(calculated from HPLC analysis of the corresponding 1-phenylethanol); ^{1}H NMR (200 MHz) δ 0.86 (m, 3 H, CH_3), 1.12–1.40 (m, 8 H, $(CH_2)_4$), 1.64 (m, 2 H, $COCH_2CH_2$), 2.39 (2 t, 2 H, J = 7.4 Hz, $COCH_2$), 3.71 (dd, 1 H, J_1 = 4.8, J_2 = 11.6 Hz, CH_2), 3.79 (dd, 1 H, J_1 = 7.6, J_2 = 11.6 Hz, CH_2), 5.96 (dd, 1 H, J_1 = 4.8, J_2 = 7.6 Hz, CH), 7.30–7.40 (m, 5-H).

Stereochemical Correlation. $LiAlH_4$ Reduction of 3; Typical Procedure. Ester **3b** [100 mg, 0.34 mmol, $[\alpha]^{25}_D$ +70.0° (*c* 3.0, $CHCl_3$)] was reduced with $LiAlH_4$ (25.8 mg, 0.68 mmol) at 0 °C in dry THF (5 mL) for 3 h. The usual workup and chromatographic purification gave (+)-1-(2-naphthyl)ethanol (25.7 mg, 44%): $[\alpha]^{25}_D$ +33.7° (*c* 1.29, EtOH) [lit.[15] $[\alpha]^{25}_D$ +41.3° (*c* 5.07, EtOH) for *R* isomer]; ^{1}H NMR (200 MHz) δ 1.58 (d, 3 H, J = 6.4 Hz, Me), 1.92 (br s, 1 H, OH), 5.07 (q, 1 H, J = 6.4 Hz, CH), 7.23–7.53 and 7.75–7.88 (m, 7-H). The ee was calculated to be 95% by HPLC (CHIRALCEL OB, hexane/propan-2-ol, 9:1, 0.3 mL/min, detected at 280 nm, t_R 43.2 (*S*) and 47.7 (*R*) min, α = 1.15).

(*R*)-(+)-1-Phenylethanol was prepared from ester **3c** [$[\alpha]^{25}_D$ +56.6° (*c* 3.4, $CHCl_3$)] by $LiAlH_4$ reduction (DME, reflux 12 h): $[\alpha]^{25}_D$ +51.4° (*c* 1.56, $CHCl_3$) [lit.[12b] $[\alpha]^{25}_D$ −50.2° (*c* 5.11, $CHCl_3$) for *S* isomer (93% ee)]; ^{1}H NMR (200 MHz) δ 1.50 (d, 3 H, J = 6.4 Hz, Me), 1.84 (s, 1 H, OH), 4.89 (q, 1 H, J = 6.4 Hz, CH), 7.20–7.45 (m, 5-H). The ee was determined as 96% by HPLC (CHIRALCEL OB, hexane/propan-2-ol, 9:1, 0.5 mL/min, detected at 254 nm, t_R 14.9 (*S*) and 18.3 (*R*) min, α = 1.50).

(*R*)-(+)-1-(4-Methoxyphenyl)ethanol was prepared from ester **3d** [$[\alpha]^{25}_D$ +73.4° (*c* 1.0, $CHCl_3$)] by $LiAlH_4$ reduction (THF, 0 °C, 3 h): $[\alpha]^{25}_D$ +31.1° (*c* 2.54, EtOH) [Lit.[16] $[\alpha]^{20}_D$ +19.4° (EtOH) for partially resolved *R* isomer]; ^{1}H NMR (200 MHz) δ 1.47 (d, 3 H, J = 6.5 Hz, Me), 1.83 (br s, 1 H, OH), 3.79 (s, 3 H, OMe), 4.84 (q, 1 H, J = 6.5 Hz, CH), 6.82–6.90 and 7.26–7.35 (m, 4-H).

Acknowledgment. We gratefully acknowledge a Grant-in-Aid from the Ministry of Education of Japan for Scientific Research on Priority Areas, Advanced Molecular Conversion.

Registry No. **1a**, 108-05-4; **1b**, 108-22-5; **1c**, 123-20-6; **1d**, 818-44-0; (±)-**2a**, 105228-01-1; (−)-**2a**, 56751-12-3; (±)-**2b**, 117465-33-5; (−)-**2b**, 85554-14-9; (±)-**2c**, 117465-34-6; (−)-**2c**, 96855-38-8; (±)-**2d**, 117340-79-1; (−)-**2d**, 117465-37-9; (±)-**2e**, 117340-80-4; (−)-**2e**, 117465-38-0; **3a**, 103665-43-6; **3b**, 117340-81-5; **3c**, 117340-82-6; **3d**, 117340-83-7; **3e**, 117340-84-8; **3f**, 117465-35-7; **3g**, 117465-36-8; 2-bromo-1-(4-bromophenyl)ethanone, 99-73-0; 2-bromo-1-(4-methoxyphenyl)ethanone, 2632-13-5; 2-bromo-1-(2-naphthalenyl)ethanone, 613-54-7; chloromethyl 3,4-dihydroxyphenyl ketone, 99-40-1; chloromethyl 3,4-dimethoxyphenyl ketone, 20601-92-7; chloromethyl phenyl ketone, 532-27-4; lipase amano p, 9001-62-1; (*R*)-(+)-1-(4-methoxyphenyl)ethanol, 1517-70-0; (+)-1-(2-naphthyl)ethanol, 52193-85-8; (*R*)-(+)-1-phenylethanol, 1517-69-7.

(*S*)-Proline Benzyl Ester as Chiral Auxiliary in Lewis Acid Catalyzed Asymmetric Diels–Alder Reactions

Herbert Waldmann

Institut für Organische Chemie, Becherweg 18-20, Joh.-Gutenberg Universität, D-6500 Mainz, Federal Republic of Germany

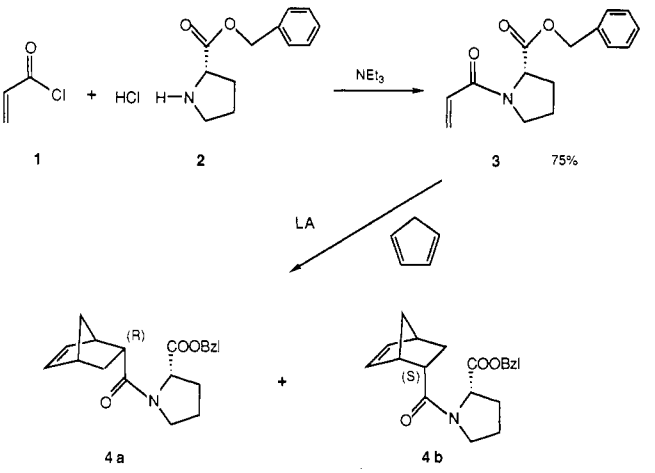
Received July 20, 1988

Asymmetric Diels–Alder reactions in which the cycloadducts are formed in high yields and with excellent diastereoselectivities have been carried out with chiral dienophilic esters,[1,5] α,β-unsaturated acyloxazolidinones[2] and -sultams.[3] In most cases reported the observed selectivities were explained exclusively by steric shielding. However, several authors recently have demonstrated that chelation with Lewis acids allows for an efficient differentiation of the diastereotopic faces of chiral acrylates.[2-5] This holds true especially for the acrylic acid ester of (*R*)-pantolactone.[5] The purpose of this paper is to describe that by using (*S*)-proline benzyl ester as chiral auxiliary high diastereoselectivities are obtained in Lewis acid catalyzed Diels–Alder reactions.

N-Acryloyl-(*S*)-proline benzyl ester (**3**) is easily prepared from acrylic acid chloride and proline benzyl ester hydrochloride.[6] It reacts with cyclopentadiene in the presence of Lewis acids in dichloromethane as solvent in good yields to provide the Diels–Alder adducts (Scheme I, Table I).

Depending on the catalyst used, either the 5*R* product **4a** or the 5*S* product **4b** is formed in excess. The best stereoselection is achieved at −10 °C in the presence of $TiCl_4$ (**4a**:**4b** = 97:3); however, at this temperature the yield

Scheme I



LA = Lewis Acid (see Table I)

Table I. Results of the Lewis Acid Catalyzed Diels–Alder Reactions between Cyclopentadiene and *N*-Acryloyl-(*S*)-proline Benzyl Ester

entry	temp, °C	Lewis acid	equiv of Lewis acid	yield, %	ratio **4a**:**4b**	endo/exo ratio
1	−10	$TiCl_4$	1	53	97:3	94:6
2	0	$TiCl_4$	1	85	96.5:3.5	92:8
3	10	$TiCl_4$	1	95	94:6	92:8
4	20	$TiCl_4$	1	95	96:4	90:10
5	30	$TiCl_4$	1	95	95:5	90:10
6	0	$TiCl_4$	0.75	83	96.3:3.7	93:7
7	0	$SnCl_4$	1	79	77:23	90:10
8	0	$ZnCl_2$	1	92	20:80	91:9
9	0	BF_3	1	80	16:84	91:9
10	0	$EtAlCl_2$	1	96	10:90	92:8

(1) For recent reviews, see: (a) Helmchen, G.; Karge, P.; Weetmann, J. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer: Berlin, 1986; vol 19, p 261. (b) Oppolzer, W. *Angew. Chem.* **1984**, *96*, 840; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876; *Tetrahedron* **1987**, *43*, 1969.

(2) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238.

(3) Oppolzer, W.; Chapuis, C.; Bernardinelli, G. *Helv. Chim. Acta* **1984**, *67*, 1397.

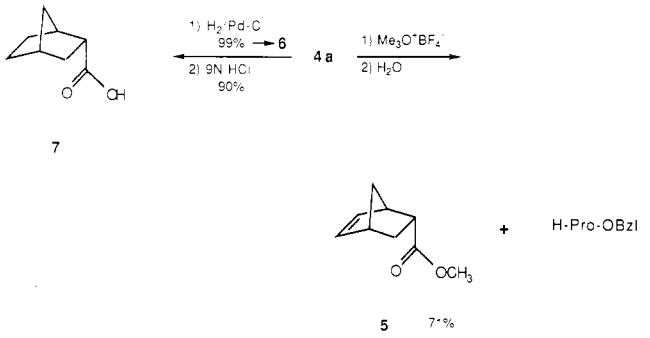
(4) (a) Mukaiyama, T.; Iwasawa, N. *Chem. Lett.* **1981**, 29. (b) Masamune, S.; Reed, L. A. III; Davis, J. T.; Choy, W. *J. Org. Chem.* **1983**, *48*, 4441. (c) Poll, T.; Helmchen, G.; Bauer, B. *Tetrahedron Lett.* **1984**, *25*, 2191. (d) Kelly, T. R.; Whiting, R.; Chandrakumar, N. S. *J. Am. Chem. Soc.* **1986**, *108*, 3510. (e) Kunz, H.; Müller, B.; Schanzenbach, D. *Angew. Chem.* **1987**, *99*, 269; *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 267.

(5) Poll, T.; Sobczak, A.; Hartmann, H.; Helmchen, G. *Tetrahedron Lett.* **1985**, *26*, 3095.

(6) Ramachandran, J.; Lin, C. H. *J. Org. Chem.* **1963**, *28*, 173.

0022-3263/88/1953-6133$01.50/0

Scheme II



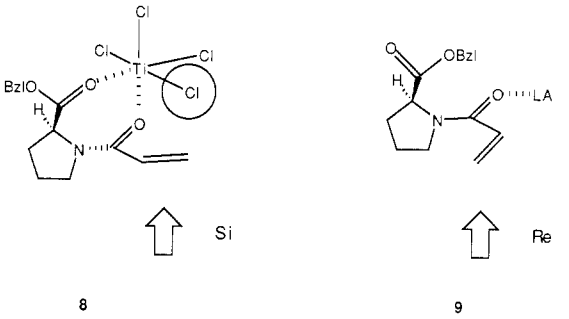
is unsatisfying. At 0 °C and higher temperatures the diastereoselectivities remain excellent, but the yield is improved. Reducing the amount of the catalyst to 0.75 equiv has only minor influence on the diastereomer ratio. If $TiCl_4$ is substituted by $SnCl_4$ the diastereomeric excess drops drastically, but **4a** is still the preferred isomer. Remarkably the application of Lewis acids that have only the capability of tetracoordination, e.g. $ZnCl_2$, BF_3, and $EtAlCl_2$, causes a reversal of the stereoselection. Here, the aluminum compound displays the best properties (**4a**:**4b** = 10:90).

In the transformations described the proline benzyl ester proves to be a very practical chiral auxiliary. Thus the composition of the reaction mixtures can be directly determined from their 400-MHz ^1H NMR spectra. Furthermore, after simple separation of the exo isomers by flash chromatography, the major diastereomers of the endo adducts can be isolated by a single recrystallization from ether.

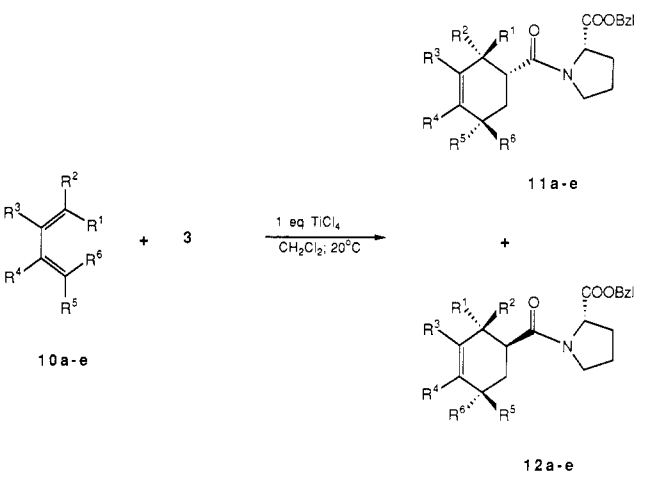
To determine the absolute configurations of the cycloadducts, the amide **4a** was transformed to the ester **5** by O-alkylation with trimethyloxonium tetrafluoroborate[7] and subsequent hydrolysis of the iminium salt generated in this reaction (Scheme II). In the hydrolysis step not only the desired ester **5** but also the starting amide **4a** is formed. It can be isolated during workup and reused for the removal of the chiral auxiliary. Compound **5** displays a specific rotation of $[\alpha]^{22}_D$ 136° (*c* 0.5, ethanol), which is in good agreement with literature data (specific rotation for the corresponding (−)-enantiomer: $[\alpha]^{26}_D$ −141° (*c* 0.5, ethanol)[8]). (*S*)-Proline benzyl ester **6** is recovered without racemization in 72% yield. Thus, by these simple transformations the auxiliary group is effectively removed from the Diels–Alder adducts. Alternatively the proline moiety can be removed by acid-catalyzed hydrolysis after simultaneous hydrogenation of the double bond and the benzyl ester function (Scheme II). A comparison of the specific rotation measured for the acid **7** ($[\alpha]^{22}_D$ 33.3° (*c* 1.1, ethanol) with the literature data ($[\alpha]^{22}_D$ 33.9° (*c* 1.06, ethanol)[2,7]) again proves the absolute configuration of **4a**.

The observed diastereoselectivities can be explained in analogy to a model that has been proposed and experimentally proven by Helmchen et al. for the acrylates of α-hydroxy carboxylic acid esters.[9] According to this model $TiCl_4$ would form a chelate **8** with the amino acid derivative in which the acrylamide moiety is in syn conformation (Scheme III). In this complex the *Re* side of the dienophile is shielded by the Lewis acid and the attack of the diene from the *Si* side is favored, resulting in the formation of **4a**. In the presence of $ZnCl_2$, BF_3, and $EtAlCl_2$ a complex **9** with an antiplanar arrangement of the acrylamide is probable (simple acrylates without additional complexation site generally prefer this conformation in the presence of Lewis acids[1,10]). As a consequence the attack of the diene is directed to the *Re* side of the double bond and **4b** is formed in excess.

Scheme III



Scheme IV[a]



[a] **10a**: R^1–R^6 = $(CH_2)_2$; R^2 = R^3 = R^4 = R^5 = H. **10b**: R^2 = CH_3; R^1 = R^3 = R^4 = R^5 = R^6 = H. **10c**: R^2 = R^5 = CH_3; R^1 = R^3 = R^4 = R^6 = H. **10d**: R^4 = CH_3; R^1 = R^2 = R^3 = R^5 = R^6 = H. **10e**: R^3 = R^4 = CH_3; R^1 = R^2 = R^5 = R^6 = H.

Table II. Results of the $TiCl_4$-Catalyzed Diels–Alder Reactions of the Proline Acrylamide 3 with the Dienes 10a–e at 20 °C

diene	yield, %	diastereomer ratio 11a–e:12a–e
10a	24	94:6
10b	41	89:6.5:2.7:1.8[a]
10c	42	90:10
10d	72	92:8
10e	75	90:10

[a] The minor diastereomers could not be assigned correctly.

The chiral dienophile **3** also reacts with less reactive acyclic dienes in the presence of $TiCl_4$ (Scheme IV). However, to obtain satisfactory yields these cycloadditions have to be carried out at 20 °C. Even at this temperature, which is high for diastereoselective reactions, the stereoselectivities are in the useful range (≥80% de; Table II). The absolute configurations of **11** and **12** were assigned, assuming that the transition states are similar to those encountered in the reactions with cyclopentadiene.

(7) Pilotti, A.; Reuterhall, A.; Torsell, K. *Acta Chem. Scand.* **1963**, *23*, 818.
(8) Berson, J. A.; Ben-Efraim, D. A. *J. Am. Chem. Soc.* **1959**, *81*, 4083.
(9) Poll, T.; Metter, J. O.; Helmchen, G. *Angew. Chem.* **1985**, *97*, 116; *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 112. The authors were able to obtain an X-ray analysis of a $TiCl_4$–lactic acid ethyl ester complex.
(10) Loncharich, R. J.; Schwartz, T. R.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 14.

In conclusion (*S*)-proline benzyl ester is an efficient auxiliary in diastereoselective Diels–Alder reactions. The facts that (*S*)- and (*R*)-proline are commercially available and that the auxiliary can be removed from the cycloadducts and recovered in good yields also render the proline ester very interesting from an economical point of view.

Experimental Section

Melting points are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 polarimeter, IR spectra with a Beckman Acculab-2; 400-MHz ^{1}H NMR and 100.6-MHz ^{13}C NMR spectra were obtained on a Bruker AM 400 spectrometer.

***N*-Acryloyl-(*S*)-proline Benzyl Ester (3).** To a solution of (*S*)-proline benzyl ester hydrochloride **2** (10 g, 41.1 mmol), in 200 mL of dichloromethane, triethylamine (8.36 g, 82.8 mmol), and 4-(dimethylamino)pyridine (1 g) at 0 °C was added dropwise 4 mL (4.5 g, 49.7 mmol; 1.2 equiv) of acrylic acid chloride. The mixture was stirred to ambient temperature for 14 h and then extracted three times with 50 mL of 1 N aqueous hydrochloric acid, 1 N sodium hydrogen carbonate solution, and water. The organic layer was dried with magnesium sulfate, filtered, and concentrated in vacuo. The product was purified by flash chromatography (petroleum ether/acetone, 2:1 (v/v)) to afford 8.0 g (75%) of the title compound: $[\alpha]^{22}_D$ −86.1° (*c* 1.1, CH_2Cl_2); IR (neat) 1735 (C=O, ester), 1640 (C=O, amide) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5 H, C_6H_5), 6.43 (d, *J* = 9.6 Hz, 1 H), 6.39 (d, *J* = 2.6 Hz, 1 H), 5.68 (dd, 1 H), 5.15 (s, 1 H, CH_{2a}-C_6H_5), 5.13 (s, 1 H, CH_{2b}-C_6H_5), 4.58 (dd, J_1 = 3.8 Hz, J_2 = 8.8 Hz, 1 H, α-CH), 3.74–3.65 (m, 1 H, NCH_{2a}), 3.62–3.54 (m, 1 H, NCH_{2b}), 2.31–1.86 (m, 4 H, CH_2CH_2). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.60; N, 5.40. Found: C, 69.52; H, 6.58; N, 5.58.

General Procedure for the Lewis Acid Catalyzed Diels–Alder Reactions. To a stirred solution of 1 g (3.8 mmol) of proline amide **3** in 50 mL of dichloromethane at the respective temperature (see Tables I and II) was added a solution of 1 equiv of the respective Lewis acid (Tables I and II) in 5 mL of dichloromethane. After the mixture was stirred for 15 min, a solution of 5 equiv of the respective diene in 5 mL of dichloromethane was added during 15 h with the aid of a motor-driven syringe. The solution was stirred for additional 5 h and then extracted three times with 0.1 N aqueous hydrochloric acid, 0.1 N sodium hydrogen carbonate, and water. The organic layer was dried with magnesium sulfate, filtered, and concentrated in vacuo. The products were purified by flash chromatography on silica gel with petroleum ether/acetone mixtures as eluents. The diastereomer ratios were obtained from 400-MHz ^{1}H NMR spectra or from 100.6-MHz ^{13}C NMR spectra recorded using the Inverse Gated technique. For yields and diastereoselectivities see Tables I and II. In the case of the cyclopentadiene adducts **4**, first the exo isomers were separated by flash chromatography, and the major endo compound **4a** was then isolated in 80–90% yield by recrystallization from ether/petroleum ether. In the cases of **11a**/**12a**–**11e**/**12e** flash chromatography and crystallization from ether/petroleum ether allowed for the isolation of enantiomerically further enriched products but did not provide an easily executable and straightforward protocol for the complete removal of the minor stereoisomers. Therefore, these adducts were characterized as mixtures of diastereomers. By this general procedure the following cycloadducts were obtained:

***N*-((1*R*,4*R*,5*R*)-Bicyclo[2.2.1]hept-2-en-5-ylcarbonyl)-(*S*)-proline benzyl ester (4a)**: mp 85 °C; $[\alpha]^{22}_D$ −23.4° (*c* 1, CH_2Cl_2); IR (KBr) 1730 (C=O, ester), 1645 (amide) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5 H, C_6H_5), 6.16 (dd, J_1 = 3.1 Hz, J_2 = 5.5 Hz, 1 H, H3), 5.97 (dd, J_1 = 2.8 Hz, J_2 = 5.5 Hz, 1 H, H2), 5.17 (d, *J* = 12.4 Hz, 1 H, CH_{2a}-C_6H_5), 5.03 (d, 1 H, CH_{2b}-C_6H_5), 4.46 (dd, J_1 = 3.9 Hz, J_2 = 8.6 Hz, 1 H, α-CH), 3.71 (m, 1 H, N-CH_{2a}), 3.62 (m, 1 H, NCH_{2b}), 2.99 (ddd, J_1 = 8.0 Hz, J_2 = 4.2 Hz, J_3 = 3.6 Hz, 1 H, H5), 2.87 (m, 1 H, H1), 2.22–1.81 (m, 5 H, CH_2-CH_2 and $H6_{eq}$), 1.47–1.39 (m, 2 H, $H6_{ax}$ and $H7_a$), 1.29–1.22 (m, 1 H, $H7_b$). Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.74; H, 7.12; N, 4.21.

***N*-((1*R*,4*R*,5*R*)-Bicyclo[2.2.2]oct-2-en-5-ylcarbonyl)-(*S*)-proline benzyl ester (11a)**: IR (neat) 1730 (C=O, ester), 1650 (amide) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.37 (m, 5 H, C_6H_5), 6.26 (m, 2 H, H2 and H3), 5.15 (d, *J* = 12.1 Hz, 1 H, CH_{2a}-C_6H_5), 5.02 (d, 1 H, CH_{2a}-C_6H_5), 4.48 (dd, J_1 = 8.2 Hz, J_2 = 3.6 Hz, 1 H, α-CH), 3.67–3.59 (m, 1 H, NCH_{2a}), 3.56–3.48 (m, 1 H, NCH_{2b}), 2.74–2.66 (m, 2 H, H4 and H5), 2.55 (m, 1 H, H1), 2.2–1.76 (m, 5 H), 1.56 (m, 2 H), 1.27–1.24 (m, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 174.2 (C=O), 172.2 (C=O), 135.7 (C3), 133.4 (ipso-C), 132.4 (C2), 128.3–128.0 (C_6H_5), 66.5 (OCH_2), 58.7 (α-C), 46.3 (NCH_2), 42.2, 31.7, 31.3, 29.3, 28.8, 26.0, 24.8, 23.9. Anal. Calcd for $C_{21}H_{25}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 75.04; H, 7.34; N, 3.92.

***N*-[(3*S*,4*R*)-3-Methylcyclohex-1-en-4-yl)carbonyl]-(*S*)-proline benzyl ester (11b)**: IR (neat) 1735 (C=O, ester), 1650 (amide) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5 H, C_6H_5), 5.66–5.59 (m, 2 H, H1 and H2), 5.21 (d, *J* = 12.4 Hz, 1 H, OCH_{2a}), 5.08 (d, 1 H, OCH_{2b}), 4.49 (dd, J_1 = 8.7 Hz, J_2 = 3.3 Hz, 1 H, α-CH), 3.74–3.69 (m, 1 H, NCH_{2a}), 3.57–3.51 (m, 1 H, NCH_{2b}), 2.79 (ddd, *J* = 11.8 Hz, J_2 = 5.5 Hz, J_3 = 3.0 Hz, 1 H, H4), 2.48 (m, 1 H, H3), 2.20–1.63 (m, 8 H), 0.91 (d, *J* = 7.1 Hz, CH_3). Anal. Calcd for $C_{20}H_{25}NO_3$: C, 72.92; H, 7.65; N, 4.25. Found: C, 72.81; H, 7.68; N, 4.31.

***N*-[((3*S*,4*R*,6*S*)-3,6-Dimethylcyclohex-1-en-4-yl)carbonyl]-(*S*)-proline benzyl ester (11c)**: IR (neat) 1730 (C=O, ester), 1655 (amide) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.24 (m, 5 H, C_6H_5), 5.59–5.55 (m, 1 H, H2), 5.47–5.44 (m, 1 H, H1), 5.21 (d, *J* = 12.3 Hz, OCH_{2a}), 5.08 (d, OCH_{2b}), 3.74–3.52 (m, 2 H, NCH_2), 2.84 (ddd, J_1 = 12.6 Hz, J_2 = 5.4 Hz, J_3 = 2.5 Hz, 1 H, H4), 0.98 (d, *J* = 7 Hz, 3 H, CH_3), 0.89 (d, *J* = 7.1 Hz, 3 H, CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 173.1 (C=O), 172.0 (C=O), 135.4 (C2), 132.2 (ipso-C), 130.4 (C1), 128.1, 127.7 and 127.6 (C_6H_5), 66.2 (OCH_2), 58.5 (α-C), 46.3 (NCH_2), 42.2, 30.5, 29.1, 28.6, 28.3, 24.4, 21.1, 16.4. Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 73.96; H, 8.16; N, 4.32.

***N*-[(4*R*)-1-Methylcyclohex-1-en-4-yl)carbonyl]-(*S*)-proline benzyl ester (11d)**: IR (neat) 1735 (C=O, ester), 1655 (amide) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 5 H, C_6H_5), 5.38 (m, 1 H, H2), 5.18 (d, *J* = 12.3 Hz, 1 H, OCH_{2a}), 5.07 (d, 1 H, OCH_{2b}), 4.52 (dd, J_1 = 8.7 Hz, J_2 = 3.7 Hz, 1 H, α-CH), 3.69–3.60 (m, 1 H, NCH_{2a}), 3.56–3.48 (m, 1 H, NCH_{2b}), 2.53 (m, 1 H, H4), 2.32–1.65 (m, 10 H), 1.62 (s, 3 H, CH_3). Anal. Calcd for $C_{20}H_{25}NO_3$: C, 72.92; H, 7.65; N, 4.25. Found: C, 72.85; H, 7.22; 4.23.

***N*-[((4*R*)-1,2-Dimethylcyclohex-1-en-4-yl)carbonyl]-(*S*)-proline benzyl ester (11e)**: IR (neat) 1735 (C=O, ester), 1655 (amide) cm^{-1}; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 174.2 (C=O), 171.5 (C=O), 135.1 (ipso-C), 127.8, 127.5 and 127.4 (C_6H_5), 124.4 and 123.5 (C2 and C3), 65.9 (OCH_2), 58.1 (α-C), 46.2 (NCH_2), 38.6, 32.8, 30.7, 28.4, 25.2, 24.2, 18.4, 18.2. Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 73.46; H, 8.08; N, 3.90.

Methyl (1*R*,4*R*,5*R*)-Bicyclo[2.2.1]hept-2-ene-4-carboxylate (5). To a solution of Diels–Alder adduct **4a** (1 g, 3 mmol) in 100 mL of dichloromethane was added 1.8 g (12 mmol) of trimethyloxonium tetrafluoroborate, and the mixture was stirred at ambient temperature for 12 h. The solvent was removed, and the remaining residue was taken up in a mixture of 3 mL of water and 5 mL of tetrahydrofuran and stirred for 30 min. To the mixture was added 50 mL of water, the pH was adjusted to 2, and the aqueous solution was extracted three times with 20 mL of ether. The combined organic layers were dried with magnesium sulfate and filtered, and the solvent was removed. The product was purified by flash chromatography with ether to afford 330 mg (71%) of the title compound: $[\alpha]^{22}_D$ 136° (*c* 0.5, ethanol) (lit.[8] $[\alpha]^{22}_D$ −141° (*c* 0.5, ethanol) for the (−)-enantiomer); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (dd, J_1 = 5.7 Hz, J_2 = 3.1 Hz, 1 H, H3), 5.90 (dd, J_1 = 5.6 Hz, J_2 = 2.8 Hz, 1 H, H2), 3.6 (s, 3 H, OCH_3), 3.17 (m, 1 H, H4) 2.92 (ddd, J_1 = 9.5 Hz, J_2 = 7.9 Hz, J_3 = 4.0 Hz, 1 H, H5), 2.88 (m, 1 H, H1), 1.88 (ddd, J_1 = 12.1 Hz, J_2 = 9.4 Hz, J_3 = 3.7 Hz, 1 H, $H3_{eq}$), 1.42–1.37 (m, 2 H, $H3_{ax}$ and $H7_a$), 1.26–1.23 (m, 1 H, $H7_b$); HRMS calcd for $C_9H_{12}O_2$ 152.084, found 152.085.

For the reisolation of proline benzyl ester from the aqueous layer the pH was adjusted to 12, and the aqueous solution was extracted three times with 20 mL of ether. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo. The remaining residue was taken up in 10 mL of anhydrous ether, and 5 mL of an ethereal solution of hydrochloric acid was added to afford 530 mg (72%) of (*S*)-proline

benzyl ester hydrochloride, $[\alpha]^{22}_D$ -43.8 (c 1, methanol) (lit.[6] $[\alpha]^{22}_D$ -43.3 (c 1, methanol).

***N*-((1*R*,2*R*,4*R*)-Bicyclo[2.2.1]heptan-2-ylcarbonyl)-(*S*)-proline (6).** To a solution of 1 g (3 mmol) of Diels-Alder adduct **4a** in 50 mL of methanol was added 400 mg of Pd on charcoal. The mixture was stirred vigorously under 1 atm of hydrogen for 24 h, filtered, and concentrated in vacuo. The remaining residue was triturated with ether to give 720 mg (99%) of the carboxylic acid **6** as a colorless solid: mp 122 °C; $[\alpha]^{22}_D$ -131° (c 0.4, CH_2Cl_2); IR (KBr) 1710 (COOH), 1650 (amide) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.8 (broad, 1 H, COOH), 4.56 (m, 1 H, α-CH), 3.64-3.59 (m, 1 H, NCH_{2a}), 3.57-3.50 (m, 1 H, NCH_{2b}), 2.87-2.83 (m, 1 H, H5), 2.49 (m, 1 H, H4), 2.42-2.38 (m, 1 H, $H3_a$), 2.26 (m, 1 H, H1), 2.06-1.92 (m, 3 H), 1.82-1.78 (m, 1 H), 1.62-1.34 (m, 7 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 176.8, 172.1, 60.3 (α-C), 47.6 (NCH_2), 45.6, 40.9, 39.2, 37.0, 32.2, 28.9, 27.1, 24.8, 24.5. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.81; H, 7.91; N, 5.90.

(1*R*,2*R*,4*R*)-Bicyclo[2.2.1]heptane-2-carboxylic Acid (7). A mixture of 430 mg (1.82 mmol) of the proline derivative **6** and 12 mL of 9 N aqueous hydrochloric acid was heated to 80 °C for 12 h and then extracted three times with 10 mL of ether. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo to afford 230 mg (90%) of the title compound as a colorless solid: $[\alpha]^{22}_D$ 33.3° (c 1, ethanol) (lit.[2] $[\alpha]^{22}_D$ 33.9° (c 1.06, ethanol)); ^1H NMR (400 MHz, $CDCl_3$) δ 10.99 (broad, 1 H, COOH), 2.80 (m, 1 H, H5), 2.57 (m, 1 H, H4), 2.53 (m, 1 H, H1), 1.69-1.22 (m, 8 H); HRMS calcd for $C_8H_{12}O_2$ 140.083, found 140.083.

Acknowledgment. This research was supported by the Degussa AG and the Fonds der Chemischen Industrie (Liebig-Stipendium).

Thermally Irreversible Photochromic Systems. A Theoretical Study

Shinichiro Nakamura[1a] and Masahiro Irie*[,1b]

Research Center, Mitsubishi Chemical Industries Limited, 1000 Kamoshida, Midoriku, Yokohama 227, Japan, and The Institute of Scientific and Industrial Research, Osaka University, Ibaraki 567, Japan

Received May 31, 1988

A guiding principle for molecular design of thermally irreversible diarylethene-type photochromic compounds has been proposed on the basis of calculations of state correlation diagrams.

Photochromic organic compounds have attracted a significant amount of attention, because of their potential ability for various applications. Among them the most promising one is to use the photochromic compounds for optical memory media.[2] Despite the recent development of laser technology, however, few applications of the compounds have been realized in optical information storage. One reason for this is the lack of thermal stability of the colored forms.

We have recently reported on a new type of thermally stable photochromic system, diarylethene derivatives having heterocyclic rings (**1a**, **1b**).[3] The colored ring-closed forms (**2a**, **2b**) remain stable for more than 12 h at 80 °C. The colored forms revert to the open ring forms (**1a**, **1b**) only when they are exposed to visible light. On the other hand, the thermal stability was not observed for 2,3-dimesityl-2-butene (**3a**), which has phenyl rings instead of the heterocyclic rings. The photogenerated colored form (**4a**) returns to the open-ring form (**3a**) in the dark with a half-life of 1.5 min at 30 °C.

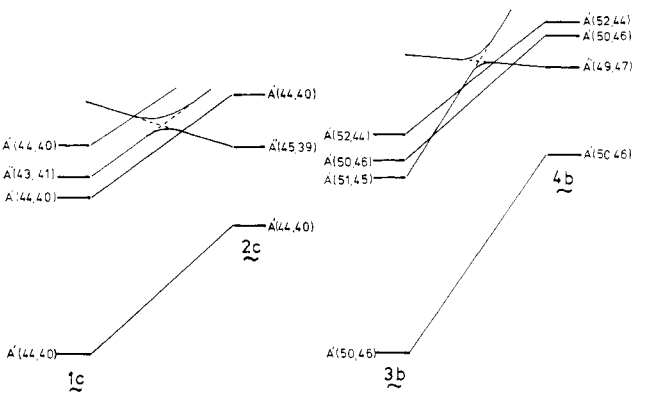
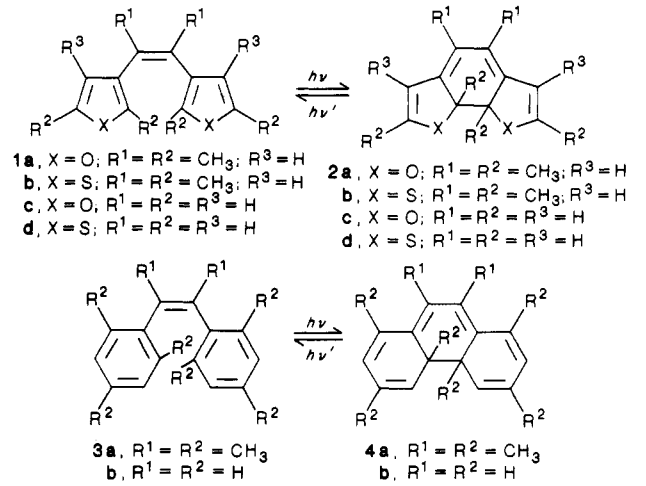
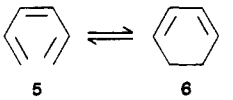


Figure 1. State correlation diagrams in disrotatory mode for the reactions from **1c** to **2c** and from **3b** to **4b**.



In order to get a guiding principle for molecular design of thermally irreversible photochromic compounds, we have carried out a theoretical study to elucidate the different thermal behavior between the diarylethene derivatives having heterocyclic rings and those having phenyl rings.

According to the Woodward-Hoffman rule based on the π orbital symmetries[4] for 1,3,5-hexatriene (**5**), which is the simplest molecular frame work of the above-mentioned compounds, a conrotatory cyclization reaction to cyclohexadiene (**6**) is brought about by light and disrotatory cyclization by heat.



5 **6**

The cycloreversion reaction is allowed both photochemically in the conrotatory mode and thermally in the disrotatory mode. From the simple symmetry consideration of the hexatriene framework, we might not expect the thermal irreversibility of the cycloreversion reaction. A state energy calculation is indispensable to discuss the thermal stability.

Semiempirical MNDO calculations[5] were carried out for 1,2-di(3-furyl)ethene (**1c**), 1,2-di(3-thienyl)ethene (**1d**),

(1) (a) Research Center. (b) The Institute of Scientific and Industrial Research.

(2) (a) Hirshberg, Y. *J. Am. Chem. Soc.* **1965**, *78*, 2304. (b) Heller, H. G. *IEEE Proc.* **1983**, *130*, 209.

(3) Irie, M.; Mohri, M. *J. Org. Chem.* **1988**, *53*, 803.

(4) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie, GmbH: Weinheim, 1970.

(5) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

0022-3263/88/1953-6136$01.50/0