MO methods give, as a first approximation, a fairly good representation of the pK: D. Beaupere, J. P. Seguin, R. Uzan, and J. P. Doucet, *Can. J. Chem.*, **54**, 297 (1976). Similarly, in a ΔE, pK plot, the methoxy-substituted compounds exhibit much smaller deviations than for 1,1-diphenylethylenes.

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Stereochemistry of the Wagner–Meerwein Rearrangement of (−)-*endo*- and (+)-*exo*-5-Bicyclo[2.2.1]heptene-2-carboxylic Acids[1]

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Stereochemistry of the acidic lactonization of *endo*- (**4**) and *exo*-5-bicyclo[2.2.1]heptene-2-carboxylic acid (**14**) has been studied with their optically active modifications. The (−)-endo isomer **4** and the (+)-exo isomer **14** both were found to give a mixture of the (−)-*endo*-lactone **15** and the (−)-*exo*-lactone **8** with retention of the optical purities of their parent acids (−)-**4** and (+)-**14**. A scheme involving the Wagner–Meerwein rearrangement and the "6,2-hydride shift" has been suggested to explain these transformations.

D_2 symmetry inherent to gyrochiral[2] (−)-twistane (**1**)[3] ($C_{10}H_{16}$) demands that its six methylene groups be classified into two categories, each comprising two and four homotopic methylenes, respectively, as shown by closed and open circles in Chart I.

Depending upon which methylene group is taken away, we have either (−)-*twist*-brendane (**2**)[4] or (−)-brexane (**3**),[2] both with C_2 symmetry, retaining one of original three C_2 axes of their parent tricyclic hydrocarbon.

It is interesting to note that this structural relationship also reflects itself in their synthetic sequences which involve *endo*-5-bicyclo[2.2.1]heptene-2-carboxylic acid (**4**) as a common starting material (Chart II). Whereas the sequence of conversions for the synthesis of (−)-*twist*-brendane (**2**) was rather straightforward involving intramolecular alkylation of the keto mesylate **6** which in turn was derived from the (−)-unsaturated carboxylic acid **4** via the *endo*-iodolactone without skeletal rearrangement, the sequence leading to (−)-brexane (**3**) involved the acidic Wagner–Meerwein type rearrangement of (+)-**4** to yield the (+)-*exo*-lactone **8** which was then transformed into (−)-brexan-2-one (**11**) via the keto mesylate **9**.

Beckmann,[5] who discovered this Wagner–Meerwein type rearrangement, reported another interesting observation, that being that both (±)-*endo*-carboxylic acid **4** (Chart III) and (±)-*exo*-carboxylic acid **14** afforded a mixture of (±)-*endo*-lactone **15** and (±)-*exo*-lactone **8**. Although prolonged heating with strong acid converted the *endo*- and *exo*-carboxylic acids **4** and **14** completely into the *endo*-lactone **15**, a difference between these diastereomeric starting materials was observed in the ratio of the two lactones **8** and **15** in their early reaction mixtures; the *endo*-lactone **15** was found to be rich in the early reaction mixture from the *endo*-carboxylic acid **4**, while the reversed ratio was found in the early reaction mixture from the *exo*-carboxylic acid **14**.

In our preceding paper,[2] which reported the first successful synthesis of optically active brexane (**2**), we briefly discussed a probable stereochemistry of this Wagner–Meerwein rearrangement which had provided us with our synthetic starting material, the (+)-*exo*-lactone **8** from the (+)-*endo*-bicyclic carboxylic acid **4** with known absolute configuration.[6]

We have studied the steric course of this remarkable rearrangement using both optically active *endo*-bicyclic carboxylic acid **4** and *exo*-bicyclic carboxylic acid **14**, and in the present paper we report the result of our recent investigation where special attention was paid to follow the configurational as well as optical purity relationship between the starting materials and the final products.[7]

Chart I

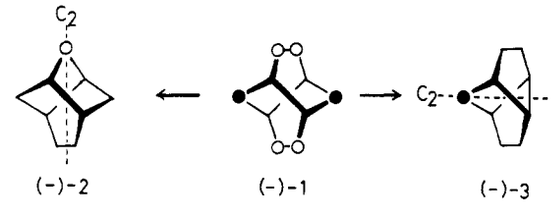


Chart II

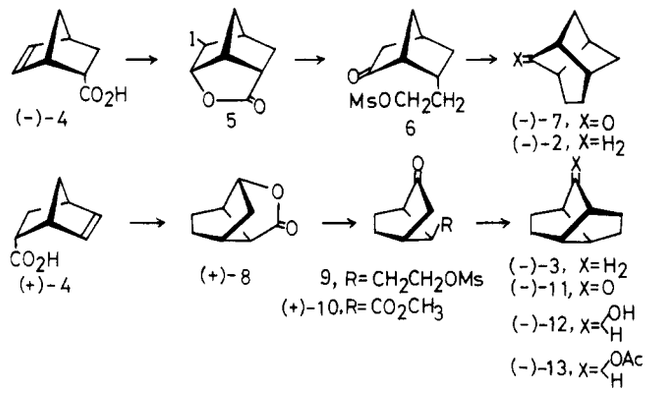
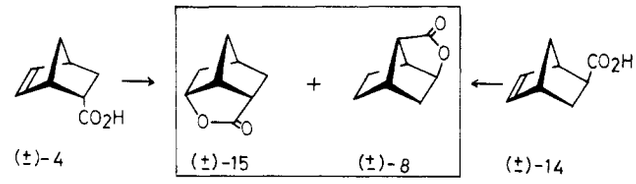


Chart III

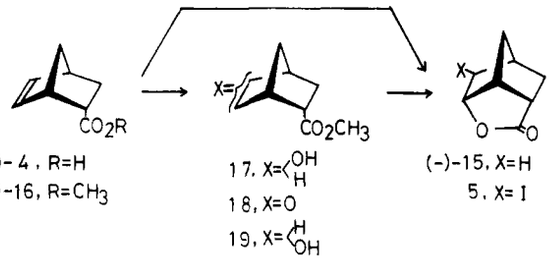


Results

Absolute Configuration and Absolute Rotation of the

0022-3263/78/1943-4947$01.00/0

Chart IV



***endo*-Lactone 15.** (−)-(1*S*,2*S*,4*S*)-*endo*-5-Bicyclo[2.2.1]-heptene-2-carboxylic acid (**4**) has been correlated with the optically active *endo*-lactone **15** in two different ways (Chart IV).

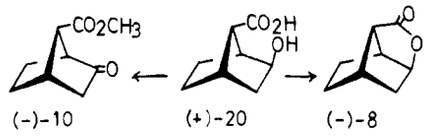
In the preceding paper,[8] we reported the conversion of (−)-*endo*-carboxylic acid **4**, $[\alpha]_D$ −96.7°(EtOH) (optical purity 67%),[6] into (−)-*endo*-lactone **15** via the alcohols **17** obtained by hydroboration–oxidation of (−)-**16**. Jones oxidation converted the mixture into a mixture of 5- and 6-*exo*-carboxylates **18** whose sodium borohydride reduction gave a mixture of 5- and 6-*endo*-hydroxy carboxylates **19**. Saponification of this product followed by acidification preferentially lactonized the 6-*endo*-hydroxy acid to furnish the (−)-*endo*-lactone **15**: mp 153.5–155 °C; $[\alpha]_D$ −2.8° (EtOH). Since all purifications were carried out by either distillation or sublimation, this sequence of conversions indicates an absolute rotation of $[\alpha]_D$ −4.18° for this *endo*-lactone **15**.

Our second procedure for the correlation started from (−)-**4**, $[\alpha]_D$ −119°(EtOH) (optical purity 83%), which was treated with iodine–potassium iodide solution to afford the iodolactone **5**. Hydrogenolysis with Adams' catalyst removed the iodine, furnishing (−)-**15**: mp 153–156 °C; $[\alpha]_D$ −3.6° (EtOH). Since the same precautions were taken not to affect optical purities during purification, this correlation gave an absolute rotation of $[\alpha]_D$ −4.33° for (−)-**15**, in agreement with the value obtained by the first method within the limit of experimental error. This agreement between two absolute rotation values obtained from rather remote sequences of conversion also supports the 1*R*,2*S*,4*S*,6*R* absolute configuration of the (−)-*endo*-lactone **15**.

Absolute Configuration and Absolute Rotation of the *exo*-Lactone 8. In the preceding paper,[2] we assigned the 1*R*,3*R*,6*S*,7*S* configuration to (−)-brexan-2-one (**11**) by analyzing its (−) Cotton effect, and this conclusion found further support in the (+) Cotton effect exhibited by the intermediate (+)-*syn*-bicyclic keto ester **10** (Chart II). Although this immediately indicated the 1*S*,2*S*,4*S*,7*R* absolute configuration for the (+)-*exo*-lactone **8**, other experimental evidence is required to correlate its absolute rotation to that of the (+)-*endo*-carboxylic acid **4** because of probable intervention of symmetrical carbonium species during the conversion which eventually lead to partially racemized final products.

We were fortunate to observe a fairly large enantiomer differential shift of $\Delta\Delta\delta$ = 0.13 ppm in the NMR signal due to CH_3CO of (−)-brexan-2-ol acetate (**13**), $[\alpha]_D$ −109° (EtOH), when the chiral shift reagent tris[3-(trifluoromethylhydroxymethylene)-*d*-camphorato]europium(III) [Eu(facam)$_3$] was added to make the molar ratio of substrate/shift reagent = 1:0.19. The ratio of integrated intensities gave an optical purity of 70.5% for this sample of (−)-brexan-2-ol (**12**). Since this acetate had been prepared from (−)-brexan-2-one (**11**), $[\alpha]_D$ −201° (EtOH), whose Wolff–Kishner reduction in turn gave (−)-brexane (**3**) with $[\alpha]_D$ −94.3° (EtOH),[2] absolute rotations of $[\alpha]_D$ −285 and −134° can be assigned to (−)-brexan-2-one (**11**) and (−)-brexane (**3**), respectively. This optical purity for (−)-brexan-2-one (**11**) can automatically be applied to its synthetic intermediates, affording an absolute rotation of $[\alpha]_D$ +4.9° to the (+)-bicyclic keto ester **10** of $[\alpha]_D$ + 3.47° (EtOH).[2]

Chart V



$[\alpha]_D$(EtOH)	−4.1° optical purity 84%	+13.9°	−141°
absolute rotation $[\alpha]_D$(EtOH)	−4.9°	+16.5°	−168°

To achieve our final object, the absolute rotation of the *exo*-lactone **8**, we used the *syn*-*exo*-hydroxy acid **20** (Chart V) as a "go-between" correlating the *exo*-lactone **8** with the *syn*-keto ester **10** whose absolute rotation we now know.

Permanganate oxidation followed by esterification converted a sample of (+)-**20** [mp 136–137 °C; $[\alpha]_D$ +13.9° (EtOH)], prepared from the (−)-*endo*-carboxylic acid **4** (see Experimental Section), into (−)-**10** with $[\alpha]_D$ −4.1° (EtOH), indicating 84% optical purity for both **10** and **20**.

Since this same (+)-**20** (optical purity 84%) sublimed at reduced pressure to yield (−)-**8** [mp 109–112 °C; $[\alpha]_D$ −141° (EtOH)], we finally have $[\alpha]_D$ −168° (EtOH) for the absolute rotation of the (−)-*exo*-lactone **8** (Chart V).

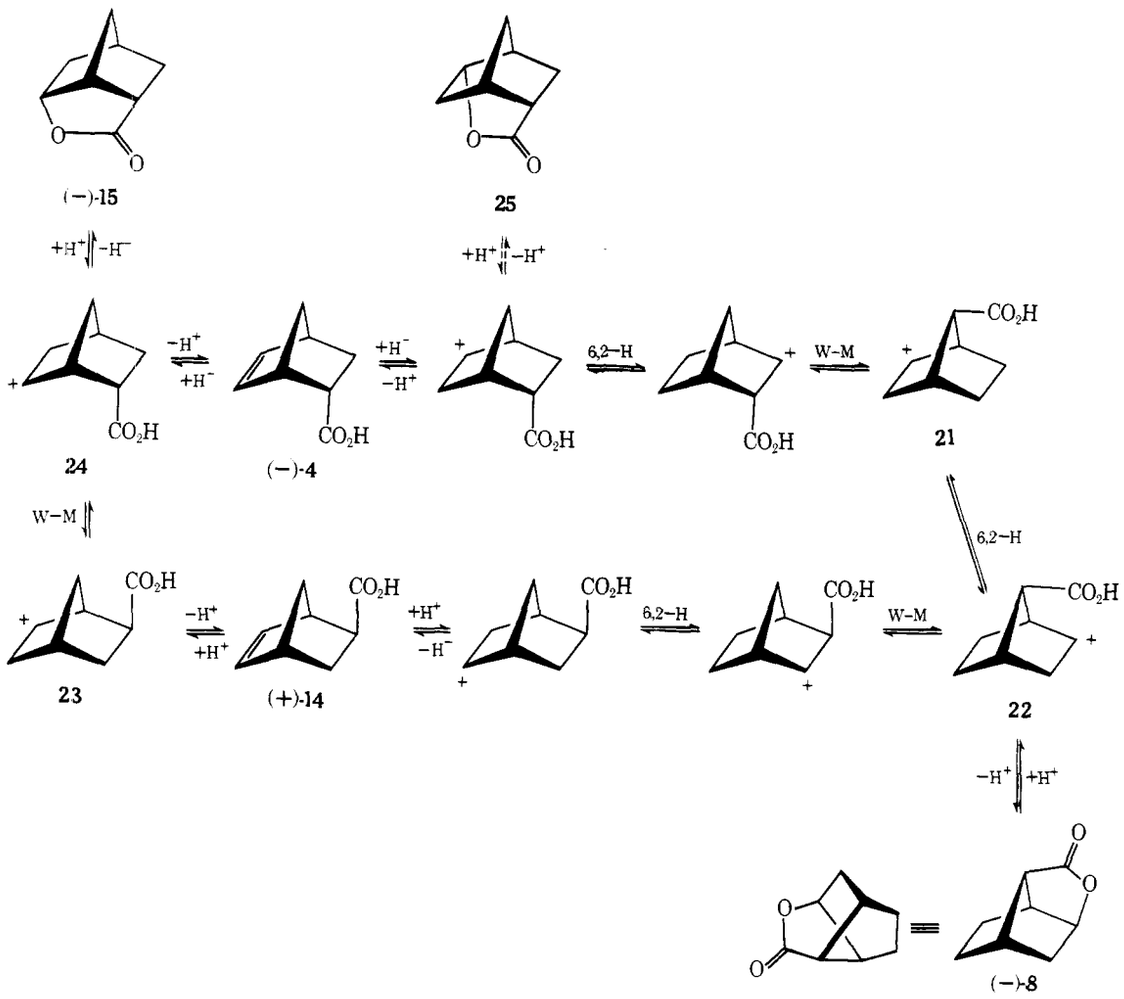
Acidic Rearrangement of (−)-*endo*-5-Bicyclo[2.2.1]-heptene-2-carboxylic Acid (4) (Chart VI). Heating (25 °C) a mixture of the (−)-endo-unsaturated carboxylic acid **4**, $[\alpha]_D$ −119° (EtOH) (optical purity 83%),[6] and 75% sulfuric acid for 4 h afforded a mixture of the *endo*-lactone **15** and the *exo*-lactone **8**, whose VPC analysis indicated a ratio of 4:1. The mixture was hydrolyzed by heating with 2 N NaOH solution, and the saponified mixture was made acidic. Separation of neutral and acidic fractions was carried out; the readily formed *endo*-lactone **15** was isolated from the neutral fraction, and from the acidic fraction was isolated the hydroxy acid **20**, whose sublimation afforded the *exo*-lactone **8**. Careful sublimation at reduced pressure purified these two lactones to show the specific rotations $[\alpha]_D$ −3.4° (EtOH) and $[\alpha]_D$ −141° (EtOH), respectively. These rotations correspond to their optical purities of 79 and 84%, respectively, indicating that this acidic rearrangement doubtlessly proceeded with no racemization within the limit of experimental error.

Acidic Rearrangement of (+)-*exo*-5-Bicyclo[2.2.1]-heptene-2-carboxylic Acid (14) (Chart VI). The (+)-exo-unsaturated acid **14**, $[\alpha]_D$ +8.6° (EtOH) (optical purity 50%),[6] was prepared by epimerization of the (+)-endo isomer **4** (see Experimental Section). Lactonization of this (+)-**14** by heating (25 °C) with 75% sulfuric acid for 4 h afforded a reaction mixture which was found to be comprised of the *endo*-lactone **15** and *exo*-lactone **8** in a ratio of 3:2. Separation and purification yielded (−)-**15** with $[\alpha]_D$ −2.1° (EtOH) and (−)-**8** with $[\alpha]_D$ −88.6° (EtOH). These values correspond to 48 and 51% optical purities for these respective lactones, indicating again that virtually no racemization took place in the acidic lactonization reaction of (+)-**14**.

Chart VI

	(−)-15	(−)-8
(−)-4 $[\alpha]_D$ −119° (EtOH) (optical purity 83%) →	$[\alpha]_D$ −34°(EtOH) (79%)	$[\alpha]_D$ −141°(EtOH) (84%)
(+)-14 $[\alpha]_D$ + 8.6° (EtOH) (optical purity 50%) →	$[\alpha]_D$ −2.1°(EtOH) (48%)	$[\alpha]_D$ −88.6°(EtOH) (51%)

Scheme I



Discussion

Chart VI summarizes our experimental results on the stereochemistry of lactonization reaction of both the (−)-*endo* acid **4** and (+)-*exo* acid **14**, emphasizing that (1) both isomeric acids give a mixture of the (−)-*endo*-lactone **15** and the (−)-*exo*-lactone **8** and that (2) no perceivable amount of racemization is observed in this reaction.

Most simply interpreted, these stereochemical behaviors seem to be rationalized by assuming the sequence of conversions illustrated in Scheme I, which involves a Wagner–Meerwein type skeletal rearrangement (W–M) together with a "6,2-hydride shift" (6,2-H). Although ample experimental examples in the literature[9] can be found which support this "6,2-hydride shift" and reluctant "3,2-hydride shift", our observation of almost no racemization in this lactonization process can be regarded as another example to exclude the "3,2-hydride shift" intervention since the "3,2-hydride shift" in the carbonium intermediates **21** and **22** (Chart VII) apparently leads to racemized products.

Although these interpretations are found to be compatible with Berson's experiment[10] on the stereochemistry of the acidic rearrangement reaction of a bicyclic unsaturated carboxylic acid closely related to the (−)-*endo*-carboxylic acid **4**, there still remain two experimental facts to be discussed: (1) relative rates of formation of the (−)-*endo*-lactone **15** and the (−)-*exo*-lactone **8** from their starting carboxylic acids **4** and **14**, and (2) almost exclusive formation of (−)-**15** from both (−)-**4** and (+)-**14** on prolonged contact with strong acid. The number of steps leading to the lactones **15** and **8** from their parent carboxylic acids **4** and **14** should simply explain the rapid appearance of (−)-**15** in the reaction mixtures, but this does not seem to hold for the explanation of the observed earlier formation of (−)-**8** from (+)-**14**. To circumvent this difficulty, we are suggesting that the Wagner–Meerwein type rearrangement **23** → **24** is a slow step involving migration of the slightly positively charged carbon atom carrying the carboxylic group to the cationic center. Finally, we invoke the calculated heats of formation ($\Delta H_f°$)[11] (Chart VIII) of brendane (**26**), brexane (**3**), and *twist*-brendane (**2**) to explain the almost exclusive appearance of the (−)-*endo*-lactone **15** on prolonged contact with strong acid. Being the ratio between the final products in the entire equilibrium processes illustrated in Scheme I, the ratio of (−)-**15** to (−)-**8** undoubtly depends upon their thermodynamic stabilities in the acidic medium, which can be safely assumed to be parallel to the stabilities of their hydrocarbon analogues, i.e., brendane (**26**) and brexane (**3**). Nearly 3 kcal/mol difference in the heat of formation between brendane and brexane will be sufficient

Chart VII

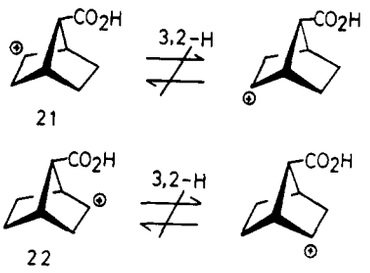


Chart VIII

	26	3	2
ΔH_f°(gas) (Kcal/mol)	-11.72	-8.82	-0.12

to explain the exclusive appearance of the (−)-*endo*-lactone **15** in the equilibrated mixture, and $\Delta H_f^\circ = -0.12$ kcal/mol[11] calculated for twist-brendane (**2**) should also explain the complete absence of the expected "twist"-*endo*-lactone **25** in the reaction mixture (Scheme I).

Experimental Section

Infrared spectral data were obtained from a Hitachi EPI-S2 spectrophotometer. Nuclear magnetic resonance spectra were recorded from a LNM-C-60HL spectrometer. Optical rotations were measured with a JASCO-DPI-SL automatic polarimeter. Elemental analyses were performed on a Yanagimoto CHN-Corder type II. All melting points and boiling points are uncorrected.

Optical Resolution of (±)-*endo*-5-Bicyclo[2.2.1]heptene-2-carboxylic Acid (4). Optical resolution of **4** with cinchonidine has been reported from our laboratory.[4] A mixture of the racemic acid **4** (107 g, 0.775 mol) and cinchonidine (228 g, 0.775 mol) gave (−)-**4** (23.5 g): bp 112–113 °C (7 mm); $[\alpha]^{17}_D$ −119° (*c* 1.10, EtOH) (optical purity 83%).[6]

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.35; H, 7.25.

From the mother liquor separated from the salt of (−)-**4**, 42.0 g of the (+)-acid **4** was obtained: bp 115–117 °C (8 mm); $[\alpha]^{18}_D$ +72.4° (*c* 2.62, EtOH) (optical purity 50%).[6]

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.39; H, 7.24.

Conversion of (−)-4 into the (−)-*endo*-Lactone 15 via Iodolactone 5. To a solution of (−)-**4**, $[\alpha]^{17}_D$ −119° (3.80 g, 0.0275 mol), in 125 mL of water was added a solution of iodine (9.40 g) and potassium iodide (19.0 g) in 112 mL of water. After stirring for 3 h at room temperature, the mixture was extracted with chloroform, and the extract was washed with sodium thiosulfate solution, saturated $NaHCO_3$ solution, and water. After drying over$MgSO_4$, the solvent was removed to yield 7.01 g of iodolactone **5** (96% yield), which without further purification was dissolved in ethyl acetate (250 mL). To the solution was added triethylamine (3.0 g) and Adams' catalyst[12] (0.40 g). The mixture was shaken at room temperature in a hydrogenation flask under 1 atm of hydrogen. After the catalyst was filtered off, the filtrate was washed with dilute HCl, saturated $NaHCO_3$ solution, and water and dried over $MgSO_4$. Evaporation of the solvent gave 3.14 g of *endo*-lactone **15** (82% yield based on **4**), which was sublimed at 85–90 °C (7 mm) to yield a pure sample: mp 153–156 °C (in a sealed tube); $[\alpha]^{25}_D$ −3.6° (*c* 2.28, EtOH).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.40; H, 7.21.

(−)-Brexan-2-ol (12). A solution of (−)-brexan-2-one (**11**), $[\alpha]^{14}_D$ −201°[2] (1.27 g, 9.34 mmol), in dry ether (50 mL) was added dropwise to a suspension of $LiAlH_4$ (350 mg, 9.34 mmol) in dry ether (50 mL). The mixture was refluxed for 5 h and then cooled in an ice bath. To the chilled reaction mixture was added carefully saturated aqueous ammonium chloride solution, and an inorganic solid was filtered off. The filtrate was dried over $MgSO_4$. After evaporation of the solvent, the residual solid was sublimed at 60 °C (20 mm) to give 1.15 g of **12** (89% yield): mp 84–85.5 °C (in a sealed tube); $[\alpha]^{21}_D$ −102° (*c* 0.218, EtOH); IR (KBr) 3300, 1078, 1060, 1010 cm^{-1}.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.23; H, 10.21.

(−)-2-Acetoxybrexane (13). To a solution of (−)-**12**, $[\alpha]^{21}_D$ −102° (864 mg, 6.26 mmol), in dry pyridine (10 mL) was added acetic anhydride (2.04 g, 20.0 mmol) at 0–5 °C, and the mixture was stirred for 3 h at this temperature. After allowing it to stand overnight at room temperature, the reaction mixture was poured onto ice and extracted with pentane. The extract was washed with dilute HCl, saturated $NaHCO_3$ solution, and water and dried over $MgSO_4$. The solvent was evaporated, and the residue was distilled to give 966 mg of **13** (86% yield): bp 118 °C (30 mm); $[\alpha]^{25}_D$ −109° (*c* 0.581, EtOH); IR (neat film) 1730, 1362, 1245, 1048, 1020 cm^{-1}; NMR (CCl_4) δ 1.50 (br s, 8 H), 1.75–2.05 (m, 3 H), 2.02 (s, 3 H), 2.25–2.45 (m, 1 H), 4.40 (d, *J* = 5.34 Hz, 1 H); NMR (CCl_4; (−)-**13**/Eu(facam)$_3$ = 1:0.19) δ 3.75 and 3.88 (anisochronous $-OCOCH_3$).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.08; H, 9.02.

Isomerization of (+)-4 into (+)-*exo*-5-Bicyclo[2.2.1]heptene-2-carboxylic Acid (14). A solution of (+)-**4**, $[\alpha]^{18}_D$ + 72.4° (40.0 g, 0.290 mol), in ether (200 mL) was treated at 0–5 °C with excess ethereal diazomethane. The usual workup gave the methyl ester (41.0 g), which was dissolved in 155 mL of absolute methanol and treated with a sodium methoxide solution prepared from 10.5 g of sodium and 100 mL of absolute methanol. After refluxing for 24 h, most of the methanol was distilled off under reduced pressure. To the residue was added 100 mL of water, and the mixture was heated at reflux for 9 h. After the resulting solution was washed with ether, the reaction mixture was neutralized with 5 N sulfuric acid and extracted with ether. The extract, after being washed with water and dried over $MgSO_4$, was concentrated to yield 34.0 g of a mixture of the acids **4** and **14**, which was dissolved in a solution of $NaHCO_3$ (72.0 g) in water (1.14 L) and treated with a solution of iodine (63.0 g) and potassium iodide (130 g) in water (745 mL). After stirring for 30 min, a solution of iodine (6.3 g) and potassium iodide (13.0 g) in 75 mL of water was added to the reaction mixture and the resulting mixture was stirred for an additional 30 min. After the iodolactone **5** that separated as a brown oil was removed with ether, the aqueous solution was decolorized with 10% sodium thiosulfate solution and carefully brought to pH 2–3 with 1 N sulfuric acid. The mixture was extracted with ether, and the extract was washed with water and dried over $MgSO_4$. Evaporation of the solvent followed by vacuum distillation gave a slightly colored sample of the acid **14**, which was dissolved in ether and decolorized by washing with 10% sodium thiosulfate. Evaporation of the solvent and redistillation afforded 5.10 g of **14** (13% yield based on **4**): bp 88–89 °C (0.6 mm); $[\alpha]^{15}_D$ +8.6° (*c* 1.25, EtOH) (optical purity 50%).[6]

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.25; H, 7.15.

Lactonization of (−)-4. To (−)-**4**, $[\alpha]^{17}_D$ −119° (17.5 g, 0.126 mol), was added dropwise 175 mL of 75% sulfuric acid with ice cooling. The mixture was stirred for 4 h at room temperature (25 °C) and then poured onto ice (1.8 kg). The mixture was extracted continuously for 3 days with ether. The extract was washed with saturated $NaHCO_3$ solution, and this alkaline solution was extracted continuously for 2 days with ether. Both ethereal extracts were combined and dried over $MgSO_4$. Removal of the solvent gave a mixture of lactones **8** and **15** (9.20 g, ratio **8**/**15** = 1:4, 52% yield) as a white solid, $[\alpha]^{15}_D$ −29.5° (*c* 0.718, EtOH). The main part of the mixture of lactones (9.00 g, 0.0652 mol) was mixed with 50 mL of 2 N NaOH solution and stirred for 1 h at room temperature. The clear solution was cooled with ice, and the pH of the chilled solution was carefully adjusted to 5 with concentrated sulfuric acid. After standing for 10 min at room temperature, the pH of the mixture was then adjusted to 8 with solid $NaHCO_3$. This slightly alkaline solution was continuously extracted for 3 days with ether. The extract was dried over $MgSO_4$. Evaporation of the solvent gave a white solid, which was sublimed at 70–80 °C (5 mm) to yield 6.70 g of (−)-*endo*-lactone **15**: mp 153–155 °C; $[\alpha]^{15}_D$ −3.4° (*c* 1.48, EtOH); IR (KBr) 1765, 1350, 1185, 1165, 1090, 1042, 1000, 982, 732, 685 cm^{-1}.

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.38; H, 7.33.

The alkaline solution freed from the *endo*-lactone **15** was acidified with HCl and extracted continuously for 2 days with ether. The extract was dried over $MgSO_4$, and evaporation of the solvent gave 1.75 g of (+)-hydroxy acid **20**: mp 136–137 °C; $[\alpha]^{15}_D$ +13.9° (*c* 0.600, EtOH); IR (KBr) 3350, 1702, 1370, 1348, 1302, 1278, 1250, 1088, 1028, 972 cm^{-1}.

Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.35; H, 7.71.

When (+)-**20**, $[\alpha]^{15}_D$ +13.9° (200 mg, 1.28 mmol), was heated at 145–150 °C under reduced pressure (5 mm), a white solid was observed to condense on the cold finger. After cooling to room temperature, the solid was collected and sublimed at 70–80 °C (5 mm) to yield 126 mg of (−)-*exo*-lactone **8** (75% yield): mp 109–112 °C; $[\alpha]^{20}_D$ −141° (*c* 0.785, EtOH); IR (KBr) 1762, 1335, 1300, 1185, 1160, 1132, 1098, 1070, 1030, 958, 935, 925, 895, 772, 698 cm^{-1}.

Anal. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.77; H, 7.37.

Lactonization of (+)-14. A mixture of (+)-**14**, $[\alpha]^{15}_D$ +8.6° (5.00 g, 0.0362 mol), and 50 mL of 75% sulfuric acid was stirred for 4 h at room temperature (25 °C). Following the same procedure described for the (−)-endo isomer **4**, 1.84 g of a mixture of lactones **8** and **15** was isolated (37% yield, ratio **8**/**15** = 2:3). A small portion of this mixture was sublimed at 110–115 °C (7 mm) to give a sample with $[\alpha]^{25}_D$

−35.0° (c 0.466, EtOH). The main part of the mixture of lactones (1.67 g, 0.0121 mol) was mixed with 12 mL of 2 N NaOH solution, and the mixture was stirred for 1 h at room temperature. The same procedure described above gave 0.80 g of *endo*-lactone **15**, $[\alpha]^{25}_D$ −2.1° (c 1.09, EtOH), and hydroxy acid **20** (0.70 g), $[\alpha]^{25}_D$ +8.5° (c 0.550, EtOH). When this hydroxy acid **20** (300 mg, 1.92 mmol) was heated at 145–150 °C (5 mm) for 30 min, a white solid was observed to condense on the cold finger. This was collected and sublimed at 70–80 °C (5 mm) to yield 125 mg of *exo*-lactone **8** (48% yield), $[\alpha]^{15}_D$ −88.6° (c 0.397, EtOH).

(−)-7-*syn*-(Methoxycarbonyl)bicyclo[2.2.1]heptan-2-one (10). To a solution of (+)-**20**, $[\alpha]^{15}_D$ +13.9° (720 mg, 4.61 mmol), in 9 mL of aqueous KOH (0.46 g) solution was added a solution of potassium permanganate (1.11 g) in 15 mL of water at room temperature, and the mixture was warmed to 35 °C. This mixture was stirred for 30 min at this temperature and then for an additional 3 h at room temperature. After addition of a small amount of ethanol to decompose the excess oxidizing agent, an inorganic solid was filtered off. The filtrate was made acidic with sulfuric acid and extracted continuously for 2 days with ether. The extract was dried over $MgSO_4$, and the solvent was evaporated to give 575 mg of the keto carboxylic acid, which was esterified with diazomethane. The crude ester was distilled to yield 367 mg of **10** (47% yield): bp 120–122 °C (10 mm); $[\alpha]^{25}_D$ −4.1° (c 1.00, EtOH).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.37; H, 7.19. Found: C, 64.03; H, 7.30.

Registry No.—(−)-**4**, 20507-53-3; (+)-**4**, 58001-99-3; (±)-**4**, 67999-50-2; **5** (isomer 1), 67999-51-3; **5** (isomer 2), 67999-52-4; **8**, 68035-50-7; **10**, 60133-56-4; **11**, 60133-48-4; **12**, 68035-51-8; **13**, 68035-52-9; **14**, 67999-53-5; **15**, 68035-53-0; **20**, 68035-54-1.

References and Notes

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4-Alkyl-5-(arylimino)-1,2,3,4-thiatriazolines as Masked 1,3-Dipoles

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The title compounds can undergo bimolecular cycloaddition–elimination reactions by two pathways (1 → **2** and 1 → **4**). The first pathway has been demonstrated in previous publications, while the second pathway is now observed with the electrophilic acyl isothiocyanates and also with sulfenes. The corresponding products of types **5** and **8** can undergo a Dimroth rearrangement under the influence of Lewis acids to give **7** and **9**, respectively. The sulfene adducts **8** react with heterocumulenes in a similar manner to give products (**11–13**) which are identical with those obtained from **1** and the same heterocumulenes. The NMR criteria used to distinguish between the isomeric reaction products are discussed.

Recent interest in the chemistry of masked 1,3-dipoles[1] has led us to investigate the behavior of 4-methyl-5-(phenylimino)-1,2,3,4-thiatriazoline (**1**) in this respect. In principle, two pathways can be considered for the reactions of **1** with unsaturated compounds, i.e., reactions involving participation of the endocyclic or exocyclic nitrogen atom of the amidine residue. We have previously reported that **1** reacts across the C=N bond of isocyanates[2] and alkyl and aryl isothiocyanates[3] to yield heterocycles of type **2** (path a). We now describe examples which can be interpreted in terms of the masked 1,3-dipole **1***, and possibly also a thiapentalene **3**, as an intermediate or transition state (path b).[4]

Reactions with Acyl Isothiocyanates. The reaction of **1** with 1 equiv of aroyl isothiocyanate or ethoxycarbonyl isothiocyanate in benzene at room temperature gave single products by NMR of structure **5**. A kinetic study of the reaction with benzoyl isothiocyanate was undertaken in two solvents of different polarity, benzene and acetonitrile.[5] The second-order rate constants and activation parameters are summarized in Table I. The small solvent effect and the moderately negative entropies of activation may indicate a concerted cycloaddition–elimination mechanism proceeding through a thiapentalene-like transition state (see structure **3** with partial bond formation of a=b and partial loss of N_2). However, these data do not rigorously exclude the alternative stepwise mechanism.[13]

When the reaction of **1** was carried out with a threefold excess of benzoyl isothiocyanate in the absence of solvent, **7a** was isolated instead of **5a**. Also, the reaction of **5a** with benzoyl isothiocyanate at room temperature produced **7a** in quantitative yield. Similarly, **5c** could be isomerized into **7c** under the influence of phenyl isothiocyanate or benzoyl isothiocyanate, but no isomerization was observed by ^1H NMR when aluminum chloride or benzoyl chloride was used as a Lewis acid. The rearrangement **5** → **7** is a typical Dimroth rearrangement[6] which probably occurs via a betaine of type **6**.

Although these results would suggest that **4** is a precursor of **2** (a = CS, b = NR) in our previously reported reactions of **1** with alkyl and aryl isothiocyanates,[3] all attempts to isolate a precursor by varying the reaction conditions were unsuccessful. In the absence of direct evidence to the contrary, we consider **2** (a = CS, b = NR) as primary cycloadducts and not as products of a Dimroth rearrangement.

Reactions with Sulfenes. Sulfenes, generated in situ from

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