Table I. Copper(I)-Catalyzed Photobicyclization of Homoallyl Vinyl Ethers[8]

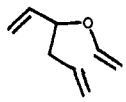
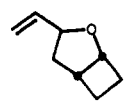
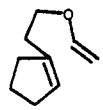
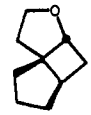
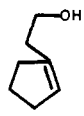
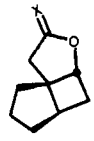
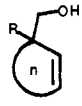
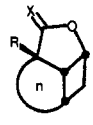
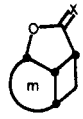
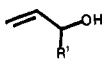
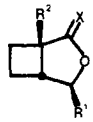
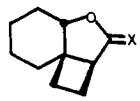
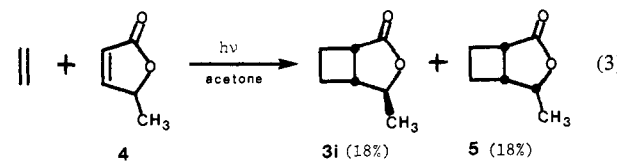
Entry	Vinyl Ether 1	Irradiation Time (h)	Photocyclization Product 2	Yield (%)
a		16		60
b		40		58
c		58		40
d	R = H, n = 5	24		92
e	R = CH_3, n = 5	24		50
f	R = H, n = 6	18		48

Table II. Synthesis of Multicyclic Butyrolactones by Selective Oxidation of Tetrahydrofuran Derivatives with Ruthenium Tetraoxide

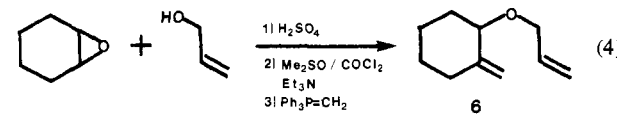
Entry	Hydroxyolefin Precursor	Ether 2 (X = H_2) Lactone 3 (X = O)	Oxidation Time (h)	Yield (%)
c			10	70
d	 R = H, n = 5		80	78
e	R = CH_3, n = 5		8	71
f	R = H, n = 6		14	85
g	 m = 5		4	73
h	m = 8		170	56
i	 R^1 = CH_3, R^2 = H		1	56
j	R^1 = n-C_4H_9, R^2 = CH_3		120	83
k	see text		16	65

of the methylene group to afford butyrolactones **3c-k** with sodium periodate and a catalytic amount of ruthenium tetraoxide (Table II).[9,15] Table II entries c–f demonstrate novel annulations of multicyclic butyrolactones from homoallyl alcohols. The cyclobutyl ring in the products **3d-f** is necessairly incorporated cis to the original alcohol substituent. Similar annulations from allylic alcohols via unsymmetrical diallyl ethers are demonstrated by Table II entries g–j. The requisite diallyl ethers for photoannulation of **2g-j** are readily available by Williamson synthesis from the hydroxy olefin precursors indicated. It is noteworthy that the stereochemistry of the substituent R^1 in **3i** and **3j** is exclusively exo.[16] This synthetically valuable stereoselectivity is in sharp contrast with a topologically different previous synthesis of **3i** by intermolecular photocycloaddition of ethylene with **4**, which affords an equal yield of the endo-epimer **5** (eq 3).[17] The requisite diallyl



4 **3i** (18%) **5** (18%) (3)

ether **6** for photoannulation of **2k** was prepared from cyclohexene oxide and allyl alcohol according to eq 4. Other synthetically



6 (4)

useful transformations of the photoproducts **2** as well as copper(I)-catalyzed photocyclizations of unsaturated ethers incorporating additional functionality are under investigation and will be described in a full account.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Foundation for support of this research. We thank Professors L. A. Paquette and H. Uda for copies of ^{1}H NMR spectra of **2a** and of **3i** and **5**, respectively.

(16) A discussion of the mechanistic basis of this stereoselectivity is deferred to a future full paper.
(17) Kosugi, H.; Sekiguchi, S.; Sekita, R.; Uda, H. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 520–28.

Conrotatory Ring Opening of Cis-Fused 3-Aminocyclobutenes. X-ray Analysis of a *cis,trans*-2*H*-Thiocin

G. W. Visser, W. Verboom, and D. N. Reinhoudt*

Laboratory of Organic Chemistry
Twente University of Technology
Enschede, The Netherlands

S. Harkema and G. J. van Hummel

Laboratory of Chemical Physics
Twente University of Technology
Enschede, The Netherlands

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The thermal valence isomerization of (hetero) cyclobutenes to (hetero) 1,3-butadienes is a classic example of a stereospecific reaction, the conrotatory mode of which is in agreement with the principle of conservation of orbital symmetry in electrocyclic reactions.[1,2] A large amount of work has been carried out on the thermal isomerization of compounds in which the cyclobutene moiety is cis annulated to another ring system. It is generally accepted that when the annulated ring possesses less than eight atoms, ring opening *must* occur by way of the symmetry-forbidden disrotatory mode[3] or by homolytic[4] or heterolytic[5] pathways, all

(1) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim, 1971.
(2) Pennings, M. L. M.; Reinhoudt, D. N.; Harkema, S.; van Hummel, G. J. *J. Am. Chem. Soc.* **1980**, *102*, 7570–7571.

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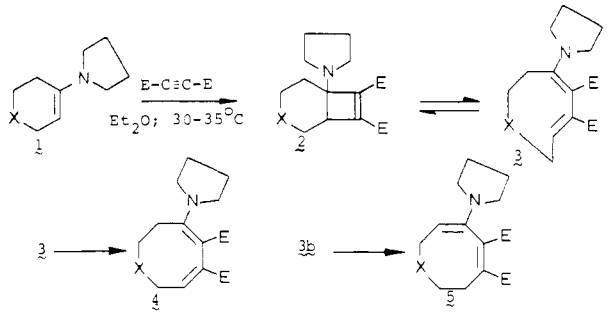
Scheme I[a,b]



[a] a, X = CH_2; b, X = S; c, X = $(CH_2)_2$; d, X = $(CH_2)_3$. [b] E = $COOCH_3$.

having a higher activation energy. Epiotis[6] has predicted that the activation energy of the ring opening will be reduced by asymmetric substitution of the cyclobutene, as experimentally observed for 3-aminocyclobutenes cis fused to 5-, 7-, 8-, and 12-membered rings. On the basis of configuration interaction analysis he concluded that in these cases the *disrotatory* process will occur. In this communication we report experimental evidence to prove that the ring opening of cis-fused 3-aminocyclobutenes proceeds in a *conrotatory* mode.

As part of our work on the mechanism of the reaction of enamines with dimethyl acetylenedicarboxylate (DMAD),[7] we synthesized cis-fused 3-aminocyclobutenes, a number of which have been reported previously. However, in our hands the reaction of DMAD and 1-(1-cyclohexen-1-yl)pyrrolidine (**1a**) in diethyl ether as described by Brannock et al.[8] did not give the dimethyl 1-(1-pyrrolidinyl)bicyclo[4.2.0]oct-7-ene-7,8-dicarboxylate (**2a**) as a pure compound. Instead we obtained a mixture of two compounds that are interconverting at room temperature as indicated by ^{1}H NMR spectroscopy. One of the compounds, showing a singlet absorption at δ 3.80 (OCH_3, 6 H) and a doublet absorption at δ 43.0 in its ^{13}C NMR spectrum, could be identified as the [2 + 2] cycloadduct **2a**. The other component, the amount of which increases in the mixture by lowering the temperature,[9] shows a doublet of a doublet at δ 5.51 (J = 5.1 and 12.0 Hz), corresponding to a vinylic proton and two singlets at δ 3.75 and 3.60 (OCH_3, 3 H).[8] After the mixture stood for some hours in $CDCl_3$ at room temperature, however, its ^{1}H NMR spectrum had changed dramatically and showed among others the absorptions characteristic of dimethyl 3-(1-pyrrolidinyl)-*cis*-*cis*-2,8-cyclooctadiene-1,2-dicarboxylate (**4a**).[8,11] Therefore, we concluded that the reaction product of **1a** and DMAD consisted of a mixture of two valence isomers, viz., the [2 + 2] cycloadduct **2a** and dimethyl 3-(1-pyrrolidinyl)-*cis*,*trans*-2,8-cyclooctadiene-1,2-dicarboxylate (**3a**). Prolonged reaction time resulted in the isomerization of the cis,trans diene to the thermodynamically more stable cis,cis-isomer **4a**. Conclusive evidence for the cis,trans-cycloalkadiene structure **3** was obtained when we reacted 1-(3,6-dihydro-2*H*-thiopyran-4-yl)pyrrolidine (**1b**)[12] with DMAD in diethyl ether. Dimethyl *cis*,*trans*-7,8-dihydro-6-(1-pyrrolidinyl)-2*H*-thiocin-4,5-dicarboxylate (**3b**) was obtained as a white crystalline solid in a yield of 82%; mp 144–145 °C (EtOH); IR (KBr) $\nu_{C=O}$ 1710, 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.50 (dd, J = 4.6, 12.6 Hz, 1 H, =CH—), 3.76 and 3.60 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 159.0 (s, C-6), 134.3 (s, C-4), 131.2 (d, C-3), 96.1 (s, C-5).[13] The structure of **3b** was determined by single-crystal X-ray analysis, and this unambiguously proved the cis,trans stereochemistry of **3b**.

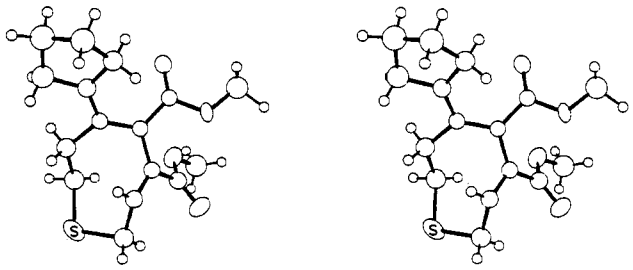


Figure 1. Stereoscopic view of **3b**.

Crystals of **3b** belong to space group $P\bar{1}$ with a = 13.600 (2) Å, b = 11.477 (2) Å, c = 10.546 (2) Å, α = 74.66 (2)°, β = 78.52 (2)°, and γ = 79.93 (4)°. Intensities were measured by using a Philips PW 1100 diffractometer [graphite monochromated Mo Kα radiation (λ 0.7107 Å), ω–2θ scan mode, $2 < \omega < 22.5°$, scan speed (ω) 0.03° s^{-1}, scan width (1.5 + 0.8 $tg\omega$)°, total number of reflections measured 4046]. The structure was solved by direct methods[14] and refined by the full-matrix least-squares method.[15] The number of reflections with $I > \sigma(I)$ (counting statistics) used for the refinement was 3497. The unit cell contains two independent molecules, having the same conformation, one of which is represented[16] in Figure 1.

Hydrogen atoms were found from difference Fourier syntheses made after refinement (on F) of positions and isotropic (anisotropic for S) thermal parameters of the heavy atoms. The highest peaks in the difference maps made at this stage were due to anisotropy of the thermal motion of the oxygen atoms. Therefore 388 parameters [scale factor, extinction parameter, positional parameters of all atoms, anisotropic thermal parameters for S and O atoms, isotropic thermal parameters for C, N, and H atoms] were refined in the last cycles. The final unweighted R factor was 5.9%. the standard deviation of an observation of unit weight was 2.7. The standard deviations of the resulting bond lengths and angles for the heavy atoms are in the range 0.004–0.006 Å and 0.2–0.4°, respectively. Mean differences in corresponding bond lengths, angles, and torsion angles for the two independent molecules are 0.005 Å, 0.4° and 1.2°. The torsion angles found for the cis and trans double bonds are −28.4 (4) and 143.0 (3)° for the first molecule and −27.2 (4) and 141.9 (3)° for the second. Details of the crystal structure of **3b**, together with the structure of the corresponding cis,cis-isomer **4b**, which also has been determined, will be published elsewhere.

The reactions of 1-(1-cyclohepten-1-yl)pyrrolidine (**1c**) and 1-(1-cycloocten-1-yl)pyrrolidine (**1d**) with DMAD in diethyl ether gave dimethyl 3-(1-pyrrolidinyl)-*cis*,*trans*-2,9-cyclononadiene-1,2-dicarboxylate (**3c**) and dimethyl 3-(1-pyrrolidinyl)-*cis*,*trans*-2,10-cyclodecadiene-1,2-dicarboxylate (**3d**), respectively. Compound **3c** was isolated in 91% yield as a crystalline solid: mp

(3) Seebach, D. In "Houben-Weyl, Methoden der organischen Chemie"; Mueller, E. Ed.; G. Thieme Verlag: Stuttgart, 1968; Vol. IV, pp 418–419.
(4) Gill, G. B. *Q. Rev. Chem. Soc.* **1968**, *22*, 338–389.
(5) Criegee, R.; Seebach, D.; Winter, R. E.; Boerretzen, B.; Brune, H.-A. *Chem. Ber.* **1965**, *98*, 2339–2352.
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(7) Visser, G. W.; Verboom, W.; Trompenaars, W. P.; Reinhoudt, D. N. *Tetrahedron Lett.* **1982**, *23*, 1217–1220.
(8) Brannock, K. C.; Burpitt, R. D.; Goodlett, V. W.; Thweatt, J. G. *J. Org. Chem.* **1963**, *28*, 1464–1468.
(9) Accordingly, at 80 °C *cis*,*trans*-1,3-cyclooctadiene cyclizes to bicyclo[4.2.0]oct-7-ene, and bicyclo[5.2.0]non-7-ene is formed at 175 °C by cyclization of *cis*,*trans*-1,3-cyclononadiene.[10]
(10) Shumate, K. M.; Neuman, P. N.; Fonken, G. J. *J. Am. Chem. Soc.* **1965**, *87*, 3996. Liu, R. S. H. *Ibid.* **1967**, *89*, 112–114.
(11) Geevers, J.; Visser, G. W.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 251–252.
(12) Kakurina, L. N.; Kucherova, N. F.; Zagorevskii, V. A. *J. Org. Chem. USSR (Engl. Transl.)* **1965**, 1118–1119.
(13) When **3b** was heated in MeOH at reflux temperature for 15 h, we obtained a 2:5 mixture of **4b** and 9-carboxy-4,6,7,8,8a,9-hexahydro-1*H*,3*H*-thiopyrano[3,4-*b*]pyrrolizine-9-acetic acid, dimethyl ester [^{1}H NMR ($CDCl_3$) δ 4.43 (dd, J = 6, 10 Hz, 1 H, N-CH-), 3.32 and 2.51 (AB q, J = 17.6 Hz, 2 H, CH_2E)]. This result shows that there exists an equilibrium between **2b** and **3b**, though at ambient temperature **2b** could not be detected by ^{1}H NMR spectroscopy. The conversion of 3-aminocyclobutenes into pyrrolizines has been reported previously.[7]
(14) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *A27*, 368–376. Main, P. In "Computing in Crystallography"; Schenk, H. Ed.; Delft University Press: The Netherlands, 1978.
(15) Busing, W. R.; Martin, K. O.; Levy, H. A. ORFLS, Report ORNL-TM-305, Oak Ridge National Laboratory, TN, 1962.
(16) Johnson, C. K. ORTEP, Report ORNL-3794, Oak Ridge National Laboratory, TN, 1965.

141.5-142.5 °C (EtOAc);[17] ^{1}H NMR ($CDCl_3$) δ 6.03 (dd, J = 3.7, 11.5 Hz, 1 H, =CH—), 3.74 and 3.57 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 167.0 (s, C-3), 152.9 (d, C-9), 132.7 (s, C-1), 97.3 (s, C-2). This compound has been described as the cis,cis-isomer by Brannock et al. (mp 109.5-110.5 °C),[8] Paquette and Begland (mp 139-141 °C),[18] and Hirsch and Cross (mp 140-142 °C).[19] Compound **3d**, mp 102-106 °C (Et_2O), was characterized by its ^{1}H NMR [($CDCl_3$) δ 5.82 (dd, J = 5.0, 12.2 Hz, 1 H, =CH—), 3.72 and 3.57 (s, 3 H, OCH_3)][20] and ^{13}C NMR spectrum [($CDCl_3$) δ 163.7 (s, C-3), 147.3 (d, C-10), 132.7 (s, C-1), 98.0 (s, C-2)]. From the reaction of 1-(1-cyclopenten-1-yl)pyrrolidine with DMAD in diethyl ether we obtained dimethyl 3-(1-pyrrolidinyl)-*cis*,*cis*-2,7-cycloheptadiene-1,2-dicarboxylate[8] without observing the corresponding cis,trans isomer by ^{1}H NMR spectroscopy as an intermediate, possibly because of a fast isomerization of the cis,trans to the cis,cis isomer.

When the thiocin **3b** was heated in toluene for 4 h at 100 °C *in the dark* the cis,cis-isomer **4b** was isolated in a 44% yield as a crystalline solid, mp 169-170 °C (toluene). Upon irradiation at room temperature, however, **3b** isomerized to dimethyl 3,8-dihydro-6-(1-pyrrolidinyl)-2*H*-thiocin-4,5-dicarboxylate (**5**). Under the prevailing reaction conditions both isomers were not interconvertible.[23] Therefore, we concluded that **5** has to be formed by a photochemical [1,5] hydrogen shift. As can be seen from Dreiding models and from the X-ray structure of **3b**, the 4π system in **3b** is twisted, thus making the antarafacial hydrogen shift sterically possible. To our knowledge this is the first example of a photochemical [1,5] hydrogen shift in a cyclic system.[25]

Our results clearly show that the ring opening of cis-fused 3-aminocyclobutenes proceeds in a *conrotatory* mode, giving (strained) cis,trans-cycloalkadienes. The rate of isomerization and the relative equilibrium concentrations of **2** and **3** at ambient temperature depend on the ring size. These results make a revision of the structural assignment of a number of compounds obtained by reaction of enamines and DMAD[8,18,19,22] necessary. Also the stereochemistry published of several other compounds[18,26] might be incorrect. Moreover the formation of "abnormal" ring opening products like **5** that have previously been reported[24,27,28] can be rationalized in terms of the intermediacy of a cis,trans isomer and a subsequent [1,5] hydrogen shift.

Registry No. 1a, 1125-99-1; **1b**, 3417-64-9; **1c**, 14092-11-6; **1d**, 942-81-4; **2a**, 3603-83-6; **3a**, 83585-93-7; **3b**, 83585-90-4; **3c**, 42205-54-9; **3d**, 42205-55-0; **4a**, 83585-94-8; **4b**, 83585-91-5; **5b**, 83585-92-6; DMAD, 762-42-5.

Supplementary Material Available: Tables of atomic positional and thermal parameters, interatomic distances and angles, and a list of observed and calculated structure factors (30 pages). Ordering information is given on any current masthead page.

(17) Before recrystallization the melting point was 105-108 °C. Recrystallization did not effect the ^{1}H and ^{13}C NMR spectrum.
(18) Paquette, L. A.; Begland, R. W. *J. Am. Chem. Soc.* **1966**, *88*, 4685-4692.
(19) Hirsch, J. A.; Cross, F. J. *J. Org. Chem.* **1971**, *36*, 955-960.
(20) Paquette and Begland[18] have reported the ^{1}H NMR ((CCl_4) δ 5.68 (q, J = 4.5 and 12.5 Hz, 1 H, =CH—), 3.60 and 3.42 (OCH_3)) and they have assigned the cis,cis configuration.
(21) Reaction of 1-(1-cyclohexen-1-yl)piperidine and -morpholine with DMAD gave the corresponding cyclobutenes as oils.[22] At room temperature these compounds produce slowly the *cis*,*cis*-2,8-cyclooctadienes, but the corresponding cis,trans-isomers could not be detected by ^{1}H NMR spectroscopy.
(22) Huebner, C. F.; Dorfman; L., Robison, M. M.; Donoghue, E.; Pierson, W. G.; Strachan, P. *J. Org. Chem.* **1963**, *28*, 3134-3140.
(23) Reinhoudt and Kouwenhoven[24] have described the formation of the 6-(1-piperidinyl) analogues of both isomers showing ^{1}H NMR spectra very similar to the spectra of our compounds. They have proposed that the 6-(1-piperidinyl) analogue of **5** is formed by a thermal [1,5] hydrogen shift concurrent with the ring opening.
(24) Reinhoudt, D. N.; Kouwenhoven, C. G. *Tetrahedron Lett.* **1973**, 3751-3754; Reinhoudt, D. N.; Kouwenhoven, C. G. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 865-878.
(25) Anh, N. T. "Die Woodward-Hoffmann Regeln und ihre Anwendung"; Verlag Chemie: Weinheim, 1972; p 78.
(26) Riviere, M.; Paillous, N.; Lattes, M. A. *Bull. Soc. Chim. Fr.* **1974**, 1911-1916.
(27) Yoshii, E.; Kimoto, S. *Chem. Pharm. Bull.* **1969**, *17*, 629-631.
(28) Stork, G.; Macdonald, T. L. *J. Am. Chem. Soc.* **1975**, *97*, 1264-1265.

General Synthesis of Chiral Borinic Acid Esters. Asymmetric Synthesis of Acyclic Ketones via Asymmetric Hydroboration-Carbenoidation

Herbert C. Brown,* Prabhakar K. Jadhav,[1] and Manoj C. Desai[1]

Richard B. Wetherill Laboratory, Purdue University West Lafayette, Indiana 47907

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Asymmetric hydroboration of prochiral alkenes with monoisopinocampheylborane in the molar ratio of 1:1, followed by a second hydroboration of nonprochiral alkenes with the intermediate dialkylboranes, provides the chiral mixed trialkylboranes. Treatment of these trialkylboranes with acetaldehyde under mild conditions results in the selective, facile elimination of the 3-pinanyl group, providing the corresponding chiral borinic acid esters with enantiomeric purities of 73-100% ee. Treatment of these intermediates with base and dichloromethyl methyl ether provides the chiral ketones, following oxidation of the intermediates, with enantiomeric purities as high as 90%.

The asymmetric synthesis of ketones has been extensively studied in the past decade.[2,3] The activity, however, is achieved primarily by the enantioselective alkylation of appropriate ketones. In the case of enantioselective alkylation of acyclic ketones, the most favorable results are realized only in the alkylation of symmetrical ketones, thereby limiting seriously the generality of the method. The present study reports a new, more general approach for the asymmetric synthesis of acyclic ketones involving asymmetric hydroboration-carbenoidation, as well as the first general synthesis of chiral borinic acid esters.

Asymmetric hydroboration has now been known for more than 2 decades,[4] and many applications of the reaction have been reported.[5] However, the high asymmetric induction achieved in the reaction has not hitherto been utilized for the asymmetric formation of carbon-carbon bonds.

It is known that under vigorous conditions trialkylboranes react with benzaldehyde to form the borinic acid esters.[6,7] Recently this reaction has been applied for a direct chiral synthesis of boronic esters.[8] However, the selective reaction of aldehydes with mixed trialkylboranes is not known.

Consequently, the strategy of the present method depends upon the successful synthesis of chiral mixed trialkylboranes, followed by selective elimination of the starting chiral auxiliary, the 3-pinanyl group, from the boron intermediate. Thus, hydroboration of *trans*-2-butene with monoisopinocampheylborane[9-11] ($IpcBH_2$) in the molar ratio of 1:1 results in the formation of 3-pinanyl-2-butylborane, which then rapidly hydroborates 1-pentene at -25 °C to provide the corresponding chiral mixed trialkylborane.

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