ISSN 1070-4272, Russian Journal of Applied Chemistry, 2006, Vol. 79, No. 10, pp. 1621–1625. © Pleiades Publishing, Inc., 2006. Original Russian Text © E.G. Mamedov, 2006, published in Zhurnal Prikladnoi Khimii, 2006, Vol. 79, No. 10, pp. 1642–1646.

> ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Asymmetric Diels-Alder Reaction between Acrylates and Cyclopentadiene in the Presence of Chiral Catalysts

E. G. Mamedov

Institute of Petrochemical Processes, National Academy of Sciences of Azerbaijan, Baku, Azerbaijan

Received August 17, 2005; in final from, March 2006

Abstract—Asymmetric Diels-Alder reaction between cyclopentadiene and alkyl and cycloalkyl acrylates in the presence of new chiral catalysts, $BBr_3 \cdot MentOEt$, $AlCl_2OMent$, BBr_2OMent , and $BBr(OMent)_2$, was studied. Optically active bicyclo[2.2.1]hept-2-ene-5-carboxylates were synthesized. The influence of the reaction conditions on the total and optical yields and on the stereoselectivity of the adducts synthesized was examined.

DOI: 10.1134/S1070427206100120

The asymmetric catalysis is currently under rapid development. The number of publications on this subject and the finance assigned to development of this line tend to increase [1–3]. Organic reactions performed in the presence of chiral catalysts underlie modern asymmetric synthesis. A key issue for achievement of high results in this field is directed synthesis of new efficient optically active catalysts [4].

Norbornene and its saturated analogue norbornane are essential fragments of many important natural compounds [5]. Today, synthesis of new compounds containing these moieties attracts the researchers' attention [6-8]. Synthesis of representatives of this class of compounds in the optically active form is of certain theoretical and practical interest.

Among the promising lines of synthesis of optically active norbornene derivatives is the asymmetric Diels-Alder reaction (ADAR) in the presence of chiral catalysts. We described the first example of ADAR with $BF_3 \cdot MentOEt$ as chiral catalyst in [9]. That study laid the foundations of an efficient method of synthesis of optically active derivatives of norbornene by ADAR, which was further developed [10, 11] using optically active methyloxy- and bornyloxyaluminum dichlorides.

Here we report the results of examination of ADAR between acrylates and cyclopentadiene (CPD) in the presence of chiral catalysts, aimed at preparation of optically active norbornene derivatives.

Chiral B- and Al-containing complex catalysts were synthesized from natural l-(–)menthol; their characteristics are listed in Table 1.

All chiral catalysts are well soluble in organic solvents (CH_2Cl_2 , CCl_4 , $CHCl_3$, C_6H_6 , C_5H_5Cl , $C_6H_5CH_3$) and can be used as homogenous catalysts.

Optically active norbornenecarboxylates **XI-XIX** are prepared by ADAR according to the scheme



where R = Et (II, XI), *n*-Pr (III, XII), *i*-Pr (IV, XIII), *n*-Bu (V, XIV), *i*-Bu (VI, XV), *t*-Bu (VII, XVI),

Catalyst	Initial compound	bp, °C (<i>P</i> , mm Hg)	$[\alpha]_D^{20}$, deg	Reference
$BBr_3 \cdot MentOEt$	MentOEt	$\begin{array}{c} 187{-}188 \ (1) \\ 181{-}182 \ (1) \\ 185{-}187 \ (1) \\ 191 \ (1) \end{array}$	-99.3	_
AlCl ₂ OMent	l-(-)-MentOH		-73.5	[10]
BBr ₂ OMent	l-(-)-MentOH		-78.5	_
BBr(OMent) ₂	l-(-)-MentOH		-91.7	_

Table 1. Characterization of chiral catalysts

Compound	bp °C (P, mm Hg)	n_{D}^{20}	d_{D}^{20}	Found, %		Earranda	Calculated, %	
				С	Н	Formula	С	Н
XI	127–128 (15)	1.4805	1.038	71.19	8.97	C ₁₀ H ₁₄ O ₂	72.28	9.03
XII	130–132 (25)	1.4795	1.0262	73.02	8.10	$C_{11}H_{16}O_2$	73.33	8.89
XIII	100-101 (10)	1.4630	0.9958	72.90	8.30	$C_{11}H_{16}O_2$	73.33	8.89
XIV	115–117 (10)	1.4602	0.9771	73.91	9.56	$C_{12}H_{18}O_{2}$	74.23	9.28
XV	104–105 (10)	1.4615	0.9794	73.50	8.89	$C_{12}^{12}H_{18}^{10}O_2^{2}$	74.23	9.28
XVI	101-103 (10)	1.4645	0.9889	75.22	8.99	$C_{12}^{12}H_{18}^{10}O_{2}^{2}$	74.23	9.28
XVII	115–117 (20)	1.5521	0.9780	74.16	8.13	$C_{13}^{12}H_{18}^{10}O_{2}^{2}$	75.72	8.73
XVIII	118–120 (20)	1.5526	0.9789	75.69	9.24	$C_{14}^{13}H_{20}^{10}O_{2}^{2}$	76.36	9.09
XIX	144–146 (5)	1.5261	0.9785	76.53	8.20	$C_{14}^{17}H_{18}^{20}O_2^2$	77.06	8.25

Table 2. Constants and elemental analysis data for compounds of optically active norbornenecarboxylates XI-XIX

Table 3. Isomeric composition and total and optical yields of XI-XIX in relation to the reaction conditions

Dieno- phile	<i>T</i> , °C	Solvent	Catalyst	Catalyst : di- enophile molar ratio	Yield of XI–XIX, %	Isomeric composition, %		Optical	$[\alpha]_{D}^{20},$
						endo	exo	yield	deg
III	20	CH ₂ Cl ₂	BBr ₂ OMent	0.25	88	94	6	35	+24.8
III	-10	CH ₂ Cl ₂	BBr ₂ OMent	0.25	87	95	5	45	+31.9
III	-40	CH ₂ Cl ₂	BBr 2OMent	0.25	87	96	4	50	+35.3
III	-70	CH ₂ Cl ₂	BBr ₂ OMent	0.25	85	99	1	92	+67.5
III	-78	CH ₂ Cl ₂	BBr ₂ OMent	0.25	82	99	1	94	+68.2
II	20	CH ₂ Cl ₂	BBr ₂ OMent	0.25	88	96	4	35	+24.8
IV	20	$CH_{2}Cl_{2}$	AlCl ₂ OMent	0.25	89	96	4	35	+24.8
V	20	$CH_{2}Cl_{2}$	AlCl ₂ OMent	0.25	89	95	5	36	+25.5
VI	20	$CH_{2}Cl_{2}$	AlCl2OMent	0.25	89	95	5	35	+24.8
VII	20	$CH_{2}Cl_{2}$	AlCl ₂ OMent	0.25	89	95	5	36	+25.5
VIII	20	CH ₂ Cl ₂	AlCl ₂ OMent	0.25	88	96	4	36	+25.5
IX	20	CH ₂ Cl ₂	AlCl ₂ OMent	0.25	89	96	4	36	+25.5
Χ	20	CH ₂ Cl ₂	AlCl ₂ OMent	0.25	88	95	5	35	+24.8
III	-10	CH ₂ Cl ₂	BBr ₂ OMent	0.5	88	96	4	45	+31.9
III	-10	CH ₂ Cl ₂	BBr ₂ OMent	0.75	89	97	3	45	+31.9
III	-70	CH ₂ Cl ₂	AlCl ₂ OMent	0.25	86	98	2	90	+63.8
III	-70	CH ₂ Cl ₂	BBr ₃ MentOEt	0.25	85	98	2	91	+64.8
III	-70	CH ₂ Cl ₂	BBr(OMent) ₂	0.25	85	98	2	91	+64.8
IV	20	$C_6H_5CH_3$	BBr ₂ OMent	0.25	84	97	3	45	+31.9
IV	20	CCl ₄	BBr ₂ OMent	0.25	83	98	2	45	+31.9
IV	20	CHCi ₃	BBr_2OMent	0.25	84	98	2	45	+31.9
IV	20	C ₆ H ₅ Čl	BBr ₂ OMent	0.25	83	97	3	45	+31.9

cyclopentyl (VIII, XVII), cyclohexyl (IX, XVIII), and cyclohex-3-enyl (X, XIX).

The reaction was run in a wide temperature range from -78 to 20°C in a CH₂Cl₂ or C₆H₅CH₃ solution. The catalyst-to-dienophile molar ratio was varied from 0.25 to 0.75. The physicochemical characteristics of adducts **XI**–**XIX** synthesized are listed in Table 2.

We examined how various reaction parameters affect the isomeric composition, as well as optical

and chemical yields of the compounds synthesized. The results are summarized in Table 3.

A mixture of *endo* and *exo* isomers of **XI–XIX** was separated by preparative chromatography. The amount of *exo* isomers was negligible; therefore, only *endo* isomers of the adducts were collected, and their optical activity was examined.

Table 3 shows that, in contrast to the noncatalyzed asymmetric Diels-Alder reaction of CPD with acrylic

diphenophiles, for which a temperature change insignificantly affects the optical yield of the adducts [12], the optical yield of **XI–XIX** significantly increases at lower temperatures in the presence of the chiral catalysts of interest. The optical yield of adduct **XII** with *endo* configuration, synthesized at -78° C, is as high as 94%.

On lowering the temperature, the stereoselectivity of the reaction increases, and the total yield of the adducts decreases. An increase in the content of chiral catalysts does not noticeably affect the optical yield of **XI–XIX**, but the total yield increases insignificantly. Table 3 also shows that the optical and total yields of the end products are virtually unaffected by the solvent.

At the reaction parameters within the limits examined, *endo* isomers of the adducts are preferentially formed. The isomeric composition of these adducts was determined by gas liquid chromatography. We found that all the Diels-Alder reactions between CPD and acrylates yield adducts with a positive rotation sign, as in the case of ADAR in the presence of Lewis acids [13]. The catalytic action of chiral catalysts can be attributed to formation of their complex with dienophiles **II**–**X**. The resulting electron deficiency on the multiple bond in dienophiles facilitates their reaction with CPD:

Here Cat.^{*} is a chiral catalyst.

This is confirmed by a shift of the absorption band v(C=O) from 1730 to 1640 cm⁻¹ on passing from dienophiles to their complexes with chiral catalysts. These data are consistent with our observation that the absorption band of the C=O group of methacrylate is shifted from 1730 to 1630 cm⁻¹ under the action of BBr₃, which suggests complexing between the catalysts and dienophiles.

All the physicochemical data for adducts **XI–XIX** synthesized by different procedures are identical.

The composition and structure of the compounds synthesized were confirmed by independent synthesis:



where R = Et, *n*-Pr, *i*-Pr, *n*-Bu, *i*-Bu, *t*-Bu, cyclopentyl, cyclohexyl, cyclohex-3-enyl.

The composition and structure of adducts XI-XIX were confirmed by their IR and ¹H NMR spectra.

In the IR spectra of the norbornenecarboxylates synthesized, the absorption bands of the ethylene moiety are observed at 1575–1550 and 3064–3040 cm⁻¹ [ν (C=C), ν (C–H)]. The unusual position of the first absorption band is attributed to the strained state of the double bond [14]. The ν (C–H) absorption is characteristic of norbornenes, which distinguishes them both from alkenes with the terminal double bond (3080 cm⁻¹) and from cyclohexene (3024 cm⁻¹).

More information can be derived from the ¹H NMR spectra of nonbornenes derivatives. The spectra of the esters synthesized contain characteristic signals due to protons of the double bond of the norbornene moiety at 5.8-6.2 ppm. The signals from protons of the olefin moieties of the *exo* isomers are close be-

cause of the spatial remoteness from magnetically anisotropic groups of the substituent. The signals from *endo* isomers are significantly nonequivalent because of the shorter distance from the substituent situated on the rear side of the bicyclic moiety. The bridgehead protons appear at 2.6-2.9 ppm as a multiplet.

To determine the optical yield of the chiral compounds **XI–XIX**, they were converted either to **XXIV** by base hydrolysis or to **XXV** by reduction with LiAlH_4 :



RUSSIAN JOURNAL OF APPLIED CHEMISTRY Vol. 79 No. 10 2006

The optical yield of **XI**–**XIX** was determined by comparing the specific rotation of the *endo*-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid **XXIV** or 2-hydroxymethylbicyclo[2.2.1]hept-5-ene **XXV** synthesized with those of the corresponding enantiomerically pure sample described by Berson et al. [15]. Based on the correlation of the optical rotation sign of compounds with the known configuration [15], the relative configuration of **XI**–**XIX** was determined to be 2R–(+) for all the adducts with *endo* configuration.

EXPERIMENTAL

The IR spectra were measured on a UR-20 spectrophotometer at 4000-400 cm⁻¹, and the ¹H NMR spectra, on a Tesla BS-48 (80 MHz) spectrometer in CCl_4 with hexamethyldisiloxane as internal reference. The optical rotation was measured on a Perkin-Elmer-141 polarimeter and on a Spektropol-1 spectropolarimeter. Preparative separation was carried out on 900×0.8 -cm columns packed with Porovina + 5% polyethylene glycol adipate; evaporator and column temperature, 240 and 170°C, respectively; carrier gas (nitrogen) flow rate 200 cm³ min⁻¹; flame-ionization detector; a Varian-Aerograph chromatograph. Chromatographic analysis of the compounds we synthesized was performed and their purity was determined with an LKhM-8MD chromatograph with a thermalconductivity detector; 300×0.3 -cm column with 5% Porovina on Dinokhrom II; carrier gas (helium) flow rate 40 cm³ min⁻¹; column and evaporator temperature, 145 and 240°C, respectively.

Acryloyl chloride **XX** was prepared by the known procedure [16].

The starting alkyl and cycloalkyl acrylates II-X were prepared by the reactions of acryloyl chloride with the corresponding alcohols [17].

The chiral catalysts were prepared by the known procedures: $BBr_3 \cdot MentOEt$ [16], $AlCl_2OMent$, BBr_2OMent , and $BBr(OMent)_2$ [18]. Alkyl and cycloalkylbicyclo[2.2.1]hept-2-ene-5-carboxylates **XI–XIX** were prepared by the reactions of CPD with the corresponding acrylates. To a 0.05 M solution of acrylate in 20 ml of CH₂Cl₂, 0.0125 mol of chiral catalyst in 10 mol of CH₂Cl₂ was added at a prescribed temperature. Next, 0.05 M of freshly distilled CPD in 10 ml CH₂Cl₂ was added dropwise with stirring.

After stirring for 0.5 h, the mixture was treated with a dilute HCl solution, washed with distilled water, and dried over MgSO₄. After the solvent was evaporated, the residue was vacuum-distilled (for conditions and results see Table 3).

Independent synthesis. Bicyclo[2.2.1]hept-2-ene-5-carboxylic acid chloride **XXI** [17] and bicyclo-[2.2.1]hept-2-ene-5-carboxylic acid **XXIII** [19] were prepared by known procedures. Independent synthesis of **XI–XIX** was carried out by the reactions of chloride **XXI** or acid **XXIII** with the corresponding alcohols. All the physicochemical characteristics of compounds **XI–XIX** prepared by independent synthesis are identical to those of the compounds prepared by condensation of CPD with acrylates **II–X** (Table 2).

CONCLUSIONS

(1) Asymmetric Diels-Alder reaction of alkyl and cycloalkyl acrylates with cyclopentadiene in the presence of chiral catalysts $BBr_3 \cdot MentOEt$, $AlCl_2OMent$, BBr_2OMent , and $BBr(OMent)_2$ yields optically active norbornenecarboxylates with R-(+) configuration.

(2) As temperature is lowered, the optical yield of norbornenecarboxylates tends to grow and reaches 94% at -78° C; with increasing temperature, the total yield tends to grow, and the stereoselectivity, to fall.

(3) An increase in the content of the chiral catalyst does not noticeably affect the optical yield, but the total yield tends to increase; the solvent only slightly affects the optical and total yields of the adducts.

REFERENCES

- 1. Pavlov, V.A., Usp. Khim., 2004, vol. 42, no. 12, pp. 1269–1304.
- Murzin, D.Yu., Myaki-Arvela, P., and Salmi, T., *Kinet. Katal.*, 2003, vol. 44, no. 3, pp. 353–364.
- 3. Stinson, S.C., *Chem. Eng. News*, 1999, no. 1, pp. 101–106.
- 4. Gavrilov, K.N., Bondarev, O.G., and Polosukhin, A.I., *Usp. Khim.*, 2004, vol. 73, no. 7, pp. 726–756.
- 5. Potapov, V.M., *Stereokhimiya* (Stereochemistry), Moscow: Khimiya, 1988.
- Kas'yan, L.I., Okovityi, S.I., Bombushkar', M.F., et al., *Zh. Org. Khim.*, 2000, vol. 36, no. 2, pp. 218–228
- Kas'yan, L.I., Tarabara, I.N., Kas'yan, A.O., et al., *Zh. Org. Khim.*, 2002, vol. 38, no. 1, pp. 29–35.
- Kas'yan, A.O., Golodaeva, A.V., and Tsygankov, A.V., *Zh. Org. Khim.*, 2002, vol. 38, no. 11, pp. 1661–1669.

- Guseinov, M.M., Akhmedov, I.M., and Mamedov, E.G., Azerb. Khim. Zh., 1976, no. 1, pp. 46–48.
- 10. JPN Patent 53–138926, *Ref. Zh. Khim.*, 1981, no. 19, 19N81P.
- 11. Bao, J. and Walf, D., J. Am. Chem. Soc., 1993, vol. 115, no. 9, pp. 3814-3815.
- 12. Farmer, R.F., and Hamer, J., J. Org. Chem., 1966, vol. 31, no. 7, pp. 2418-2419.
- 13. Mamedov, E.G., *Zh. Org. Khim.*, 2001, vol. 37, no. 2, pp. 230–235.
- 14. Zefirov, N.S. and Sokolov, V.I., Usp. Khim., 1967, vol. 36, no. 2, pp. 243-268.

- Berson, J.A., Remaninck, A., Suzuki, S., et al., J. Amer. Chem. Soc., 1961, vol. 83, no. 8, pp. 3986–3997.
- 16. Weigand-Hilgetag, Organisch-Chemische Experimentierkunst, Hilgetag, H.G. and Martini, A., Eds. Leipzig: Johann Ambrosius Barth, 1964, 3d Ed.
- 17. Akhmedov, I.M., Mamedov, E.G., Kyazimov, E.A., et al., Azerb. Khim. Zh., 1980, no. 5, p. 5155.
- 18. Mamedov, E.G., Azerb. Khim. Zh., 2001, no. 3, pp. 27–31.
- 19. Nody, C.D., J. Amer. Chem. Soc., 1954, vol. 76, no. 11, pp. 2907–2910.