield [2(OAc),3(SAr)] adducts.[8]

Diels–Alder Reactions and Products

The reactions of 1,3-butadiene (**6a**), isoprene (**6b**), and 2-methyl-1,3-pentadiene (**6d**) with 4,4-dimethyl-2-cyclohexenone (**7a**),[3a,5,9] 5,5-dimethyl-2-cyclohexenone (**7b**),[1,3a]



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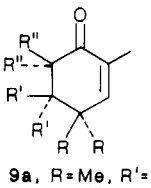
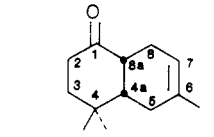


9a, R = Me, R' = R'' = H
b, R = R'' = H, R' = Me
c, R = R' = H, R'' = Me

2,4-dimethyl-2-cyclohexenone (**8**),[10] 2,4,4-trimethyl-2-cyclohexenone (**9a**),[1] 2,5,5-trimethyl-2-cyclohexenone (**9b**),[1] and 2,6,6-trimethyl-2-cyclohexenone (**9c**)[1] were performed in various diene–dienophile combinations under aluminum chloride catalysis in toluene solution at 40–70 °C for 2–80 h and led to 62–96% yields of octalones, as depicted in Tables I and IV. The angularly methylated octalones were kinetically based Diels–Alder adducts, as indicated by the constancy of the product ratios throughout the course of each reaction, and the kinetic basis of the octalones derived from α-unsubstituted 2-cyclohexenones was reflected by the constancy of the ratios of the cis–trans product couples. In the reactions of the latter cyclohexenones the *cis*-octalones undergo bridgehead isomerization into the more stable trans compounds. Base-induced equilibration of the angularly unalkylated bicycles gave trans/cis equilibrium ratios of 9.8, 5.7, and 110 for the **10**–**13**, **11**–**14**, and **12**–**15** ketone pairs, respectively.



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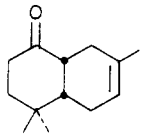

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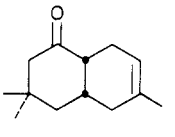

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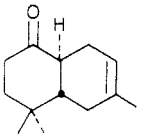

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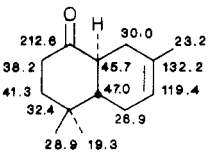

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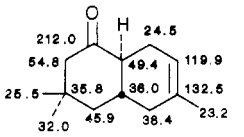
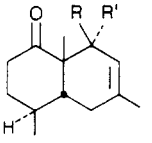
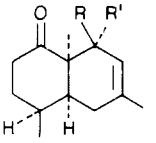


15

The structure of the Diels–Alder adducts (**10**, **11**, **16**–**21**) and the trans isomers (**13**,[3a] **14**, and **15**) were determined



16 **a**, R = R' = H
b, R = Me, R' = H
c, R = H, R' = Me



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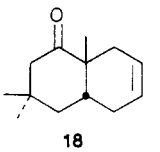

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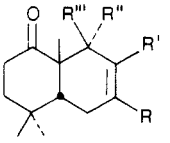
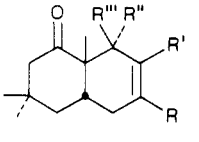
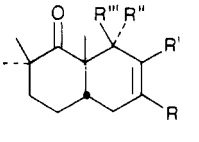


19a-d



20a-d



21a-d

a, R = Me, R' = R'' = R''' = H; **b**, R = R'' = H, R''' = H, R' = Me; **c**, R = R'' = Me, R' = R''' = H; **d**, R = R''' = Me, R' = R'' = H

by ^{13}C NMR spectroscopy, the carbon shifts of the *cis*-octalones being listed in Table II and those of the trans-ketones **14** and **15** appearing on their formulas.

With 4,6-didemethyl-**16a**[3a] and 6-demethyl-**16b**[10] as NMR models the carbon shifts of octalones **16a**, **16b**, **18**,

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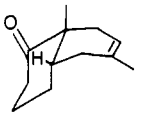
Table I. Aluminum Chloride Catalyzed Diels–Alder Reactions of Dienes 6 with Cyclohexenones 7, 8, and 9[a]

reactants	products	product ratios
6a–9b	**18**	
6b–7a[b]	**10, 11, 13, 14**	1:1.8:6.7:5.8
6b–7b[c]	**12, 15**	1.4:1
6b–8[d]	**16a, 17a**	8:1
6b–9a	**19a, 19b**	1.4:1
6b–9b[e]	**20a**	
6b–9c	**21a, 21b**	13.3:1
6d–8	**16b, 16c, 17b, 17c**	5:15.8:3.3:1
6d–9a	**19c, 19d**	1:1.4
6d–9b	**20c, 20d**	6.2:1
6d–9c	**21c, 21d**	2.7:1

[a] The reaction conditions are listed in Table IV. [b] Reference 5. [c] Two more compounds account for 7.5% of the reaction mixture. They are cis–trans isomers of probably [2] adduct structure. [d] Two more compounds (in 1.5:1 ratio) account for 10% of the reaction mixture. They are anti and syn diastereomers of probably [2] adduct structure. [e] One more product, probably a [2] adduct, accounts for 8% of the reaction mixture.

20a, and **20d** could be assigned easily and their conformation shown to be that indicated in formula **22**. The



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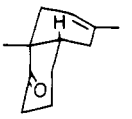


23

3,3-dimethylated ketones within this group reveal the *gem*-dimethyl function by the shielding of C(4a) due to the γ-effect exerted thereon by the 3β-methyl group. 3α,6-Didemethyl-**12**[3a] and 6-demethyl-8α-methyl-**10**[3a] served as models for the analysis of octalones **10** and **11** and 6-demethyl-**17a**[10] and 6-demethyl-**17c**[10] acted in the same capacity for ketones **17a–c**. The five new compounds existed in conformation **23**. The presence of the 8β-methyl group in ketone **17b** was reflected by the shielding of C(4a) as a consequence of the axiality of the methyl function. Application of the above data to the remaining, new octalones permitted their shift assignment and their classification into two categories, octalones **19a,b,d** and **21a,b,d** belonging to conformation **22** with the ketonic ring in a nonchair form and Diels–Alder products **16c**, **19c**, **20c**, and **21c** to conformation **23** with their ketonic ring also in distorted form. Finally, shift assignment and structure analysis of *trans*-octalones followed a well-established routine.[1,10]

[2]–[3] Regioselectivity

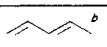
The Diels–Alder reactions of 2-cyclohexenones with (*E*)-piperylene (**6c**) have been shown to proceed exclusively to [1] adducts[1,3,5,10] and with isoprene (**6b**) preponderantly (≥90%) to [3] adducts.[1,3,5,10] As an inspection of Table III reveals, this regiochemical bias has been maintained for the reactions of all geminally dimethylated ketones except for those of the 4,4-dimethyl compounds. The reactions with 2-methyl-1,3-pentadiene (**6d**), a previously uninvestigated diene of both the piperylene and isoprene types, were totally regioselective, showing the compound to imitate the behavior of piperylene. The pentadiene cycloadditions showed high endo selectivity, albeit less than the Diels–Alder reactions of (*E*)-piperylene (**6c**), except for those with the 4,4-dimethylated 2-cyclohexenones. Whereas the regiochemistry of the reactions of the latter ketones with (*E*)-piperylene (**6c**) and the pentadiene **6d** was normal, that of the cycloadditions with isoprene (**6b**), leading to ca. 1:1 mixtures of [2] and [3] adducts, was unexpected.[5] Relatedly, whereas the 4,4-dimethyl ketones

Table II. ^{13}C Chemical Shifts of *cis*-Octalones[a]

	10	**11**	**16a**	**16b**	**16c**	**17a**	**17b**	**17c**	**18**	**19a**	**19b**	**19c**	**19d**	**20a**	**20c**	**20d**	**21a**	**21b**	**21c**	**21d**
C(1)	211.9	211.9	215.7	215.6	216.3	214.7	215.1	214.3	215.4	216.3	216.0	217.5	215.9	215.9	215.9	215.7	219.6	219.4	221.8	217.9
C(2)	37.8	37.8	37.2	37.6	40.3	36.3	35.8	38.2	50.1	34.8	34.8	36.6	35.2	50.1	54.9	50.4	43.3	43.3	43.3	43.5
C(3)	35.5	35.5	34.9	35.5	32.4	29.9	29.5	30.8	34.5	40.6	40.6	35.5	41.5	34.5	32.7	35.0	38.2	38.2	33.8	38.9
C(4)	32.9	32.9	29.6	29.1	29.3	28.0	28.2	28.2	41.8	33.8	33.6	33.0	34.0	42.0	42.7	41.5	25.1	24.8	24.5	24.9
C(4a)	46.4	45.9	47.7	50.3	46.6	46.2	41.3	49.1	35.8	48.7	47.6	50.0	51.8	36.5	36.2	38.7	39.8	38.6	36.8	42.2
C(5)	29.2	24.5	28.7	28.9	28.8	26.6	27.4	26.9	27.7	27.9	23.3	28.5	28.1	32.7	33.2	33.1	33.6	28.8	33.3	33.9
C(6)	131.3	118.6	130.6	130.5	129.1	131.0	129.0	128.9	123.9	131.9	119.3	132.8	131.6	130.6	129.4	130.5	130.5	117.8	129.4	130.1
C(7)	118.6	131.7	116.9	123.9	124.7	119.1	126.5	126.3	122.5	117.5	129.8	126.0	124.4	116.3	124.2	123.4	117.1	132.3	125.4	124.0
C(8)	23.9	28.5	32.3	33.0	37.9	33.5	33.1	40.3	30.6	33.5	37.6	38.1	33.4	31.1	37.5	31.9	31.7	36.0	39.4	30.6
C(8a)	43.4	44.4	46.7	50.8	49.1	47.8	50.3	51.0	46.4	46.4	47.3	49.8	50.9	46.2	48.3	50.2	46.5	46.5	48.8	50.4
2-Me α																	28.6[b]	28.6[b]	27.2[b]	28.2[b]
β																	29.3[b]	29.3[b]	28.9[b]	29.0[b]
3-Me α									32.2					32.2	27.8	32.2				
β									26.2					26.2	32.2	26.5				
4-Me α	27.7[b]	27.8[b]	19.8[b]	20.0	21.3	18.4	18.3	18.4		32.1	32.0	29.8[b]	32.6							
β	26.7[b]	26.7[b]								20.8	20.8	31.0[b]	21.2							
6-Me	23.6		23.7	23.5	23.9	23.4	23.3	23.4		23.5[b]		23.3	23.3	23.7	23.9	23.4	23.6		23.6	23.4
7-Me		23.1									23.6[b]							23.6		
8-Me				15.0	20.8		16.4	16.1				17.2	16.9		21.5	15.2			19.0	14.9
8a-Me			20.0[b]	14.8	25.1	26.5	22.6	23.0	19.5	23.1[b]	23.2[b]	24.5	15.9	19.5	24.9	14.3	21.6	21.6	26.5[b]	15.9

[a] The δ values are in parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [b] Signals in any vertical column may be interchanged.

Table III. Regio- and Diastereoselectivity of Diels–Alder Reactions[a]

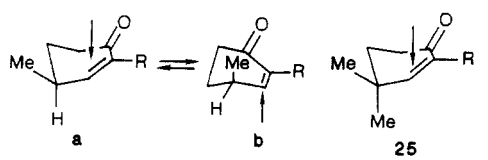
	 [b]					
	endo	[1]	[3]	[2]	endo	[1,3]
7a[c]	≥99	100	50	50		
7b	≥99	100	93	7		
9a	≥97	100	58	42	41	100
9b	≥97	100	92	(8)	86	100
9c	78	100	93	7	73	100
8	79	100	90	(10)	67	100

	syn[d]		anti[d]		syn		anti		syn		anti	
	endo	exo	endo	exo	[3]	[2]	[3]	[2]	endo	exo	endo	exo
8	40	9	39	12	11	(4)	79	(6)	4	13	63	20

[a] In % of adduct in the reaction mixture. A number in parentheses refers to an uncharacterized structure. [b] From ref 1. [c] Isoprene values from ref 5. [d] From ref 10.

have shown normal endo–exo diastereoisomerism behavior in their reactions with (*E*)-piperylene (**6c**),[1,3a] they veered from the expected path in the reactions with the pentadiene. Finally, the reactions of 2,4-dimethyl-2-cyclohexenone (**8**), with isoprene (**6b**) and 2-methyl-1,3-pentadiene (**6d**), were highly regioselective. Whereas the reaction of the ketone with (*E*)-piperylene (**6c**) has been shown to take place with similar endo–exo product ratios in both the syn- and anti-addition modes, the reaction with the pentadiene **6d** occurred with sharp drop of endo-syn addition. The major avenue for the production of the [3] adduct in the reaction with isoprene (**6b**) was the anti-addition route.

In attempting to interpret the above unusual results, three parameters affecting the transition state of the Diels–Alder reaction and thus controlling the outcome of the reaction had to be kept in constant consideration: (a) primary HOMO (diene)–LUMO (dienophile) orbital interactions,[4,11] (b) secondary orbital interaction,[4,12] and (c) nonbonded, steric interactions.[1,10] In an earlier analysis of the stereochemistry of the cycloaddition of 4-methyl-2-cyclohexenone (**24**, R = H) with isoprene (**6b**), 90% of whose product mixture was derived from an anti-[3] adduct of assumed endo-addition origin (by analogy with the stereochemical result of the reaction of the ketone with (*E*)-piperylene),[3c] it was emphasized that stereoelectronic control restricted the reaction to diene attack on either dienophile conformer in antiparallel modes as indicated in the formulas and that nonbonded repulsions in the reaction of the equatorially methylated conformer (**24a**, R = H) between the methyl group and the developing carbon–carbon bond at C(3) (a 1,2-gauche interaction) and between the methyl functions would suppress this reaction path in favor of reaction with the axially methylated conformer (**24b**, R = H).[10] The formation of an anti-endo-[3] adduct had followed the energetically most favored route from the vantage point of each of the aforementioned factors **a**–**c**.



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Antiparallel approach of isoprene (**6b**) to the 4,4-dimethyl-2-cyclohexenones (**7a** and **9a**) (see arrow in **25**) suffers from methyl–methyl repulsions in a transition state leading to endo-[3] adduct, thus opening the energetically more favorable paths of endo-[2] and/or exo-[3] addition. As Table III indicates, the reaction yields a ca. 1:1 mixture of [2] and [3] adducts, showing that an energy compromise had been struck between the parameters a–c. By analogy with the results of the cycloadditions with 2-methyl-1,3-pentadiene (**6d**) (vide infra) the [2] and [3] products must have been formed by endo and by exclusively or preponderantly *exo* addition, respectively. The production of a ca. 3:2 mixture of exo-[1,3] and endo-[1,3] adducts in the reaction between 2,4,4-trimethyl-2-cyclohexenone (**9a**) and the pentadiene **6d** can be explained in the following manner. Since the terminal methyl group of the diene exerts a stronger directing influence than the central methyl function,[13] the reaction follows the normal regiochemistry observed for (*E*)-piperylene.[1] However, in view of the methyl–methyl repulsion in the transition state leading to the endo-[1,3] adduct, production of the exo-[1,3] adduct is preferred.

In the face of the above interpretation of the cycloaddition of 4,4-dimethyl-2-cyclohexenone (**7a**) with isoprene (**6b**) in terms of ca. 1:1 endo-[2] and exo-[3] additions, it is possible to explain the formation of a [2] adduct from the reaction of isoprene (**6b**) with 4,4-dimethyl-2,5-cyclohexadienone.[6,14] Since introduction of a second double bond into the ketonic ring removes a 1,3-diaxial interaction between the developing bond at C(3) and axial H(5), the reaction proceeds preferentially by endo-[2] addition (a result which probably reflects also the electronic dissimilarity of enone from dienone). The maintenance of the latter cycloaddition preference in the boron trifluoride catalyzed reaction of isoprene (**6b**) with 2-carbomethoxy-4,4-dimethyl-2,5-cyclohexadienone can be attributed to the reaction taking place mostly via the Lewis acid complex of the ketone carbonyl group. On the other hand, the reversal of regiochemistry in the Diels–Alder reaction of the two compounds under stannic chloride catalysis may be due to predominant Lewis acid complexation of the ester carbonyl group (and/or of both the ketone and ester carbonyl groups, e.g., by chelation) leading preferentially to exo-[3] addition with secondary orbital overlap (parameter **b**) with the ester function.

An earlier study of the reactions of 5,5-dimethyl-2-cyclohexenones (**7b** and **9b**) and 2,6,6-trimethyl-2-cyclohexenone (**9c**) with (*E*)-piperylene (**6c**) had shown the additions to proceed in the expected endo-[1] manner (Table III).[1] The reactions of the three ketones with

(11) Fleming, I.; Michael, J. P.; Overman, L. E.; Taylor, G. F. *Tetrahedron Lett.* **1978**, 1313.
(12) Alston, P. V.; Ottenbrite, R. M. *J. Org. Chem.* **1975**, *40*, 1111.
(13) A behavior pattern reminescent of that of the methyl groups of 3-methyl-1,3-pentadiene: Alston, P. V.; Ottenbrite, R. M.; Cohen, T. *J. Org. Chem.* **1978**, *43*, 1864.
(14) Fringuelli, F.; Minuti, L.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1983**, *48*, 1810.

Table IV. Reaction Conditions of the Diels–Alder Reactions of Dienes 6 with 2-Cyclohexenones 7–9[a]

reactants	diene/ketone[b]	$AlCl_3$/ketone[b]	reactn temp, °C	reactn time, h	product yield, %[c]
6a–9b	6	0.9	70	46	75
6b–7a	15	0.25	40	80	75
6b–7b	9	0.25	60	15	95
6b–8	9	0.25	40	17	85
6b–9a	9	0.25	40	63	96
6b–9b	9	0.25	60	63	83
6b–9c	6	0.25	40	8	85
6d–8	9	0.25	40	2	85
6d–9a	15	0.25	40	3	62
6d–9b	15	0.15	60	6	94
6d–9c	9	0.20	40	3	85

[a] Complexation time—40 min; complexation temperature—22 °C; ketone concentration—0.1 M. [b] Ratio of equivalents. [c] GC based.

isoprene (**6b**) and pentadiene **6d** now gave products, [3] and endo-[1,3] adducts, respectively, indicating once again normal addition behavior. Whereas the reactions of ketone **9c** had involved sterically unencumbered, energetically favored antiparallel addition, those of the 5,5-dimethyl compounds must have proceeded by parallel addition in the face of the energetically unfavorable, 1,3-diaxial, nonbonded interaction between the axial 5-methyl function and the developing bond at C(3) in the antiparallel addition mode.

The results of the cycloaddition of 2,4-dimethyl-2-cyclohexenone (**8**; **24**, R = Me) with isoprene (**6b**) and pentadiene **6d** can be interpreted easily in the light of the above discussion of various 2-cyclohexenones. The percentages of syn and anti adducts (from reactions indicated by the arrows in formulas **24a** and **24b**, R = Me) in the reaction with isoprene (**6b**), 15 and 85%, respectively, resemble those of the reaction with pentadiene **6d**, 17 and 83%, respectively, but differ sharply from those of the reaction with (*E*)-piperylene (**6c**), 49 and 51%. Furthermore, the anti/syn ratios of the piperylene reaction are 1.3 and 1 for the exo and endo addition modes, respectively. Whereas the ratio for the pentadiene exo addition remains nearly the same (1.6), that for the endo addition increases to 16. Thus in the exo addition frame the pentadiene shows the same behavior as piperylene, but in the endo mode the reaction via conformer **24b** (R = Me) is favored greatly by all three parameters **a–c**. Finally, the [3] adducts of the reaction with isoprene must come mostly from anti-endo (79%) and some from syn-exo (11%) addition (Table III).

Experimental Section

The experimental details of the Diels–Alder reactions and of the base-induced product equilibrations as well as the specifics on the spectral analyses of all octalones and on the instruments used for the work are delineated in the Experimental Section of the publication 9.[10] The carbon shifts on formulas **14** and **15** are in parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) - 76.9$ ppm. Ketone **12** could not be characterized in view of easy isomerization. Ketones **10**, **11**, **13**, and **14** have been described previously.[5] The 2,4-dinitrophenylhydrazones were recrystallized in 95% ethanol and those of ketones **21a–d** could not be prepared because of steric hindrance.

Diels–Alder Reactions. The reactions and their workup followed a previous prescription,[3a] and the conditions are detailed in Table IV.

Octalone 15: IR 1715 (s, C=O), 1670 (w, C=C) cm^{-1}; ^1H NMR δ 0.87, 1.06, 1.63 (s, 3 each, methyls), 5.37 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 182–183 °C. Anal. Calcd for $C_{19}H_{24}O_4N_4$: C, 61.26; H, 6.51; N, 15.05. Found: C, 61.52; H, 6.68; N, 14.84.

Octalone 16a: mp 48–49 °C; IR 3010 (w, olefinic CH), 1710 (s, C=O) cm^{-1}; ^1H NMR δ 0.94 (d, 3 J = 6 Hz, Me), 1.08, 1.68 (s, 3 each, methyls), 5.34 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 174–175 °C. Anal. Calcd for $C_{19}H_{24}O_4N_4$: C, 61.26, H, 6.51; N, 15.05. Found: C, 61.55; H, 6.42; N, 14.70.

Octalone 16b: mp 57–58 °C; IR 1708 (s, C=O), 1665 (w, C=C) cm^{-1}; ^1H NMR δ 0.73 (d, 3, J = 7 Hz, Me), 0.87, 1.68 (s, 3 each, methyls), 0.94 (d, 3, J = 6 Hz, Me), 5.10 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 176–177 °C. Anal. Calcd for $C_{20}H_{26}O_4N_4$: C, 62.15; H, 6.79; N, 14.50. Found: C, 61.41; H, 6.72; N, 14.35.

Octalone 16c: mp 30–31 °C; IR 3018 (w, olefinic CH), 1702 (s, C=O) cm^{-1}; ^1H NMR δ 0.95 (d, 3, J = 6 Hz, Me), 1.01 (d, 3, J = 7 Hz, Me), 1.12, 1.70 (s, 3 each, methyls), 5.23 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 167–168 °C. Anal. Calcd for $C_{20}H_{26}O_4N_4$: C, 62.15; H, 6.79; N, 14.50. Found: C, 61.80; H, 6.78; N, 14.60.

Octalone 17a: mp 70–71 °C; IR 1713 (s, C=O) cm^{-1}; ^1H NMR δ 0.98 (d, 3, J = 7 Hz, Me), 1.30, 1.60 (s, 3 each, methyls), 5.30 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 179–180 °C. Anal. Calcd for $C_{19}H_{24}O_4N_4$: C, 61.26; H, 6.51; N, 15.05. Found: C, 61.09; H, 6.55; N, 14.88.

Octalone 17b: IR 1713 (s, C=O) cm^{-1}; ^1H NMR δ 0.82 (d, 3, J = 7 Hz, Me), 1.00 (d, 3, J = 7 Hz, Me), 1.15, 1.60 (s, 3 each, methyls), 5.26 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 202–203 °C. Anal. Calcd for $C_{20}H_{26}O_4N_4$: C, 62.15; H, 6.79; N, 14.50. Found: C, 61.90; H, 6.79; N, 14.55.

Octalone 17c: IR 1715 (s, C=O) cm^{-1}; ^1H NMR δ 0.94 (d, 3, J = 7 Hz, Me), 1.22 (d, 3, J = 7 Hz, Me), 1.42, 1.62 (s, 3 each, methyls), 5.20 (br s, 1, olefinic H). Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.70; H, 10.90.

Octalone 18: IR 3022 (w, olefinic CH), 1705 (s, C=O), 1655 (w, C=C) cm^{-1}; ^1H NMR δ 0.90, 1.03, 1.03 (s, 3 each, methyls), 5.57 (m, 2, olefinic Hs). 2,4-Dinitrophenylhydrazone: mp 173–174 °C. Anal. Calcd for $C_{19}H_{24}O_4N_4$: C, 61.26; H, 6.51; N, 15.05. Found: C, 61.64; H, 6.65; N, 15.13.

Octalone 19a: IR 1710 (s, C=O) cm^{-1}; ^1H NMR δ 0.99, 0.99, 1.07, 1.69 (s, 3 each, methyls), 5.30 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 171–172 °C. Anal. Calcd for $C_{20}H_{26}O_4N_4$: C, 62.15; H, 6.79; N, 14.50. Found: C, 62.01; H, 6.81; N, 14.45.

Octalone 19b: IR 1710 (s, C=O) cm^{-1}; ^1H NMR δ 0.98, 0.98, 1.06, 1.63 (s, 3 each, methyls), 5.33 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 173–174 °C. Anal. Calcd for $C_{20}H_{26}O_4N_4$: C, 62.15; H, 6.79; N, 14.50. Found: C, 62.10; H, 6.80; N, 14.48.

Octalone 19c: IR 1705 (s, C=O) cm^{-1}; ^1H NMR δ 0.90, 1.00, 1.15, 1.73 (s, 3 each, methyls), 0.93 (d, 3, J = 7 Hz, Me), 5.33 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 149–150 °C. Anal. Calcd for $C_{21}H_{28}O_4N_4$: C, 62.99; H, 7.05; N, 13.94. Found: C, 63.19; H, 7.01; N, 14.05.

Octalone 19d: mp 56–57 °C; IR 1707 (s, C=O) cm^{-1}; ^1H NMR δ 0.73 (d, 3, J = 7 Hz, Me), 0.90, 0.97, 1.03, 1.68 (s, 3 each, methyls), 5.07 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 203–204 °C. Anal. Calcd for $C_{21}H_{28}O_4N_4$: C, 62.99; H, 7.05; N, 13.99. Found: C, 62.47; H, 7.04; N, 13.86.

Octalone 20a: IR 3018 (w, olefinic CH), 1706 (s, C=O), 1665 (w, C=C) cm^{-1}; ^1H NMR δ 0.88, 1.00, 1.03, 1.67 (s, 3 each, methyls), 5.27 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 160–161 °C. Anal. Calcd for $C_{20}H_{26}O_4N_4$: C, 62.15; H, 6.79; N, 14.50. Found: C, 61.92; H, 6.82; N, 14.28.

Octalone 20c: IR 1700 (s, C=O) cm^{-1}; ^1H NMR δ 0.95, 0.99, 1.15, 1.70 (s, 3 each, methyls), 1.04 (d, 3, J = 7 Hz, Me), 5.30 (br s, 1, olefinic H). 2,4-Dinitrophenylhydrazone: mp 127 °C. Anal.

Calcd for $C_{21}H_{28}O_4N_4$: C, 62.98; H, 7.05; N, 13.99. Found: C, 62.56; H, 7.09; N, 13.95.

Octalone 20d: IR 1700 (s, C=O) cm^{-1}; ^1H NMR δ 0.75 (d, 3, J = 7 Hz, Me), 0.89, 0.89, 1.04, 1.67 (s, 3 each, methyls), 5.10 (br s, 1, olefinic H). Anal. Calcd for $C_{15}H_{24}O$: C, 81.77; H, 10.98. Found: C, 81.41; H, 10.95.

Octalone 21a: IR 1697 (s, C=O) cm^{-1}; ^1H NMR δ 1.09, 1.12, 1.18, 1.65 (s, 3 each, methyls), 5.28 (m, 1, olefinic H). Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.77; H, 10.79.

Octalone 21b: IR 1697 (s, C=O) cm^{-1}; ^1H NMR δ 1.07, 1.09, 1.17, 1.64 (s, 3 each, methyls), 5.27 (br s, 1, olefinic H). Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.25; H, 10.85.

Octalone 21c: IR 1700 (s, C=O) cm^{-1}; ^1H NMR δ 1.00 (d, 3, J = 8 Hz, Me), 1.04, 1.18, 1.21, 1.68 (s, 3 each, methyls), 5.35 (br s, 1, olefinic H). Anal. Calcd for $C_{15}H_{24}O$: C, 81.77; H, 10.98. Found: C, 82.02; H, 10.91.

Octalone 21d: IR 1695 (s, C=O) cm^{-1}; ^1H NMR δ 0.78 (d, 3, J = 7 Hz, Me), 0.95, 1.08, 1.17, 1.66 (s, 3 each, methyls), 5.07 (br s, 1, olefinic H). Anal. Calcd for $C_{15}H_{24}O$: C, 81.77; H, 10.98. Found: C, 81.70; H, 11.05.

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Reduction of α-Halo Ketones by Organotin Hydrides. An Electron-Transfer-Hydrogen Atom Abstraction Mechanism[1]

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The mechanism for the reduction of α-chloro- and α-bromoacetophenone with triphenyltin hydride was investigated. The reductions were found to follow the same reduction pathways as has previously been reported for the reduction of α-fluoroacetophenone. Both homolytic and heterolytic reactions could be recognized since the homolytic reactions yield acetophenone and the heterolytic reactions yield α-(halomethyl)benzyl alcohol. The homolytic reductions proceed by a free-radical chain process where the initiation step and one of the propagation steps involve SET reactions. The reduction apparently does not proceed by a direct halogen transfer since no secondary deuterium isotope effect was observed on reduction of α,α-dideuterio-α-haloacetophenone.

Introduction

Early work on the triorganotin hydride reduction of alkyl halides established that the reagents selectively reduce the carbon-halogen bond in the presence of a number of other functional groups which are themselves unaffected.[3] Two of the substrates used to demonstrate this selective reactivity were α-chloro- and α-bromoacetophenone (eq 1, X = Cl, Br). Recently[4] we have demonstrated that the

$$PhC(=O)CH_2X + n\text{-}Bu_3SnH \rightarrow PhC(=O)CH_3 + n\text{-}Bu_3SnX \quad (1)$$

triphenyltin hydride reduction of α-fluoroacetophenone (I) proceeds by homolytic and heterolytic pathways depending upon the conditions under which the reaction is carried out. The heterolytic reaction of I leads, after hydrolysis, to α-fluoromethylbenzyl alcohol (II) (see Scheme Ia), while the homolytic pathway yields acetophenone (see Scheme Ib), which under the reaction conditions is unreactive.

The defluorination was rationalized by a chain mechanism whose initiation step (eq 4) and one of its propagation steps (eq 5) both involved a single-electron-transfer (SET) reaction. The homolytic mechanism yielded acetophenone as the sole product.

Since the formation of dehalogenated ketone is indicative of a radical chain process which involves a SET-hydrogen atom transfer sequence, it was of interest to examine more closely the reduction of α-chloro- and α-bromoacetophenone.

Results

The reduction of both α-chloro- and α-bromoacetophenone was carried out in several solvents. The effect, on the product distribution and their relative rates of formation, of an added initiator, azobisisobutyronitrile (AIBN), or an inhibitor, p-dinitrobenzene (DNB), was examined. The results of the studies are listed in Tables I and II.

By analogy to the results previously reported for the reduction of α-fluoroacetophenone,[4] the reductions, at least in the less polar solvents, appear to follow the homolytic pathway. Qualitatively the reduction of these halo ketones appear to be faster than the reduction of the fluoride.

Electrolytic reduction at a dropping mercury electrode (DME) of the α-halosubstituted acetophenones were com-

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