  Bull. Chem. Soc. Jpn., 56, 1669—1677 (1983)

Stereoselective Intramolecular Diels-Alder Reactions of α,β-Unsaturated Amides Using Internal Coordination of Metal Salts

Toyonori TAKEBAYASHI,** Nobuharu IWASAWA, Teruaki MUKAIYAMA,* and Tadashi HATA†

Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

†Analytical and Metabolic Laboratories, Sankyo Co., Ltd., Hiromachi, Shinagawa-ku, Tokyo 140

(Received October 9, 1982)

The intramolecular Diels-Alder reactions between acyclic dienes and α,β-unsaturated amides utilizing the internal coordination of the metal salts have been studied in detail. When the magnesium salts of *N*-(*trans*, *trans*-2,4-alkadienyl)-*N*-(2-hydroxyphenyl)acrylamide derivatives are employed, the intramolecular Diels-Alder reactions are remarkably accelerated and the corresponding cycloadducts are obtained in high yields with isomeric ratios (*exo*-adducts: *endo*-adducts) of about 3 : 2. And the same reactions of *N*-(*trans*, *trans*-2,4-alkadienyl)-*N*-(2-hydroxyphenyl)-1-cyclopentenecarboxamide afford predominantly (60 : 40 to 85 : 15 selectivity) *trans*-fused cycloadducts (*exo*-adducts) in good yields.

The intramolecular Diels-Alder reaction has become one of the most powerful methods for the construction of a variety of interesting ring systems, and has been applied to the syntheses of various natural products.[1]

Though the efficiency of this reaction, derived from the entropical factor, is well established, it sometimes needs high temperature to perform the reaction, and, in some cases, the desired cycloadducts cannot be obtained at all even by the intramolecular Diels-Alder reaction. Moreover, the stereochemical features must be well-defined for this reaction to become widely accepted as a synthetic method.

As for the former problems, we recently reported an efficient method for the acceleration of the intramolecular Diels-Alder reaction between furan derivatives and α,β-unsaturated amide derivatives employing the internal coordination of magnesium salt or internal hydrogen bonding.[2] As for the stereochemical problems, a large amount of work has recently been reported by Roush,[3] Boeckmann,[4] White,[5] and so on. They, in most cases, have dealt with terminally activated trienoate systems, and made it clear that when acyclic diene is employed, two stereoisomers (*endo* and *exo* adducts) are produced, and that non-bonded interaction plays more important role in the stereoselection of this reaction than the secondary orbital control.

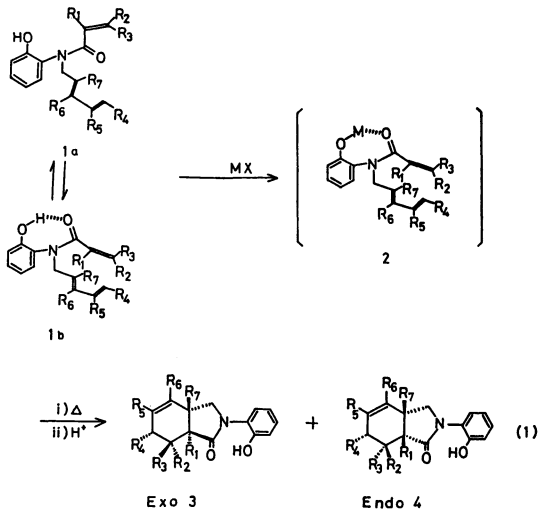
In this paper, we would like to describe our recent results about the reaction rate and stereoselection of the intramolecular Diels-Alder reaction between acyclic diene and α,β-unsaturated carbonyl unit connected by the amide bond, with the assumption that the formation of internal chelate complex not only accelerates the reaction but also alters the stereochemical course of this reaction.

Results and Discussion

Only a few examples have been known about the intramolecular Diels-Alder reaction of an acyclic diene and a dienophile linked by the amide bond,[6] and only one report was published on the stereoselection of these compounds by Gschwend *et al.*[7]

Our recent results on the intramolecular Diels-Alder reaction between furan derivatives and α,β-unsaturated amides, utilizing the internal coordination of the magnesium salt and the internal hydrogen bonding, prompted us to examine the reactivity and stereoselection of the reaction between acyclic dienes and α,β-unsaturated carboxyl compounds linked by the amide bond.

Among various conformers of *o*-aminophenol derivative **1**, only conformer **1b** in which diene and dienophile groups are located nearby would contribute to the cycloaddition reaction, and it is assumed that by the employment of the internal interaction (the internal hydrogen bonding or the internal coordination of the metal salt of compound **1**), the conformation of amide **1** would be fixed to **1b** and, combined with the Lewis acid character of the metal salt, the cycloaddition reaction would be accelerated efficiently. Moreover, it is expected that the formation of this rigid internal chelate complex **2** would result in the more efficient stereoregulation by the nonbonding steric repulsion combined with the enhanced secondary orbital control caused by the Lewis acid character of the metal salts (Eq. 1).



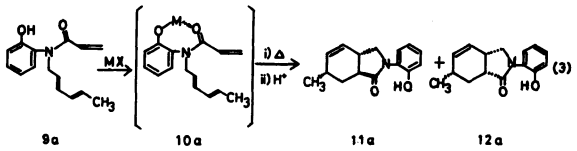
(1)

Based on these assumptions, various *N*-(*trans*,*trans*-2,4-alkadienyl)-*N*-(2-hydroxyphenyl)acrylamide derivatives **9** were prepared as shown in Eq. 2.

In the first place, the intramolecular Diels-Alder reaction of acrylamide derivative **9a** and its magnesium

** Present address: Product Development Laboratories Sankyo Co., Ltd., Hiromachi, Shinagawa-ku, Tokyo 140.

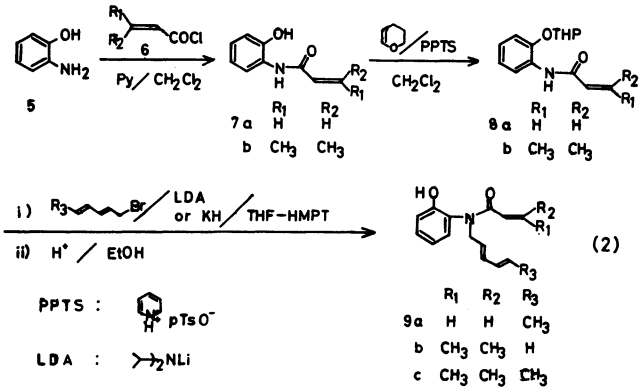
Table 1. The Diels-Alder reaction of the amide **9a**[a)]



9a **10a** **11a** **12a**

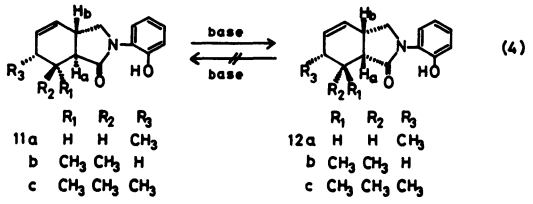
Metal salt	Solvent	Reaction time/h	Yield/% of cycloadduct	Ratio **11a** : **12a**
None	Toluene	20	16	45 : 55
-OMgBr	Toluene	9	72	59 : 41
-OMgBr	Benzene	10	69	55 : 45
-OMgBr	Dichloromethane	36	21	52 : 48
-OMgCl	Toluene	16	77	58 : 42

a) The reaction was performed in refluxing solvent under an argon atmosphere.



salt was examined and the results were summarized in Table 1.

As shown in this Table, when the toluene solution of amide **9a** was refluxed for 20 h, nearly equal amounts of two cycloadducts (that is, *trans*-fused **11a** and *cis*-fused **12a**) were obtained in only 16% yield along with substantial amount of polymerized product. These two isomers were separated by silica-gel thin-layer chromatography (hexane–ethyl acetate, 3 : 2) and the structures were determined by ^{1}H-NMR (270 MHz).



The proton H_a in **11a** appears at δ 2.42 as a doublet-triplet splitting. Coupling constants are $J_{H_a-H_b}=J_{H_a-R_2}=13$ Hz, and $J_{H_a-R_1}=3$ Hz, indicating the trans ring fusion of this compound. On the other hand, the proton H_a in **12a** appears at δ 2.82 as a doublet-doublet-doublet splitting. Coupling constants are $J_{H_a-H_b}=8$ Hz, $J_{H_a-R_1}=5$ Hz, $J_{H_a-R_2}=13$ Hz, indicating the cis ring fusion of this compound. Further, the examination of Dreiding models of **11a** and **12a** suggested the *trans*-fused product is more strained than the *cis*-fused one. In accordance with this, it is observed that trans **11a** was completely isomerized to cis **12a** by the treatment of 0.1 equivalent of sodium methoxide in refluxing methanol. On the other hand, treatment of cis **12a** under the same conditions resulted in the complete recovery of **12a** (Eq. 4).

The IR spectrum of amide **9a** indicates that the internal hydrogen bonding exists in this molecule (carboxyl absorption appears at 1610 cm^{-1}). However, above result indicates that the fixation of the conformation of **9a** by the hydrogen bonding is not enough to promote the cycloaddition reaction effectively.

Next, with the expectation that the formation of internal chelate complex not only accelerate the reaction, but also alter the stereoselection, amide **9a** was converted to its bromomagnesium salt and heated for 9 h in refluxing toluene. As expected, the yield of cycloadducts **11a** and **12a** increased up to 72%, and the ratio of **11a** and **12a** also changed from 45 : 55 to 59 : 41. However, further examination of reaction temperature did not alter the stereoselectivity dramatically.

Next, we examined various metal salts such as Al, Sn, Zn, and B, based on the consideration that stronger Lewis acid than Mg would enhance the secondary orbital control and *endo*-mode of cyclizations would be preferred. And the results are summarized in Table 2.

Table 2. The Diels-Alder reaction of various metal salts of amide **9a**[a)]

Metal salt	Solvent	Reaction time/h	Yield/% of cycloadduct	Ratio **11a** : **12a**
-OAl(Et)Cl	Toluene	11	36	25 : 75
-OAl(Et)$_2$	Toluene	17	37	38 : 62
-OSn(Bu)$_2$Cl	Toluene	17	84	42 : 58
-OZnCl	Toluene	17	43	48 : 52
-OBBr$_2$	Toluene	9	16	38 : 62
-OB  [b)]	Toluene	9	43	32 : 68
-OB(OEt)$_2$	Toluene	17	31	41 : 59
-OB(Ph)Cl	Toluene	11	42	14 : 86
-OB(Ph)OH	Toluene	11	28	29 : 71

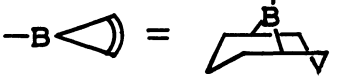
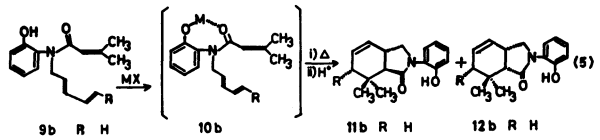
a) The reaction was performed in refluxing toluene under an argon atmosphere. b) 

Table 3. The Diels-Alder reaction of amide **9b**[a] (R=H)



9b R H 10b 11b R H 12b R H
9c R CH_3 10c 11c R CH_3 12c R CH_3

Metal salt	Solvent	Additive[b]	Reaction time/h	Yield/% of cycloadduct	Ratio[c] 11b : 12b
None	Toluene	—	60	12	55 : 45
–OMgCl	Toluene	—	20	52	52 : 48
–OMgBr	Toluene	—	20	31	62 : 38
–OAl(Et)Cl	Toluene	—	48	24	53 : 47
$-OSn(Bu)_2Cl$	Toluene	—	20	17	52 : 48
None	Xylene	—	20	32	64 : 36
None	Xylene	tBC	20	42	65 : 36
–OMgCl	Xylene	tBC	7	85	59 : 41
–OMgCl	Xylene	tBC	3	75	58 : 42
–OMgBr	Xylene	tBC	7	71	69 : 31
–OAl(Et)Cl	Xylene	tBC	14	27	69 : 31
$-OSn(Bu)_2Cl$	Xylene	tBC	7	41	41 : 59

a) The reaction was performed in refluxing solvent under an argon atmosphere. b) The catalytic amount of 4-*t*-butylcatechol (tBC) was added. c) Two stereoisomers of the cycloadduct were separated by silica-gel chromatography.

Table 4. The Diels-Alder reaction of amide **9c**[a] (R=CH_3)

Metal salt	Solvent	Additive[b]	Reaction time/h	Yield/% of cycloadduct	Ratio 11c : 12c
None	Toluene	—	30	16	68 : 32
–OMgBr	Toluene	—	24	53	60 : 40
–OAl(Et)Cl	Toluene	—	24	35	40 : 60
$-OSn(Bu)_2Cl$	Toluene	—	24	64	49 : 51
None	Xylene	tBC	20	49	68 : 32
–OMgCl	Xylene	tBC	14	77	57 : 43
–OMgCl	Xylene	tBC	7	78	60 : 40
–OMgBr	Xylene	tBC	14	61	58 : 42
–OAl(Et)Cl	Xylene	tBC	14	54	59 : 41
$-OSn(Bu)_2Cl$	Xylene	tBC	14	55	62 : 38

a) The reaction was performed in refluxing solvent under an argon atmosphere. b) The catalitic amount of 4-*t*-butylcatechol (tBC) was added. c) Two stereoisomers of the cycloadduct were separated by silica-gel thin-layer chromatography.

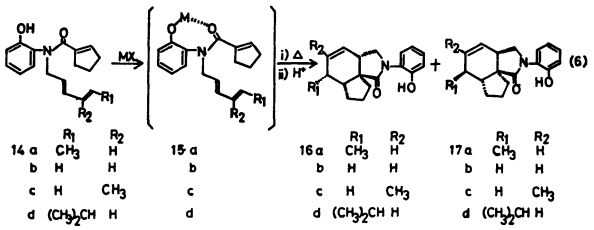
Though the acceleration of the reaction is rather modest compared to the magnesium salt (one serious problem is the polymerization of starting material caused by the existence of Lewis acid), the preferred formation of *endo*-cycloadduct **12a** should be noted and when phenyldichloroborane is added to the solution of sodium salt of amide **9a**, up to 86 : 14 stereoselection could be achieved.

Next, we examined the reaction of more sterically hindered 3-methyl-2-butenamide derivatives **9b** and **9c** using various metal salts. And the results are summarized in Tables 3 and 4.

As shown in these Tables, the reaction proceeded rather slowly in refluxing toluene even when the magnesium salt was employed. However, the xylene solutions of the magnesium salts of **9b** and **9c** were refluxed with catalytic amount of 4-*t*-butylcatechol as a radical scavenger, high yields of the corresponding cycloadducts were realized. However, remarkable change in the stereoselection of the two cycloadducts was not observed in these cases.

The structures of these stereoisomers were determined by ^{1}H-NMR. The proton H_a in **11b** appears at δ 2.21 as a doublet with a coupling constant of 12 Hz, indicating the trans ring fusion of this compound. On the other hand, the proton H_a in **12b** appears at δ 2.56 as a doublet with a coupling constant of 8 Hz, indicating the cis ring fusion of this compound (Eq. 4). Treatment of **11b** with 0.1 equivalent of sodium methoxide in refluxing methanol completely isomerized **11b** to **12b**. On the other hand, treatment of **12b** under the same conditions resulted in the complete recovery of **12b**. The structures of **11c** and **12c** were assigned similarly. That is, ^{1}H-NMR analysis indicates that coupling constants of proton H_a in **11c** and **12c** are 12 Hz and 8 Hz, respectively, and isomerization of **11c** proceeded smoothly by the treatment of **11c** with NaH in refluxing THF, but when **12c** was treated in the same manner,

TABLE 5. THE DIELS-ALDER REACTION OF AMIDE **14**[a)]



Amide	Metal salt	Reaction time/h	Yield/% of cycloadduct	Ratio **16 : 17**
14a	None	17	46	50 : 50[b)]
	-OMgCl	10	80	85 : 15[b)]
	-OMgBr	10	78	80 : 20[b)]
	-OMgI	10	78	83 : 17[b)]
	-OAl(Et)Cl	24	58	60 : 40[b)]
	$-OSn(Bu)_2Cl$	10	58	54 : 46[b)]
14b	None	6	29	40 : 60[c)]
	-OMgCl	4	91	62 : 38[c)]
	-OMgBr	4	86	62 : 38[c)]
	-OMgI	4	81	60 : 40[c)]
	-OAl(Et)Cl	5	31	38 : 62[c)]
	$-OSn(Bu)_2Cl$	4	43	35 : 65[c)]
14c	None	20	30	42 : 58[c)]
	-OMgCl	10	71	60 : 40[c)]
	-OMgBr	10	75	65 : 35[c)]
	-OMgI	10	75	61 : 39[c)]
	-OAl(Et)Cl	10	38	38 : 63[c)]
	$-OSn(Bu)_2Cl$	10	50	38 : 62[c)]
14d	None	11	25	60 : 40[b)]
	-OMgCl	10	74	76 : 24[b)]
	-OMgBr	10	70	80 : 12[b)]
	-OMgI	10	70	88 : 12[b)]
	-OAl(Et)Cl	10	21	58 : 42[b)]
	$-OSn(Bu)_2Cl$	10	33	62 : 39[b)]

a) The reaction were carried out in refluxing toluene. b) GC analysis were performed on 2 m, 2% OV-17 Chromosorb W column at 200 °C. c) In separable by TLC or GC. Product ratio were determined by ^{1}H-NMR.

complete recovery of **12c** was observed.

Finally, we examined the reaction of cyclic α,β-unsaturated amide compounds to construct polycyclic systems in a single step.

Amides **14** were prepared by the same procedure described in Eq. 1, and the results are shown in Table 5.

As shown in Table 5, when the toluene solution of amide **14a** was refluxed for 17 h, equal amounts of two stereoisomeric adducts **16a** and **17a** were obtained in 46% yield. On the other hand, when toluene solution of the chloromagnesium salt of amide **14a** was refluxed for 10 h, adduct **16a** and **17a** were obtained in 80% yield and the isomeric ratio of the products came up to 85 : 15. The ratio of these two stereoisomers was determined by gas chromatography and the configuration of the predominantly formed adduct was defined from X-ray analysis to be *trans*-fused (*i.e.* **16a**). Similar reactions of the magnesium salts of amides **14b—d** showed that the reaction is surely accelerated by the formation of internal chelate complex and that, in these cases, the *exo*-cycloadducts are predominantly formed.[8)] Recently, Roush[3c)] has reported the Lewis acid catalyzed

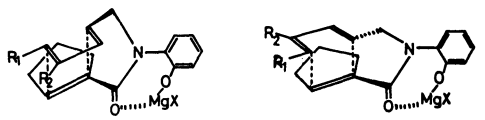


Fig. 1. Transition states of cycloaddition reaction.

intramolecular Diels-Alder reaction of terminally activated trienoates, and, in his case, the *endo*-cycloadducts were preferentially obtained, probably because of the enhanced secondary orbital control by the Lewis acid. But in our cases, the *exo*-cycloadducts were predominantly formed by the employment of magnesium salt. This result is interpreted as that, in our magnesium salt mediated intramolecular Diels-Alder reaction, steric control is more important than the secondary orbital control in the stereoselection of the products.

When the reaction is carried out without converting to the metal salt, there is little energy difference between

TABLE 6. POSITIONAL PARAMETERS OF THE NON-HYDROGEN ATOMS FOR **18a**, WITH THEIR ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Positional parameters have been multiplied by 10^4.

Atom	x	y	z	B_{ep}/Å^2	Atom	x	y	z	B_{eq}/Å^2
N(1)	3062(7)	130(4)	5531(7)	4.45(24)	C(17)	−178(9)	1119(5)	3454(10)	5.22(34)
C(2)	3478(8)	69(5)	6773(9)	4.70(31)	C(18)	66(9)	1945(5)	3658(9)	5.20(34)
C(3)	4258(8)	761(5)	7298(8)	4.32(29)	O(19)	1047(6)	2185(4)	4330(7)	6.38(26)
C(4)	5309(9)	738(5)	8577(10)	5.41(35)	C(20)	−935(8)	2467(5)	2924(8)	4.39(30)
C(5)	6544(9)	1025(6)	8438(11)	6.18(38)	C(21)	−626(9)	3175(6)	2662(10)	5.47(35)
C(6)	6271(10)	1693(6)	7591(11)	6.75(42)	C(22)	−1489(9)	3670(6)	1959(10)	5.78(36)
C(7)	5406(10)	1659(6)	6489(10)	6.08(38)	C(23)	−2721(9)	3459(5)	1589(9)	5.32(34)
C(8)	4694(9)	937(5)	6224(10)	5.50(35)	C(24)	−3045(9)	2768(6)	1792(11)	6.31(39)
C(9)	3554(10)	787(6)	5104(10)	5.82(35)	C(25)	−2177(9)	2269(5)	2502(10)	5.82(37)
C(10)	2139(9)	−326(5)	4729(9)	4.81(33)	Br(26)	−3917(1)	4147(1)	624(2)	9.27(7)
C(11)	2277(9)	−1077(5)	4650(11)	6.01(38)	O(27)	3258(6)	−436(4)	7372(6)	5.92(24)
C(12)	1364(10)	−1519(6)	3877(12)	7.13(43)	C(28)	3344(9)	1344(5)	7485(10)	5.37(35)
C(13)	262(10)	−1210(6)	3174(11)	6.60(40)	C(29)	3533(10)	1280(7)	8839(11)	7.24(44)
C(14)	35(9)	−446(6)	3241(10)	5.79(36)	C(30)	4907(10)	1207(6)	9460(10)	6.36(39)
C(15)	972(9)	−4(5)	4026(10)	5.23(35)	C(31)	7522(11)	1162(8)	9696(13)	8.84(52)
O(16)	898(6)	745(3)	4189(6)	5.69(23)					

TABLE 7. THERMAL PARAMETERS OF THE NON-HYDROGEN ATOMS FOR **18a**, WITH THEIR ESTIMATED STANDARD DEVIATIONS

All parameters have been multiplied by 10^4. The thermal parameters are of the form

$$T=\exp[-(B_{11}h_2+B_{22}k^2+B_{33}l^2+2B_{12}hk+2B_{13}hl+2B_{23}kl)].$$

Atom	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N(1)	107(8)	30(3)	79(8)	−3(4)	20(7)	5(4)
C(2)	89(10)	25(3)	129(12)	0(5)	39(9)	5(5)
C(3)	94(9)	27(3)	95(11)	8(5)	29(8)	4(5)
C(4)	109(11)	28(4)	140(13)	1(5)	30(10)	9(6)
C(5)	85(10)	44(5)	168(15)	9(6)	28(10)	−2(7)
C(6)	112(12)	44(5)	182(16)	−13(6)	54(11)	−12(7)
C(7)	121(12)	36(4)	157(14)	−5(6)	60(11)	9(6)
C(8)	118(11)	34(4)	125(12)	−1(5)	44(10)	2(6)
C(9)	133(12)	40(4)	113(12)	0(6)	40(10)	12(6)
C(10)	104(11)	30(4)	104(12)	−3(5)	31(9)	−5(5)
C(11)	109(11)	33(4)	166(15)	7(5)	44(11)	0(6)
C(12)	140(13)	29(4)	212(18)	0(6)	52(13)	−16(7)
C(13)	138(13)	39(4)	152(15)	−10(6)	36(11)	−19(7)
C(14)	98(11)	33(4)	151(14)	−5(5)	7(10)	−9(6)
C(15)	117(11)	25(4)	132(13)	3(5)	46(10)	1(5)
O(16)	109(7)	28(2)	148(9)	3(3)	10(6)	−1(4)
C(17)	101(10)	29(4)	135(13)	6(5)	33(10)	−1(5)
C(18)	103(10)	34(4)	124(12)	−4(5)	43(9)	0(6)
O(19)	105(7)	36(3)	171(10)	−2(4)	13(7)	−5(4)
C(20)	99(10)	26(3)	99(11)	2(5)	37(8)	−1(5)
C(21)	97(11)	36(4)	136(13)	−3(5)	36(10)	−8(6)
C(22)	115(11)	35(4)	145(14)	−1(6)	54(10)	13(6)
C(23)	111(11)	32(4)	127(13)	15(5)	42(10)	18(6)
C(24)	90(10)	43(5)	181(16)	2(6)	52(11)	4(7)
C(25)	103(11)	32(4)	167(15)	−4(5)	51(10)	9(6)
Br(26)	133(1)	62(1)	266(2)	31(1)	66(1)	44(1)
O(27)	135(8)	32(3)	132(9)	−11(4)	26(7)	12(4)
C(28)	107(11)	33(4)	131(13)	11(5)	39(10)	0(6)
C(29)	126(13)	59(6)	162(16)	21(7)	63(12)	0(8)
C(30)	145(13)	46(5)	117(13)	−2(6)	44(11)	−3(6)
C(31)	111(13)	81(7)	194(19)	−7(8)	3(13)	−17(9)

endo-mode and *exo*-mode in the transition state. However, when amide **14** is converted to its magnesium salt, the coordination of the Mg to the carbonyl oxygen should make the conformation of the molecule more rigid and the *endo*-mode of cyclization (A) would become more strained compared with the *exo*-mode of cyclization (B), because of the planarity of the amide group (Fig. 1). When the stronger Lewis acid such as

TABLE 8. POSITIONAL AND ISOTROPIC THERMAL PARAMETERS OF THE HYDROGEN ATOMS FOR **18a**, WITH THEIR ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

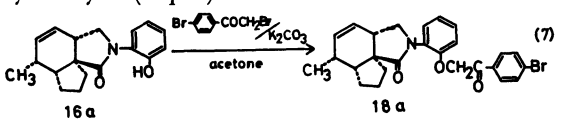
Positional parameters have been multiplied by 10^3.

Atom	x	y	z	B/Å^2
H(4)	539(6)	21(4)	897(6)	3(2)
H(5)	681(7)	59(5)	795(8)	6(2)
H(6)	677(7)	218(4)	792(7)	5(2)
H(7)	512(7)	203(4)	589(7)	5(2)
H(8)	538(8)	58(5)	622(8)	7(2)
H(9A)	297(8)	118(5)	495(8)	7(2)
H(9B)	376(7)	69(5)	437(7)	6(2)
H(11)	304(8)	−123(5)	517(8)	7(2)
H(12)	143(7)	−201(4)	381(7)	5(2)
H(13)	−36(8)	−149(5)	252(8)	6(2)
H(14)	−70(7)	−17(4)	267(7)	4(2)
H(17A)	−79(6)	99(4)	373(7)	4(2)
H(17B)	−39(7)	103(4)	241(7)	4(2)
H(21)	19(8)	326(5)	291(8)	6(2)
H(22)	−119(9)	407(6)	159(9)	9(3)
H(24)	−382(8)	256(5)	165(8)	7(2)
H(25)	−240(7)	182(4)	258(7)	5(2)
H(28A)	254(8)	122(5)	682(8)	7(2)
H(28B)	366(9)	183(6)	741(9)	9(3)
H(29A)	318(10)	77(6)	916(10)	10(3)
H(29B)	321(9)	169(6)	916(10)	10(3)
H(30A)	515(8)	181(5)	944(8)	7(2)
H(30B)	522(7)	102(4)	1050(7)	4(2)
H(31A)	783(9)	76(5)	1050(9)	8(3)
H(31B)	732(9)	161(6)	1011(10)	9(3)
H(31C)	830(9)	135(6)	969(9)	9(3)

Al or Sn were employed, there would be some delicate balance between steric control and enhanced secondary orbital control, and two cycloadducts were obtained in almost the same ratio with the noncatalyzed reaction.

Thus, magnesium salt is the most effective both for the acceleration of the reaction and for the stereoselective formation of the cycloadducts.

X-Ray analysis revealed the relative configuration of the predominantly afforded cycloadduct to be the *exo*-mode cycloadduct (trans ring junction; **16a**). The analysis was carried out as follows. The preferentially formed cycloadduct was obtained by the recrystallization of the mixture of two stereoisomers from cyclohexane. This isomer was converted to its *p*-bromobenzoylmethyl ether **18a** to get a good single crystal for X-ray analysis (Eq. 7).



(7)

16a 18a

The crystal data for this compounds are: $a=11.611(4)$ Å, $b=17.874(5)$ Å, $c=11.480(5)$ Å, $\beta=110.50(3)°$, space group $P2_1/c$, $D_c=1.43$ g/cm^3. Intensities of 1896 independent reflection within the limited sphere $2\theta=110°$ were collected on a fully automated diffractometer with graphic-monochromated Cu-$K\alpha$ radiation using ω-2θ scan technique. The structure was solved by the heavy atom method. All non-hydrogen atoms were found in the E-map and subsequent Fourier syntheses. A three dimentional difference Fourier map showed the positions of all H atoms. Block-diagnoal least-squares refinement reduced final R-value and R_w-value to 0.082 and 0.087, respectively. The function minimized was $(\sum w||F_o|-|F_c||^2)$, where the weights w are $1/\sigma(F)$. The atomic parameters with their estimated standard deviations are listed in Tables 6, 7, 8, and 9.[9] The numbering system and a stereoscopic view of the molecule are shown in Figs. 2 and 3, respectively. The bond distances and angles are given in Tables 10 and 11, respectively.

TABLE 10. BOND DISTANCES OF **18a**, WITH THEIR ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Bond distance	l/Å	Bond distance	l/Å
N(1)–C(2)	1.340(13)	C(23)–Br(26)	1.895(9)
N(1)–C(9)	1.464(14)	C(24)–C(25)	1.379(13)
N(1)–C(10)	1.404(11)	C(28)–(29)	1.496(17)
C(2)–C(3)	1.527(12)	C(29)–C(30)	1.508(15)
C(2)–O(27)	1.216(13)		
C(3)–C(4)	1.547(12)	C(4)–H(4)	1.04(7)
C(3)–C(8)	1.522(16)	C(5)–H(5)	1.06(9)
C(3)–C(28)	1.555(15)	C(6)–H(6)	1.05(8)
C(4)–C(5)	1.583(16)	C(7)–H(7)	0.92(8)
C(4)–C(30)	1.510(17)	C(8)–H(8)	1.02(9)
C(5)–C(6)	1.501(16)	C(9)–H(9A)	0.95(9)
C(5)–C(31)	1.512(15)	C(9)–H(9B)	0.97(9)
C(6)–C(7)	1.313(14)	C(11)–H(11)	0.92(8)
C(7)–C(8)	1.505(14)	C(12)–H(12)	0.91(8)
C(8)–C(9)	1.512(12)	C(13)–H(13)	0.99(8)
C(10)–C(11)	1.359(14)	C(14)–H(14)	1.00(7)
C(10)–C(15)	1.433(12)	C(7)–H(17A)	0.92(8)
C(11)–C(12)	1.370(14)	C(17)–H(17B)	1.15(8)
C(12)–C(13)	1.368(15)	C(21)–H(21)	0.90(8)
C(13)–C(14)	1.397(15)	C(22)–H(22)	0.95(11)
C(14)–C(15)	1.390(13)	C(24)–H(24)	0.95(9)
C(15)–O(16)	1.360(11)	C(25)–H(25)	0.87(8)
O(16)–C(17)	1.409(11)	C(28)–H(28A)	1.00(8)
C(17)–C(18)	1.507(13)	C(28)–H(28B)	0.96(11)
C(18)–O(19)	1.209(11)	C(29)–H(29A)	1.11(12)
C(18)–C(20)	1.499(12)	C(29)–H(29B)	0.96(12)
C(20)–C(21)	1.376(14)	C(30)–H(30A)	1.11(9)
C(20)–C(25)	1.397(13)	C(30)–H(30B)	1.16(7)
C(21)–C(22)	1.368(13)	C(31)–H(31A)	1.12(9)
C(22)–C(23)	1.394(14)	C(31)–H(31B)	0.99(11)
C(23)–C(24)	1.334(15)	C(31)–H(31C)	0.97(11)

As shown in Fig. 3, the ring junction between the ring A and the ring B is *trans*-configuration and the ring B links to the ring C with *cis*-configuration. The ring B is boat conformation, the atom C(5) and C(8) being displaced by 0.57 and 0.65 Å, respectively, form the plane of the other four atoms in this ring. The five-membered ring A and C both take an envelop conformation where the atoms C(8) and C(29) lie 0.63 and 0.59 Å, respectively, out of the plane composed of the other atoms. The atomic configuration of N(1) atom is estimated to be sp^2 hybrid orbital, since this atom is displaced by 0.06 Å from the plane consisted of three attached carbon atoms.

In conclusion, it is noted that an efficient and general method is established for the stereoselective intramolecular Diels-Alder reaction by employing internal coordination of the magnesium salt. By employing this

TABLE 11. BOND ANGLES OF **18a**, WITH THEIR ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Bond angle	ϕ/°	Bond angle	ϕ/°
C(2)–N(1)–C(9)	112.6(7)	C(11)–C(10)–C(15)	118.0(8)
C(2)–N(1)–C(10)	123.9(8)	C(10)–C(11)–C(12)	122.0(9)
C(9)–N(1)–C(10)	123.0(8)	C(11)–C(12)–C(13)	120.1(10)
N(1)–C(2)–C(3)	107.3(8)	C(12)–C(13)–C(14)	121.2(9)
N(1)–C(2)–O(27)	126.4(8)	C(13)–C(14)–C(15)	118.1(9)
C(3)–C(2)–O(27)	126.3(9)	C(10)–C(15)–C(14)	120.5(8)
C(2)–C(3)–C(4)	121.0(8)	C(10)–C(15)–O(16)	114.3(7)
C(2)–C(3)–C(8)	99.7(8)	C(14)–C(15)–O(16)	125.2(8)
C(2)–C(3)–C(28)	105.0(8)	C(15)–O(16)–C(17)	118.1(7)
C(4)–C(3)–C(8)	113.5(8)	O(16)–C(17)–C(18)	107.0(7)
C(4)–C(3)–C(28)	103.7(8)	C(17)–C(18)–O(19)	122.1(8)
C(8)–C(3)–C(28)	114.2(8)	C(17)–C(18)–C(20)	117.1(7)
C(3)–C(4)–C(5)	109.7(9)	O(19)–C(18)–C(20)	120.7(9)
C(3)–C(4)–C(30)	107.2(8)	C(18)–C(20)–C(21)	118.9(8)
C(5)–C(4)–C(30)	113.1(8)	C(18)–C(20)–C(25)	122.8(8)
C(4)–C(5)–C(6)	109.2(8)	C(21)–C(20)–C(25)	118.3(8)
C(4)–C(5)–C(31)	111.1(11)	C(20)–C(21)–C(22)	122.0(9)
C(6)–C(5)–C(31)	114.0(9)	C(21)–C(22)–C(23)	117.8(10)
C(5)–C(6)–C(7)	120.3(10)	C(22)–C(23)–C(24)	121.3(9)
C(6)–C(7)–C(8)	114.5(10)	C(22)–C(23)–Br(26)	117.8(7)
C(3)–C(8)–C(7)	109.2(9)	C(24)–C(23)–Br(26)	120.6(7)
C(3)–C(8)–C(9)	102.2(9)	C(23)–C(24)–C(25)	120.7(9)
C(7)–C(8)–C(9)	125.5(9)	C(20)–C(25)–C(24)	119.5(9)
N(1)–C(9)–C(8)	100.7(8)	C(3)–C(28)–C(29)	103.4(8)
N(1)–C(10)–C(11)	122.5(8)	C(28)–C(29)–C(30)	104.1(11)
N(1)–C(10)–C(15)	119.3(8)	C(4)–C(30)–C(29)	104.8(9)

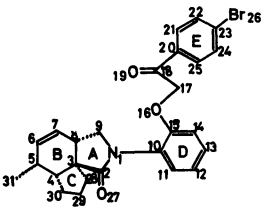


Fig. 2. Atomic numbering system of compound **18a**. Unaccampanied numbers indicate C atoms.

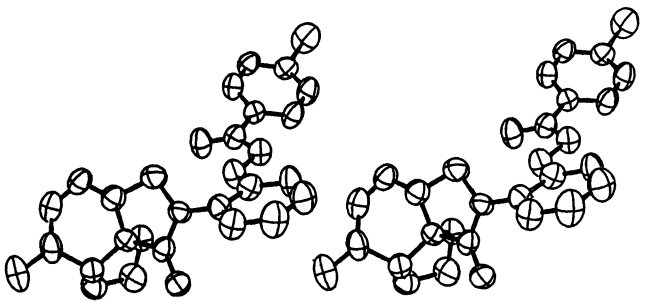


Fig. 3. Stereoscopic view of **18a**. Thermally vibrating Ellipsoids are drawn at the 50% probability level.

method, various cycloadducts, which cannot be prepared in the previous intramolecular Diels-Alder reaction, have become obtainable stereoselectively and in good yield.

Experimental

Measurements. All the melting points were uncorrected. ^{1}H-NMR spectra were recorded on a Bruker WH-270 (270 MHz) or a JEOL FX-90Q (90 MHz)or a Varian Model T-60 (60 MHz). IR spectra were taken on a Hitachi 260-50 spectrometer. Mass spectra were measured with JEOL JMS 01-SG. The intensity of crystal were collected on a Rigaku AFC-5 four-circle diffractomer. GC analyses were done on a Hitachi 163.

Materials. N-*(2-Hydroxyphenyl)acrylamide (7a)*: Under an argon atmosphere acryloyl chloride (9.06 g, 0.1 mol) was added to the suspension of 2-aminophenol **5** (10.91 g, 0.1 mol) and dry pyridine (8.1 ml) in dichloromethane (40 ml) at 0—5 °C and stirred at room temperature for 2 h. To the reaction mixture 2 M hydrochloric acid (5 ml)†† was added and the organic layer was washed with water (15 ml×3). After being dried over Na_2SO_4, the solution was evaporated *in vacuo*. The residue was recrystallized from benzene to afford amide **7a** (13.06 g, 80%). Mp 114.5—115.5 °C (benzene); IR (KBr) 3405, 3092 and 1685 cm^{-1}; NMR ($CDCl_3$) δ=5.50—5.97 (1H, m), 6.17—6.50 (2H, m), 6.70—7.27 (4H, m), 7.50—8.00 (1H, broad), 8.73 (1H, s); Found: C, 66.21; H, 5.49; N, 8.43%. Calcd for $C_9H_9NO_2$: C, 66.24; H, 5.56; N, 8.58%. By similar procedure amide **7b** was prepared. **7b**: Mp 147.0—148.5 °C (benzene); IR (KBr) 3291 and 1627 cm^{-1}; NMR ($CDCl_3$) δ=1.87 (3H, s), 2.17 (3H, s), 5.83 (1H, m), 6.50—6.97 (3H, m), 7.30—7.60 (1H, m), 8.98 (1H, s), 9.33—9.87 (1H, broad); Found: C, 69.03; H, 6.84; N, 7.48%. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33%.

N-[*2-(Tetrahydropyranyloxy)phenyl*]*acrylamide (8a)*. To the solution of amide **7a** (5.23 g, 32.0 mmol) and pyridinium *p*-toluenesulfonate (0.81 g, 3.2 mmol) in dichloromethane (150 ml), 3,4-dihydro-2*H*-pyran (5.11 g, 60.5 mmol) was added dropwise. After being stirred for 2 h at room temperature, 2 M sodium hydroxide (30 ml) was added to the mixture. The organic layer was washed with water (3×30 ml) and dried over Na_2SO_4. After the solvent was evaporated *in vacuo*,

†† 1 M=1 mol dm^{-3}.

residual oil was crystallized from petroleum ether to afford amide **8a** as white needles (6.42 g, 81%). Mp 81.0—82.0 °C (hexane); IR (KBr) 3408 and 1680 cm^{-1}; NMR ($CDCl_3$) δ= 1.50—2.20 (6H, m), 3.30—4.17 (2H, m), 5.20 (1H, m), 5.47—5.73 (1H, m), 6.03—6.33 (2H, m), 6.70—7.13 (3H, m), 7.73—8.00 (1H, broad), 8.03—8.37 (1H, m); Found: C, 67.92; H, 7.08; N, 5.55%. Calcd for $C_{14}H_{17}NO_3$: C, 67.99; H, 6.93; N, 5.66%. By similar procedure amide **8b** was prepared. **8b**: Mp 88.5—89.5 °C (hexane); IR (KBr) 3354 and 1667 cm^{-1}; NMR ($CDCl_3$) δ=1.40—2.07 (6H, m), 1.90 (3H, s), 2.20 (3H, s), 3.37—4.00 (2H, m), 5.30 (1H, m), 5.33 (1H, m), 6.80—7.23 (3H, m), 7.57—7.97 (1H, broad), 8.07—8.50 (1H, m); Found: C, 69.50; H, 7.83; N, 4.98%. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09%.

N-(trans, trans-2,4-Hexadienyl)-N-(2-hydroxyphenyl)acrylamide (9a). Under an argon atmosphere, amide **8a** (3.93 g, 15.9 mmol) in dry THF (15 ml) was added slowly at 0 °C to the suspension of potassium hydride (0.64 g, 15.9 mmol) in dry THF (15 ml) and the mixture was further stirred at room temperature for 15 min. To the mixture *trans,trans*-2,4-hexadienyl bromide (2.55 g, 15.9 mmol) was added dropwise at −76 °C over 10 min. After being stirred at room temperature overnight, the reaction mixture was quenched with water (10 ml) and extracted with ethyl acetate (3×20 ml). The extracts were dried over Na_2SO_4 and evaporated *in vacuo*. The residual oil was purified by the silica-gel column chromatography using hexane–ether (2 : 1). Then, the product was dissolved in ethanol (15 ml) and 2 M hydrochloric acid (2 ml). After being heated at 50—55 °C for 2 h, the reaction mixture was neutralized with 5% sodium hydrogencarbonate and extracted with dichloromethane (2×15 ml). The organic layer was washed with water and dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the residual oil was purified by the silica-gel column chromatography using dichloromethane to afford amide **9a** (2.68 g, 70%). Oil; IR (liquid) 3150, 1630, and 1610 cm^{-1}; NMR ($CDCl_3$) δ=1.67 (3H, d, J=6 Hz), 3.87 (1H, dd, J=5 and 14 Hz), 4.70 (1H, dd, J=5 and 14 Hz), 5.13—6.33 (6H, m), 6.70—7.40 (5H, m), 8.60 (1H, s).

N-(trans, trans-2,4-Pentadienyl)-N-(2-hydroxyphenyl)-3-methyl-2-butenamide (9b). Under an argon atmosphere, amide **8b** (5.51 g, 0.02 mol) in dry THF (15 ml) was added dropwise at 0 °C to the solution (THF 50 ml–HMPT 10 ml) of lithium diisopropylamide (0.02 mol) and the mixture was further stirred at room temperature for 30 min. Then *trans,trans*-2,4-pentadienyl bromide (2.96 g, 0.02 mol) was added dropwise to the reaction mixture at −76 °C. After being stirred at room temperature for 2 h, the reaction mixture was quenched with 2 M hydrochloric acid (20 ml) and water (30 ml), and extracted with dichloromethane (3×30 ml). The extracts were washed with water (3×30 ml), dried over Na_2SO_4 and evaporated *in vacuo*. The residual oil was purified by the silica-gel column chromatography using hexane–ether (2 : 1). The product was hydrolyzed with 2 M hydrochloric acid in ethanol in the same way with the preparation of amide **9a** to afford amide **9b** (3.86 g, 75%). Mp 140.5—142.0 °C (hexane); IR (KBr) 3170, 1642, and 1604 cm^{-1}; NMR ($CDCl_3$) δ=1.65 (3H, s), 2.08 (3H, s), 3.58—4.10 (1H, m), 4.28—4.57 (1H, m), 4.83—5.55 (3H, m), 5.62—6.47 (3H, m), 6.67—7.28 (4H, m), 7.42 (1H, s); Found: C, 74.77; H, 7.31; N, 5.72%. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44%. By similar procedure amides **9c** and **14a—d** were prepared. **9c**: Mp 69.0—70.0 °C (hexane–cyclohexane); IR (KBr) 3220, 1644, and 1608 cm^{-1}; NMR ($CDCl_3$) δ=1.63 (3H, s), 1.70 (3H, d, J=6 Hz), 2.07 (3H, s), 3.50—4.07 (1H, m), 4.20—4.83 (1H, m), 5.10—6.17 (5H, m), 6.53—7.27 (4H, m), 7.67 (1H, s); Found: C, 75.19; H, 7.57; N, 5.25%. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16%. **14a**: Oil; IR (liquid) 3170, 1610, and 1580 cm^{-1}; NMR ($CDCl_3$) δ=1.33—1.93 (2H, m), 1.67 (3H, d, J=6 Hz), 1.97—2.47 (4H, m), 3.70—4.73 (2H, m), 5.13—6.20 (4H, m), 6.50—7.37 (5H, m), 7.60 (1H, s); Found: *m/e* 283.1603. Calcd for $C_{18}H_{21}NO_2$: M, 283.1572. **14b**: Oil; IR (liquid) 3140, 1604, and 1580 cm^{-1}; NMR ($CDCl_3$) δ=1.27—1.90 (2H, m), 1.93—2.60 (4H, m), 3.60—4.33 (1H, m), 4.40—5.33 (3H, m), 5.37—6.47 (4H, m), 6.53—7.20 (4H, m), 8.73—9.93 (1H, broad); Found: *m/e* 269.1421. Calcd for $C_{17}H_{19}NO_2$: M, 269.1415. **14c**: Oil; IR (liquid) 3140, 1605, and 1580 cm^{-1}; NMR ($CDCl_3$) δ=1.33—1.97 (2H, m), 1.77 (3H, s), 2.03—2.60 (4H, m), 3.70—4.40 (1H, m), 4.47—5.27 (1H, m), 4.83 (2H, s), 5.40—6.37 (3H, m), 6.53—7.20 (4H, m), 8.43—9.43 (1H, broad); Found: *m/e* 283.1607. Calcd for $C_{18}H_{21}NO_2$: M, 283.1572. **14d**: Oil; IR (liquid) 3150, 1610, and 1570 cm^{-1}; NMR ($CDCl_3$) δ=0.93 (6H, d, J=6 Hz), 1.30—1.90 (2H, m), 1.93—2.60 (5H, m), 3.60—4.20 (1H, m), 4.23—4.83 (1H, m), 5.00—6.13 (5H, m), 6.40—7.10 (4H, m), 7.70—8.20 (1H, broad); Found: *m/e* 311.1858. Calcd for $C_{20}H_{25}NO_2$: M, 311.1885.

Intramolecular Diels-Alder Reaction Using Magnesium Salt. 3a,6,7,7a-Tetrahydro-2-(2-hydroxyphenyl)-6-methyl-1-isoindolinone (11a and 12a): To a solution of amide **9a** (314 mg, 1.29 mmol) in dry THF (3 ml) was added dropwise butylmagnesium chloride (1.42 ml, 0.91 mol/l ether solution) at −78 °C under an argon atmosphere. After the solvent was concentrated under the reduced pressure at room temperature, toluene (10 ml) was added and the reaction mixture was refluxed for 16 h under an argon atmosphere. To the solution was added 2 M hydrochloric acid (2 ml) and the products were extracted with ethyl acetate. The extract was washed with water and dried over Na_2SO_4. The solution was evaporated *in vacuo* and the crude product was purified on a silica-gel thin-layer chromatography using hexane–ethyl acetate (3 : 2) to afford the cycloadduct (**11a** and **12a**) (241 mg, 77%). Two stereoisomers **11a** and **12a** were cleanly separable by the silica-gel thin-layer chromatography (**11a** : **12a**=58 : 42). **11a**: Mp 136.0—137.0 °C (cyclohexane); IR (KBr) 3070, 3030, 1658, and 1595 cm^{-1}; NMR (270 MHz) ($CDCl_3$); δ= 1.10 (3H, d, J=7 Hz), 1.84 (1H, dt, J=7 and 13 Hz), 2.00 (1H, dd, J=3 and 13 Hz), 2.42 (1H, dt, J=13 and 3 Hz), 2.56 (1H, m), 2.78 (1H, m), 3.75 (2H, m), 5.77 (1H, dt, J=10 and 3 Hz), 5.81 (1H, dt, J=10 and 1.5 Hz), 6.77—7.40 (4H, m), 8.76 (1H, s); Found: C, 74.00; H, 7.00; N, 5.78%. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76%. **12a**: Mp 135.0—136.0 °C (hexane); IR (KBr) 3090, 2095, 1658, and 1595 cm^{-1}; NMR (270 MHz) ($CDCl_3$); δ=1.09 (3H, d, J=7 Hz), 1.39 (1H, dt, J=13 and 10 Hz), 2.10 (1H, dt, J=13 and 5 Hz), 2.27 (1H, m), 2.82 (1H, ddd, J=13, 8, and 5 Hz), 3.12 (1H, m), 3.75 (1H, t, J=9 Hz), 3.94 (1H, t, J=9 Hz), 5.65 (1H, ddd, J=10, 3.5, and 2.5 Hz), 5.79 (1H, broad d, J=10 Hz), 6.99—7.37 (4H, m), 8.59 (1H, s); Found: C, 74.04; H, 7.03; N, 5.81%. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76%. By similar procedure cycloadducts **11b—c** and **12b—c** were afforded. **11b**: Mp 95.0—96.0 °C (cyclohexane); IR (KBr) 3050, 2880, 1652, and 1595 cm^{-1}; NMR (90 MHz) ($CDCl_3$); δ=1.04 (3H, s), 1.36 (3H, s), 1.99 (2H, m), 2.21 (1H, d, J=12 Hz), 2.57—3.17 (1H, broad), 3.70 (2H, d, J=6 Hz), 5.74 (2H, m), 6.81—7.41 (4H, m), 8.80 (1H, s); Found: C, 74.45; H, 7.42; N, 5.47%. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44%. **12b**: Mp 130.0—131.0 °C (cyclohexane); IR (KBr) 3045, 2950, 1633, and 1595 cm^{-1}; NMR (90 MHz) ($CDCl_3$) δ=1.10 (3H, s), 1.27 (3H, s), 1.60—2.36 (2H, m), 2.56 (1H, d, J=8 Hz), 2.89—3.29 (1H, broad), 3.52 (1H, dd, J=5 and 9 Hz), 4.03 (1H, dd, J=7 and 9 Hz), 5.41—5.99 (2H, m), 6.67—7.36 (4H, m), 8.47 (1H,

s); Found: C, 74.54; H, 7.54; N, 5.46%. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44%. **11c**: Mp 112.0—113.0 °C (cyclohexane); IR (KBr) 3040, 2960, 1659, and 1595 cm^{-1}; NMR (90 MHz) ($CDCl_3$) δ=0.99 (3H, d, J=7 Hz), 1.06 (3H, s), 1.33 (3H, s), 1.68—2.04 (1H, m), 2.24 (1H, d, J=12 Hz), 2.64—3.11 (1H, m), 3.68 (2H, m), 5.68 (2H, m), 6.68—7.29 (4H, m), 8.75 (1H, s); Found: C, 75.54; H, 7.73; N, 5.02%. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16%. **12c**: Mp 142.0—143.0 °C (cyclohexane); IR (KBr) 3040, 2960, 1645, and 1595 cm^{-1}; NMR (90 MHz) ($CDCl_3$) δ=0.97 (3H, s), 1.03 (3H, d, J=8 Hz), 1.26 (3H, s), 1.86—2.25 (1H, m), 2.51 (1H, d, J=8 Hz), 2.93—3.36 (1H, m), 3.77 (2H, m), 5.60 (2H, s), 6.60—7.29 (4H, m), 8.46 (1H, s); Found: C, 75.38; H, 7.91; N, 5.12%. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16%. In the case of the cycloaddition reactions of amides **14a—d**, the reactions were carried out in the same way, but two stereoisomers could not be separated eacho ther by silica-gel thin-layer chromatography. The predominantly formed cycloadducts **16a—d** were isolated by the recrystallization from cyclohexane after the purification of cycloadducts (one spot of two stereoisomers) from other miner spots by silica-gel thin-layer chromatography using hexane–ethyl acetate (3 : 2). Physical properties and spectral data of **16a—d** are as follows. **16a**: Mp 100.0—101.0 °C (cyclohexane); IR (KBr) 2960 and 1651 cm^{-1}; NMR ($CDCl_3$) δ=1.11 (3H, d, J=7 Hz), 1.23—1.90 (6H, m), 2.07—3.07 (3H, m), 3.50—4.20 (2H, m), 5.50—6.13 (2H, m), 6.67—7.23 (4H, m), 8.77 (1H, s); Found: C, 76.10; H, 7.48; N, 5.00%. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94%. **16b**: Mp 113.0—114.0 °C (cyclohexane); IR (KBr) 2960 and 1651 cm^{-1}; NMR ($CDCl_3$) δ=1.05—2.38 (8H, m), 2.38—3.28 (2H, m), 3.43—4.10 (2H, m), 5.91 (2H, m), 6.63—7.17 (4H, m), 8.72 (1H, s); Found: C, 75.76; H, 7.13; N, 5.25%. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20%. **16c**: Mp 129.0—130.0 °C (cyclohexane); IR (KBr) 2970 and 1642 cm^{-1}; NMR ($CDCl_3$) δ=1.42 (3H, s), 1.10—1.90 (6H, m), 1.96—3.08 (4H, m), 3.48—3.98 (2H, m), 5.44—5.60 (1H, m), 6.68—7.28 (4H, m), 8.86 (1H, s); Found: C, 76.27; H, 7.53; N, 4.95%. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94%. **16d**: Mp 142.0—143.0 °C (cyclohexane): IR (KBr 2960 and 1648 cm^{-1}; NMR ($CDCl_3$) δ=1.02 (6H, d, J=5 Hz), 1.08—2.08 (8H, m), 2.58—2.96 (2H, m), 3.58—4.18 (2H, m), 5.98 (2H, s), 6.72—7.24 (4H, m), 8.84 (1H, s); Found: C, 76.92; H, 8.01; N, 4.57%. Calcd for $C_{20}H_{25}NO_2$: C, 77.13; H, 8.09; N, 4.50%.

Isomerization of Cycloadducts 11a to 12a. A solution of adduct **11a** (99.5 mg, 0.39 mmol) and 28% sodium methoxide (0.15 ml, commercially available in methanol solution) was refluxed for 20 h. The mixture was neutralized with 2 M hydrochloric acid and extracted with dichloromethane. The organic layer was washed with water and dried over Na_2SO_4. The needles obtained by the evaporation of the solvent *in vacuo* was identical in all respects with adduct **12a** (99.0 mg, 99%). By similar procedure adduct **11b** was isomerized to adduct **12b**, but, in the case of adduct **11c**, sodium hydride was used as base instead of sodium methoxide.

2,3,3a,6,6a,7,8,9-Octahydro-2-[2-(4-bromobenzoylmethoxy)phenyl]-1H-cyclopent[d]isoindol-1-one (18a). To the suspension of adduct **16a** (413.2 mg, 1.46 mmol) and potassium carbonate (111.9 mg, 0.81 mmol) in aceton (20 ml) 4-bromophenacyl bromide (446.6 mg, 1.61 mmol) was added. After the mixture was refluxed for 2 h, water (10 ml) was added. After the extraction with dichloromethane (2×20 ml) the organic layer was dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by silica-gel column chromatography using ether–hexane (1 : 1) to afford **18a** (547.1 mg, 80%). Mp: 188.0—189.0 °C (methanol); IR (KBr) 1702, 1681, and 1588 cm^{-1}; NMR ($CDCl_3$) δ=1.11 (3H, d, J=7 Hz), 1.21—1.78 (6H, m), 2.20 (1H, m), 2.40—2.80 (2H, m), 3.78 (2H, m), 5.20 (2H, s), 5.76 (1H, m), 5.91 (1H, m), 6.84—7.44 (4H, m), 7.62 (2H, d, J=8 Hz), 7.84 (2H, d, J=8 Hz).

References

1) W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977).

2) a) T. Mukaiyama, T. Tsuji, and N. Iwasawa, *Chem. Lett.*, **1980**, 697; b) T. Mukaiyama and T. Takebayashi, *ibid*, **1980**, 1013.

3) a) W. R. Roush, *J. Org. Chem.*, **44**, 4008 (1979); b) W.R. Roush, A. I. Ko and H. R. Gillis, *ibid*, **45**, 4264 (1980); c) W. R. Roush and H. R. Gillis, *ibid*, **45**, 4267 (1980); d) W. R. Roush and S. M. Peseckis, *J. Am. Chem. Soc.*, **103**, 6696 (1981); e) W. R. Roush and H. R. Gillis, *J. Org. Chem.*, **45**, 4283 (1980); f) W. R. Roush and S. E. Hall, *J. Am. Chem. Soc.*, **103**, 5200 (1981); g) W. R. Roush, H. R. Gillis and I. K. Albert, *ibid.*, **104**, 2269 (1982).

4) a) R. K. Boekman, Jr., and S. S. Ko, *J. Am. Chem. Soc.*, **102**, 7149 (1980); b) R. K. Boeckman, Jr., and S. S. Ko, *ibid*, **104**, 1033 (1982); c) R. K. Boeckmen, Jr., and T. R. Alessi, *ibid*, **104**, 3216 (1982); d) R. K. Boeckman, Jr., and D. M. Demko, *J. Org. Chem.*, **47**, 1792 (1982).

5) a) J. D. White, B. G. Sheldon, B. A. Solheim, and J. Clardy, *Tetrahedron Lett.*, **1978**, 5189; b) J. D. White and B. G. Sheldom, *J. Org. Chem.*, **46**, 2273 (1981).

6) G. Brieger and J. N. Benett, *Chem. Rev.*, **80**, 63 (1980).

7) H. W. Gschwend, A. L. Lee, and H. D. Meier, *J. Org. Chem.*, **38**, 2169 (1973).

8) We did not perform X-ray analysis of predominantly formed cycloadducts **16b—d**, but from the retention time of GC analysis and spectral analogy of ^{1}H-NMR we assume that cycloadducts (**16b—d**) are the same *exo*-mode cycloadducts as cycloadduct **16a**.

9) Table 9 shows observed and calculated structure factors. The complete F_o-F_c data are deposited as Document No. 8323 at the Office of the Editor of the Bulletin of the Chemical Society of Japan.