JOC Article

1,3-Dipolar Cycloaddition of Diazoalkanes to (*S*)-(+)-3-[(4-Methylphenyl)sulfinyl]-5,6-dihydropyran-2-one. Synthesis of Optically Pure Cyclopropanes by Denitrogenation of Sulfinyl and Sulfonyl Pyrazolines

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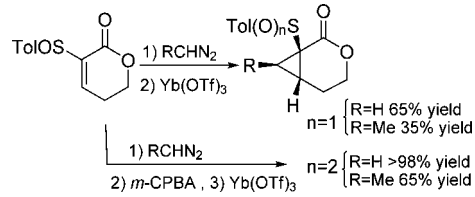

The addition of diazomethane and diazoethane to enantiopure (*S*)-(+)-3-[(4-methylphenyl)sulfinyl]-5,6-dihydropyran-2-one (**3**) afforded the corresponding pyrazolines **4** and **6**-*exo* in good yields and with almost complete π-facial selectivity. When the reaction is effected in the presence of $Yb(OTf)_3$, the facial selectivity is inverted to give the pyrazolines **5** and **7**-*exo*. The denitrogenation of optically pure sulfinyl pyrazolines **4**−**7**-*exo* into the corresponding cyclopropanes with $Yb(OTf)_3$ occurred with complete retention of configuration but moderate chemoselectivity and yields. These results were significantly improved starting from sulfonyl pyrazolines, which afforded optically pure 3-oxabicyclo[4.1.0]heptan-2-ones with yields ranging between 65% (**17** and *ent*-**17**) and ≥95% (**16** and *ent*-**16**).

Introduction

Cyclopropanes are extremely versatile building blocks in organic synthesis owing to their ready accessibility and good reactivity.[1,2] This smallest cycloalkane class is found as a basic structural element in a wide range of naturally occurring and synthetic compounds with important biological and pharmaceutical applications.[3] As a consequence, many recent studies have been devoted to the development of enantioselective synthesis of such compounds.[4] 3-Oxabicyclo[4.1.0]heptan-2-ones are interesting intermediates in the synthesis of pyrethroids,[5] mitoxanes,[6] and conformationally constrained analogues of glutamate.[7] Despite this interest, only two strategies (starting from enantiomerically pure cyclopropane[7,8] or homoallylic diazoacetates and chiral catalysts[9]) have been used for the preparation of these skeletons in optically pure form, which justifies the search for new methods of preparing them.

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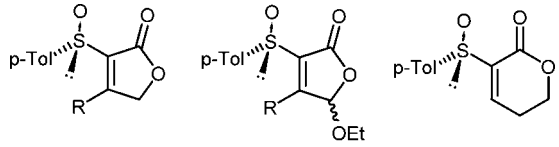
SCHEME 1. Sulfinyllactones Used As Dipolarophiles



1a R = H
1b R = Me

2a R = H
2b R = Me

(+)-**3**

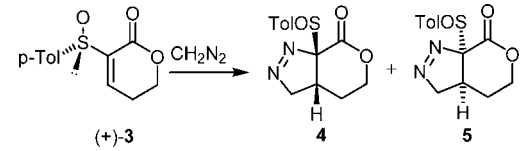
The synthesis of cyclopropanes by extrusion of nitrogen from pyrazolines is a well-known reaction.[10] Recently, we reported a highly stereoselective and efficient method to transform sulfinyl furopyrazolines into sulfinyl cyclopropanes, which can be easily desulfinylated.[11] We had previously reported efficient and highly stereoselective syntheses of the sulfinyl furopyrazolines by reaction of diazoalkanes with optically pure 3-[(4-methylphenyl)sulfinyl]furan-2(5*H*)-ones[12] **1** and with both C-5 epimers of 5-ethoxy-3-[(4-methylphenyl)sulfinyl]furan-2(5*H*)-ones[13] **2** (Scheme 1). Our success in this area suggested to us that a new method for synthesizing 3-oxabicyclo[4.1.0]heptan-2-ones could be achieved by addition of the diazoalkanes to (*S*)-(+)-3-[(4-methylphenyl)sulfinyl]-5,6-dihydropyran-2-one **3** and subsequent nitrogen extrusion from the product(s) obtained thereby. In this paper, we report the results obtained in this study as well as some mechanistic aspects related to the conversion of pyrazolines into cyclopropanes by extrusion of nitrogen.

Results and Discussion

This study was initiated by examining the reaction of the recently described[14] (+)-sulfinylpyranone **3** with diazomethane under various conditions (Table 1). In all cases, a separable mixture of the two isomeric bicyclic pyrazolines **4** and **5** was obtained. The ratio of **4**:**5** varied somewhat with the solvent used and the reaction temperature, but isomer **4** was always the strongly predominant product (de >96%; entries 3 and 5). When the cycloaddition reaction was effected in the presence of an equivalent of $Yb(OTf)_3$, compound **5** became the predominant product with the best de being observed in THF at −78 °C (entry 6). Under these conditions, the solvent was partially converted into a polymeric material which could not be separated from compound **5**, and thus this product was not characterized spectroscopically. The impurity could, however, be removed in the next step of the synthetic sequence.

The reaction of **3** with diazoethane gave results which closely resembled those obtained with diazomethane, in that the formation **6**-*exo* was very strongly favored in the absence of a Lewis acid (Table 2). Compound **7**-*exo* was not observed under these conditions, but a minor unidentified substance was formed in each case. When the addition reaction was conducted in the presence of 1 equiv of $Yb(OTf)_3$ at −78 °C in THF, the **7**-*exo* compound predominated over the **6**-*exo* isomer with a de >80% (entry 5).

TABLE 1. Reactions of (+)-3 with Diazomethane

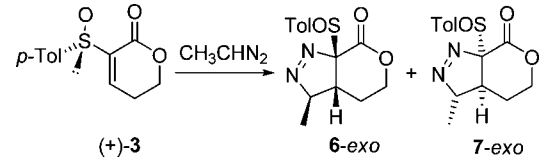


(+)-**3** **4** **5**

entry	solvent	*T*, °C	*t*, min	**4**:**5** ratio[a]	**4** (%)[b]
1	Et_2O/MeOH	0	10	95:5	92
2	Et_2O/MeOH	−40	15	>95:5	95
3	Et_2O/MeOH	−78	20	>98:2	97
4	CH_3CN	−40	15	95:5	92
5	THF	−78	15	>98:2	97
6	THF[c]	−78	30	20:80	
7	Et_2O/MeOH[c]	−78	30	~40:60	
8	CH_3CN[c]	−40	30	50:50	

[a] Determined by ^{1}H NMR. [b] Isolated yield. [c] In the presence of 1 equiv of $Yb(OTf)_3$.

TABLE 2. Reactions of (+)-3 with Diazoethane



(+)-**3** **6**-*exo* **7**-*exo*

			ratio[a]			
entry	solvent	*T*, °C	**6**-*exo*	**7**-*exo*	other	yield %
1	*b*	0	95		5	95
2	*b*	−78	>98		<2	97
3	THF	0	95		5	95
4	THF	−78	>98		<2	97
5	THF[c]	−78	<10	>90		>80
6	*d*	−78	~60	~40		95

[a] Determined by ^{1}H NMR. [b] Et_2O/MeOH. [c] With 1 equiv of $Yb(OTf)_3$. [d] Et_2O/MeOH and 1 equiv of $Yb(OTf)_3$.

With the pyrazolines in hand, the susceptibility thereof to thermal and Lewis acid induced nitrogen elimination was studied (Table 3). When solutions of **4**, **5**, **6**-*exo*, or **7**-*exo* in toluene were briefly heated at 100 °C, aromatization to the pyrazoles **14** (from **4** or **5**, entries 1 and 2) or **15** (from **6**-*exo* or **7**-*exo*, entries 11 and 12) occurred nearly quantitatively, instead of nitrogen loss, which indicates that desulfinylation is strongly favored under these conditions. The pyrazole **15** was also produced in high yield at room temperature in a THF solution of **6**-*exo* containing an equivalent of $Eu(fod)_3$ (entry 20). In contrast, in THF solution containing $Yb(OTf)_3$, the pyrazolines **4** or **5** were converted into mixtures of the desired cyclopropanes **8** or **9** and the olefin **12**. The cyclopropane/olefin ratio was independent of the number of equivalents of $Yb(OTf)_3$ used but increased from 70:30 at room temperature (entries 3 and 4, and 7−10) to 80:20 at −40 °C (entries 5 and 6) with the isolated cyclopropane yields ranging from 65 to 73%. No reaction occurred at −78 °C. Under similar conditions, the **6**-*exo* or **7**-*exo* pyrazolines were converted into the cyclopropanes **10** or **11**, each of which was admixed with the olefin **13**, which was now the major product (entries 13 and 14, and 16−19). Lowering the reaction temperature did not improve the cyclopropane content of the mixture (entry 15), and a small amount of the pyrazole **15** was also obtained. It is remarkable that the tendency

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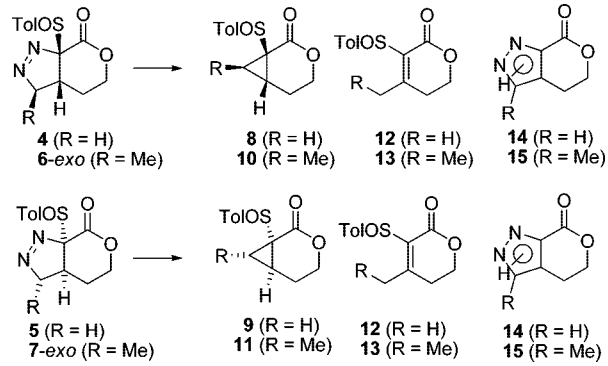
TABLE 3. Decomposition of Pyrazolines 4−7-*exo* under Different Conditions



entry	pyrazoline	solvent	Lewis acid (equiv)	*T*, °C	*t*	products (ratio)[a]	isolated yield, %
1	**4**	toluene		100	30 min	**14**	97
2	**5**	toluene		100	30 min	**14**	97
3	**4**	THF	$Yb(OTf)_3$ (0.5)	25	10 min	**8** (70) **12** (30)	66[b]
4	**5**	THF	$Yb(OTf)_3$ (0.5)	25	10 min	**9** (70) **12** (30)	65[b]
5	**4**	THF	$Yb(OTf)_3$ (0.5)	−40	24 h	**8** (80) **12** (20)	73[b]
6	**5**	THF	$Yb(OTf)_3$ (0.5)	−40	24 h	**9** (80) **12** (20)	70[b]
7	**4**	THF	$Yb(OTf)_3$ (1)	25	10 min	**8** (70) **12** (30)	66[b]
8	**5**	THF	$Yb(OTf)_3$ (1)	25	10 min	**9** (70) **12** (30)	65[b]
9	**4**	THF	$Yb(OTf)_3$ (3)	25	10 min	**8** (70) **12** (30)	66[b]
10	**5**	THF	$Yb(OTf)_3$ (3)	25	10 min	**9** (70) **12** (30)	65[b]
11	**6**-*exo*	toluene		100	30 min	**15**	97
12	**7**-*exo*	toluene		100	30 min	**15**	97
13	**6**-*exo*	THF	$Yb(OTf)_3$ (0.5)	25	1 h	**10** (45) **13** (55)	37[b]
14	**7**-*exo*	THF	$Yb(OTf)_3$ (0.5)	25	3 h	**11** (45) **13** (55)	35[b]
15	**7**-*exo*	THF	$Yb(OTf)_3$ (0.5)	−20	48 h	**11** (40) **13** (50) **15** (10)	
16	**6**-*exo*	THF	$Yb(OTf)_3$ (1)	25	30 min	**10** (45) **13** (55)	37[b]
17	**7**-*exo*	THF	$Yb(OTf)_3$ (1)	25	30 min	**11** (45) **13** (55)	35[b]
18	**6**-*exo*	THF	$Yb(OTf)_3$ (3)	25	30 min	**10** (45) **13** (55)	37[b]
19	**7**-*exo*	THF	$Yb(OTf)_3$ (3)	25	30 min	**11** (45) **13** (55)	35[b]
20	**6**-*exo*	THF	$Eu(fod)_3$ (1)	25	3 days	**15**	97

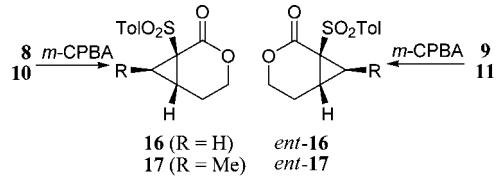
[a] Determined by ^1H NMR. [b] Yield of cyclopropane.

to form cyclopropanes by the denitrogenation of these (6 + 5) bicyclic pyrazolines **4**−**7**-*exo* is lower than that observed for the corresponding (5 + 5) bicyclic pyrazolines.[11] In Table 3, it can be seen that olefins **12** or **13** are always obtained as a significant or even the major product. By contrast, cyclopropanes were obtained as exclusive products in most of the reactions described in ref 11.

The absolute configurations of (S_S)-1-[(4-methylphenyl)sulfinyl]-3-oxabicyclo[4.1.0]heptan-2-one (**8**)[15] and of (S_S)-7-methyl-1-[(4-methylphenyl)sulfinyl]-3-oxabicyclo[4.1.0]heptan-2-one (**10**)[15] were unequivocally established by X-ray diffraction analysis as (1*R*,6*R*) and (1*R*,6*R*,7*R*), respectively. The configurational assignment of their stereoisomers **9** and **11** as (1*S*,6*S*) and (1*S*,6*S*,7*S*) was determined by chemical correlation with **8** and **10** through the corresponding sulfones (Scheme 2).

The absolute configuration of compounds **8** and **10** at C-1 and C-6 is that which is expected based on the observed stereochemical course of the cycloaddition of diazoalkanes to the sulfinylfuranones **1a** and **1b** (Scheme 1) and the denitrogenation of the pyrazolines so obtained.[11,12] The configurations assigned to pyrazolines **4**−**7**-*exo* can be rationalized on steric grounds, whereby the diazoalkanes approach the less hindered face of the presumably most stable *s-cis* **A** conformation

SCHEME 2. Chemical Correlation of Cyclopropanes 8 and 10 with 9 and 11



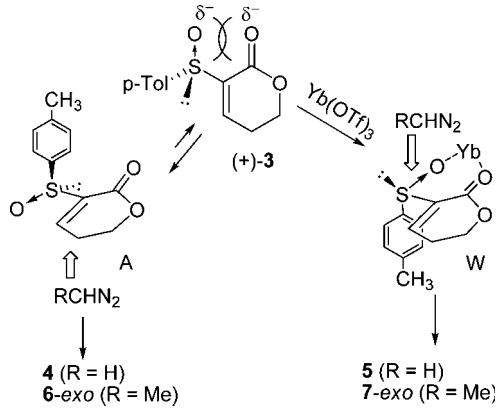
(electrostatic repulsion between the sulfinyl and carbonyl oxygen atoms is minimized) of compound **3**, yielding adducts **4** and **6**-*exo* (Scheme 3). When the cycloadditions are effected in the presence of $Yb(OTf)_3$, the *s-trans* conformation is likely to be preferred due to the formation of the chelated species **W**. The change in the spatial arrangement of the *p*-tolyl group is responsible for the inversion of the facial selectivity in these cases, giving rise to **5** and **7**-*exo*.

The complete *exo* selectivity of the reactions with diazoethane (compounds **6**-*exo* and **7**-*exo* are exclusively formed) was previously also observed with sulfinylbutenolides,[12] and therefore, it can be explained on the basis of the different steric repulsions affecting the *endo* and *exo* approaches (Scheme 4). A more detailed explanation can be found in ref 12.

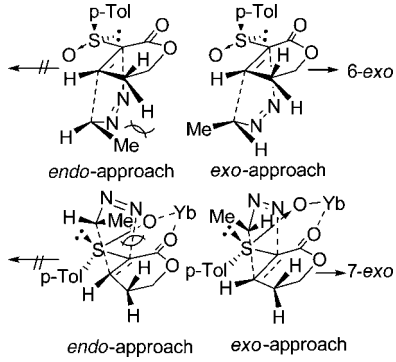
A comparison of the results observed for compounds **4**−**7**-*exo* (Table 3) with those previously reported for the pyrazolines derived from sulfinylbutenolides[12] shows that the product spectra are significantly different. These results stem from the structural differences between the two bicyclic systems. The 7a-(*p*-

(15) Crystallographic data (excluding structure factors) for **8** and **10** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC- 718417 (**8**) and CCDC- 718418 (**10**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44−(0)1223−336033 or e-mail: deposit@ccdc.cam.ac.uk).

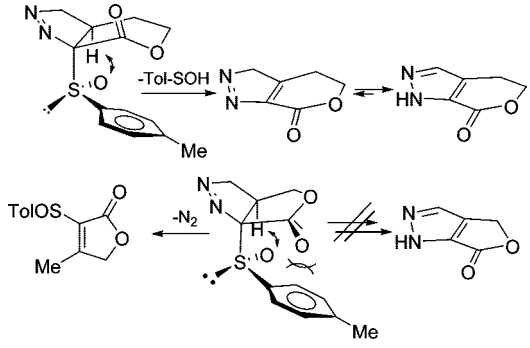
SCHEME 3. Stereochemical Course of the Reactions of (+)-3 with Diazoalkanes



SCHEME 4. Rationalization of the *endo/exo* Selectivity

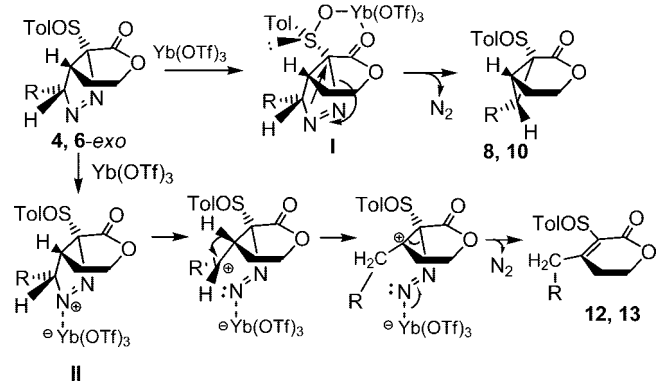


SCHEME 5. Thermolysis of Sulfinyl Pyrano[3,4-*c*]pyrazol-7-ones and Furo[3,4-*c*]pyrazol-6-ones



tolylsulfinyl)tetrahydropyrano[3,4-*c*]pyrazol-7-ones (5 + 6 bicyclic system) undergo desulfinylation and are transformed exclusively into the pyrazoles **14** and **15** on thermolysis (entries 1, 2, 11, and 12, Table 3) or on treatment with Eu(fod)$_3$ (entry 20). In contrast, the 6a-(*p*-tolylsulfinyl)furo[3,4-*c*]pyrazol-6-ones[12] (5 + 5 bicyclic system) are converted into 3-sulfinyl-4-alkylfuran-2(5*H*)-ones by extrusion of nitrogen. The facile desulfinylation of compounds **4**−**7**-*exo* implies that these bicyclic systems adopt the conformation shown in Scheme 5, wherein the sulfinyl group and H-3 are nearly eclipsed. Thus, the transition state for the cycloelimination of *p*-tolylsulfenic acid would be readily accessible in this conformation.[16] The analogous transition state for the furo[3,4-*c*]pyrazolines would be strongly destabilized by an unfavorable interaction of the *p*-tolyl group with the carbonyl oxygen atom, which would explain the low tendency of these compounds to undergo pyrolytic desulfinylation to pyrazoles.

SCHEME 6. Yb(OTf)$_3$-Induced Decomposition of 7a-(*p*-Tolylsulfinyl)tetrahydropyrano[3,4-*c*]pyrazol-7(7a*H*)-ones



The effect of the Yb(OTf)$_3$ on the reaction course of the 7a-(*p*-tolylsulfinyl)tetrahydropyrano[3,4-*c*]pyrazol-7-ones (5 + 6 bicyclic system) can be rationalized (Scheme 6) by means of a model similar to that used to explain the completely stereoselective transformation of 6a-(*p*-tolylsulfinyl)furo[3,4-*c*]pyrazol-6-one (5 + 5 bicyclic pyrazoline) into cyclopropanes.[11] The chelation of the catalyst to the sulfinyl and carbonyl oxygens (species **I**) decreases the electron density at C-7a, provoking the concerted migration of C-3 with extrusion of nitrogen. This migration would be more difficult when R = Me for steric reasons, thus explaining the larger proportion of **13** from **6**-*exo* (Table 3). In contrast, the association of the metal to the less hindered nitrogen (species **II**) would explain the formation of the 3-sulfinyl-5,6-dihydropyran-2-ones. This association decreases the electron density at C-3, facilitating the breaking of the N(2)−C(3) bond, forming secondary (from **6**-*exo*) or primary (from **4**) carbocations which are transformed into the most stable tertiary carbocations by hydrogen migration. These species easily extrude nitrogen forming sulfinyl pentenolides **12** and **13**.[17] The different orientation of the carbonyl oxygen in (5 + 5) and (6 + 5) bicyclic pyrazolines (see Scheme 5) explains their differing behavior under denitrogenation conditions. Chelation of Yb(OTf)$_3$ with the (6 + 5) systems brings the sulfinyl and carbonyl oxygens into closer proximity, consequently inducing conformational changes which are less favorable to cyclopropane formation.

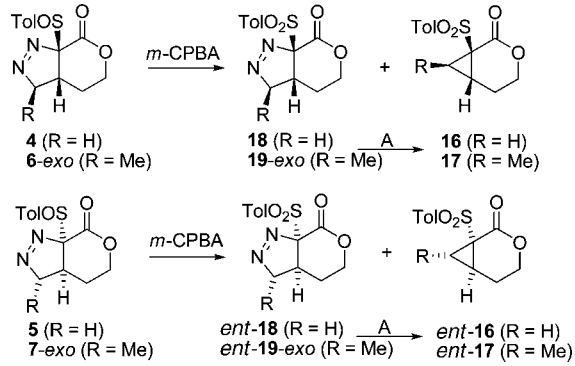
The Yb(OTf)$_3$-provoked increase in the electron-withdrawing character of the substituents on the pyrazoline ring of the sulfinyl pyrazolines is clearly an important factor in the conversion thereof into cyclopropanes. On this basis, as well as on literature precedent,[18] we predicted that oxidation of the sulfinyl group to the sulfone would favor cyclopropane formation. Indeed, reaction of the sulfinyl pyrazoline **4** with excess *m*-CPBA (2 equiv, at 0 °C for 30 h) gave the sulfonyl cyclopropane **16** as the only product (77% yield, Table 4, entry 1). When the reaction was stopped after 24 h, a 70:30 mixture of the intermediate sulfonyl pyrazoline **18** and the cyclopropane **16**

(16) Analogous situation is produced when the reaction is conducted under Eu(fod)$_3$ catalysis (entry 20, Table 3) because Eu will be joined to the nitrogen (see ref 11).

(17) In ref 12, it was proposed that migration of H at C-3a is concerted with the extrusion of nitrogen. As both alternatives are reliable, we are currently performing studies on isotopically marked substrates to clarify this point.

(18) García Ruano, J. L.; Alonso, S. A.; Martín, M. R.; Torrente, E.; Martín, A. M. *Org. Lett.* **2004**, *6*, 4945.

TABLE 4. Reaction of Pyrazolines 4−7-*exo* with *m*-CPBA and Yb(OTf)$_3$



entry	pyrazoline	*T*, °C	*t*	products (ratio)[a]	A	product (isolated yield %)
1	**4**	0	30 h	**16**		**16** (77)
2	**4**	0	24 h	**18** (70) **16** (30)	Yb(OTf)$_3$[b]	**16** (100)
3	**5**	0	24 h	*ent*-**18** (70) *ent*-**16** (30)	Yb(OTf)$_3$[b]	*ent*-**16** (95)
4	**6**-*exo*	0	7 days	**17** (78) **15** (22)		**17** (65)
5	**7**-*exo*	0	7 days	*ent*-**17** (78) **15** (22)		*ent*-**17** (65)
6	**6**-*exo*	25	19 h	**17** (78) **15** (22)		**17** (65)
7	**7**-*exo*	25	19 h	*ent*-**17** (78) **15** (22)		*ent*-**17** (65)

[a] Determined by ^{1}H NMR. [b] Conditions: 0.5 equiv of Yb(OTf)$_3$ in THF, rt, 5 min.

was obtained. Addition of Yb(OTf)$_3$ (0.5 equiv) to a room temperature THF solution of this mixture produced cyclopropane **16** quantitatively in 5 min (entry 2). The sulfinyl pyrazoline **5**, when subjected to the same reaction sequence, gave the sulfonyl cyclopropane *ent*-**16** (95%, entry 3). No 3-sulfonyl-5,6-dihydropyran-2-one was detected in these reaction mixtures. The **6**-*exo* and **7**-*exo* sulfinyl pyrazolines gave, respectively, cyclopropanes **17** and *ent*-**17**, accompanied by significant amounts of the pyrazole **15** (cyclopropane/pyrazole ratios of 78:22; entries 4 and 5).

Under these conditions, sulfonyl pyrazolines **19**-*exo* or *ent*-**19**-*exo* could not be detected in the reaction mixtures. When the reaction was carried out at room temperature, the reaction time was reduced (entries 6 and 7), but the composition of the reaction mixtures was unaltered. The cyclopropanes **17** or *ent*-**17** were easily purified by flash chromatography.

The absolute configuration of the sulfonyl cyclopropanes obtained from sulfinyl pyrazolines was determined by comparison of the [α] values and spectroscopic data with those of the sulfonyl cyclopropanes obtained by oxidation of corresponding sulfinyl cyclopropanes.

Experimental Section

A. Dipolar Cycloadditions. Method A. To a solution of 0.05 g (0.21 mmol) of (*S*)-(+)-3-[(4-methylphenyl)sulfinyl]-5,6-dihydropyran-2-one (**3**), in the solvent (5 mL) indicated in Tables 1 and 2, cooled at the temperature indicated in Tables 1 and 2, was added an excess of an ethereal solution of diazomethane (0.6 M) or diazoethane (0.6 M). The reaction was kept at the same temperature for the time indicated in Tables 1 and 2. The solvent was removed under vacuum, and the residue was analyzed by ^{1}H NMR and purified as indicated in each case.

Method B. To a solution of Yb(OTf)$_3$ (0.13 g, 0.21 mmol) in the solvent indicated in Tables 1 and 2 (0.1 M), at room temperature, was added a solution of (*S*)-(+)-3-[(4-methylphenyl)sulfinyl]-5,6-dihydropyran-2-one (**3**) (0.05 g, 0.21 mmol) in the same solvent (5 mL). The mixture was stirred for 1 h and cooled at −78 °C. Then, an excess of an ethereal solution of diazomethane (0.6 M) or diazoethane (0.6 M) was added. The reaction was kept at the same temperature for 1 h and then was quenched with aqueous saturated potassium sodium tartrate and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were washed with brine, dried and concentrated. The residue was analyzed by ^{1}H NMR and purified as indicated in each case.

(3a*R*,7a*R*,*S*$_S$)-7a-[(4-Methylphenyl)sulfinyl]-3,3a,4,5-tetrahydropyrano[3,4-*c*]pyrazol-7(7a*H*)-one (4). Compound **4** was obtained from **3** and diazomethane by method A (entry 5 in Table 1) and purified by crystallization from Et_2O: white solid (97% yield), mp 86−87 °C; $[\alpha]_D$ +93.1 (*c* 0.45, acetone); IR (KBr) ν_{max} 1722, 1084 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.35−1.48 (m, 1H), 1.75−1.84 (m, 1H), 2.46 (s, 3H), 2.73−2.83 (m, 1H), 2.98 (dt, 1H, *J* = 2.4 and 11.4 Hz), 3.87 (td, 1H, *J* = 4.2 and 11.4 Hz), 4.62 (dd, 1H, *J* = 2.7 and 18.6 Hz), 4.90 (dd, 1H, *J* = 8.4 and 18.6 Hz), 7.41 and 7.65 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 25.4, 27.3, 66.4, 86.8, 116.6, 125.5, 130.4, 134.1, 143.8, 160.6; EIMS *m*/*z* 278 (5%, M$^+$), 246 (22), 214 (13), 139 (100), 138 (55), 108 (75), 53 (50); HRMS (EI) *m*/*z* calcd for $C_{13}H_{14}O_3N_2S$ [M$^+$] 278.0725, found 278.0736.

(3a*S*,7a*S*,*S*$_S$)-7a-[(4-Methylphenyl)sulfinyl]-3,3a,4,5-tetrahydropyrano[3,4-*c*]pyrazol-7(7a*H*)-one (5). Compound **5** was obtained from **3** and diazomethane by method B (entry 6 in Table 1). In this reaction, decomposition of THF was observed giving a nonidentified polymeric product. Therefore, the spectroscopic data of **5** were not possible to obtain.

(3*R*,3a*R*,7a*R*,*S*$_S$)-3-Methyl-7a-[(4-methylphenyl)sulfinyl]-3,3a,4,5-tetrahydropyrano[3,4-*c*]pyrazol-7(7a*H*)-one (6-*exo*). Compound **6**-*exo* was obtained from **3** and diazoethane by method A (entry 4 in Table 2) and purified by crystallization from Et_2O: white solid (97% yield), mp 71−73 °C; $[\alpha]_D$ +284 (*c* 0.45, acetone); IR (KBr) ν_{max} 1720, 1273, 1086 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.40−1.65 (m, 2H), 1.65 (d, 1H, *J* = 7.5 Hz), 2.20 (ddd, 1H, *J* = 4.5 and 7.2 Hz), 2.45 (s, 3H), 3.14 (ddd, 1H, *J* = 3.3, 8.1, and 11.4 Hz), 3.82 (ddd, 1H, *J* = 3.3, 7.2, and 11.4 Hz), 4.65 (dq, 1H, *J* = 4.5 and 7.2 Hz), 7.38 and 7.63 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.6, 21.5, 26.5, 30.9, 65.8, 94.7, 117.0, 125.6, 130.2, 134.2, 143.6, 160.7; EIMS *m*/*z* 278 (12%, M$^+$ − 14), 152 (84), 139 (100), 122 (70), 91 (69), 53 (68).

(3*S*,3a*S*,7a*S*,*S*$_S$)-3-Methyl-7a-[(4-methylphenyl)sulfinyl]-3,3a,4,5-tetrahydropyrano[3,4-*c*]pyrazol-7(7a*H*)-one (7-*exo*). Compound **7**-*exo* was obtained from **3** and diazoethane by method B (entry 5 in Table 2) and purified by crystallization from CH_2Cl_2/hexane: white solid (80% yield), mp 87−90 °C; $[\alpha]_D$ +113.8 (*c* 0.45, acetone); IR (KBr) ν_{max} 1732, 1268, 1047; ^{1}H NMR ($CDCl_3$, 300

MHz) δ 0.85 (d, 3H, J = 7.2 Hz), 1.58−1.70 (m, 1H), 2.24−2.30 (m, 2H), 2.41 (s, 3H), 4.13 (ddd, 1H, J = 3.3, 5.7, and 11.4 Hz), 4.38 (m, 2H), 7.33 and 7.47 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.5, 21.5, 27.8, 33.8, 66.6, 93.5,113.2, 126.6, 129.5, 135.4, 143.7, 162.5; EIMS *m*/*z* 278 (7%, $M^+ - 14$), 264 (44), 152 (29), 139 (100), 125 (38), 91 (47), 53 (25).

B. Extrusion of Nitrogen from Pyrazolines 4−7-*exo* under Lewis Acid Catalyst. To a solution of $Yb(OTf)_3$ (0.056 g, 0.09 mmol) in THF (2 mL) under argon was added a solution of pyrazolines **4**−**7**-*exo* (0.18 mmol) in THF (3 mL). The mixture was stirred at the temperature and time indicated in Table 3. Then, the reaction was quenched with aqueous saturated potassium sodium tartrate at the indicated temperature and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were washed with brine and dried. The solvent was removed under vacuum and purified as indicated in each case.

(1*R*,6*R*,*S*$_S$)-1-[(4-Methylphenyl)sulfinyl]-3-oxabicyclo[4.1.0]heptan-2-one (8). Compound **8** was obtained from **4** (entry 3 in Table 3) and was purified by flash chromatography (ethyl acetate−hexane 80:20): white crystals (66% yield), mp 140−143 °C; $[\alpha]^{20}_D$ +79.8 (*c* 0.5, acetone); IR (KBr) ν_{max} 1709, 1119, 1041 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.73−1.84 (m, 1H), 1.81 (t, 1H, J = 6.3 Hz), 1.85 (dd, 1H, J = 6.3 and 8.7 Hz), 1.97−2.05 (m, 1H), 2.27−2.34 (m, 1H), 4.01−4.16 (m, 2H), 7.28 and 7.61 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.4, 14.3, 20.5, 21.4, 43.2, 64.3, 125.1, 129.7, 139.3, 142.1, 167.7; EIMS *m*/*z* 250 (100%, M^+), 234 (3), 222 (9), 139 (72), 111 (16), 92 (34), 53 (15); HRMS (FAB^+) *m*/*z* calcd for $C_{13}H_{15}O_3S$ [M + 1] 251.0742, found 251.0740.

(1*S*,6*S*,*S*$_S$)-1-[(4-Methylphenyl)sulfinyl]-3-oxabicyclo[4.1.0]heptan-2-one (9). Compound **9** was obtained from **5** (entry 4 in Table 3) and was purified by flash chromatography (ethyl acetate−hexane 80:20): opaque oil (65% yield); $[\alpha]^{20}_D$ +120 (*c* 0.5, acetone); IR (film) ν_{max} 1715, 1121, 1015 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.48 (dd, 1H, J = 6.3 and 9.0 Hz), 1.63 (t, 1H, J = 6.6 Hz), 2.07−2.13 (m, 1H), 2.27 (ddt, 1H, J = 3.3, 6.0, and 14.7 Hz), 2.40 (s, 3H), 2.51 (m, 1H), 4.07 (dt, 1H, J = 3.3 and 12.0 Hz), 4.29−4.35 (m, 1H), 7.29 and 7.74 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.0, 20.4, 21.3, 21.4, 43.4, 64.4, 125.3, 129.5, 139.9, 141.7, 168.3; EIMS *m*/*z* 250 (100%, M^+), 234 (3), 222 (9), 139 (91), 111 (20), 92 (41), 53 (24); HRMS (FAB^+) *m*/*z* calcd for $C_{13}H_{15}O_3S$ [M + 1] 251.0742, found 251.0737.

(1*R*,6*R*,7*R*,*S*$_S$)-7-Methyl-1-[(4-methylphenyl)sulfinyl]-3-oxabicyclo[4.1.0]heptan-2-one (10). Compound **10** was obtained from **6**-*exo* (entry 13 in Table 3) and was purified by flash chromatography (ethyl acetate−hexane 80:20): white crystals (37% yield), mp 151−152 °C; $[\alpha]^{20}_D$ +142 (*c* 0.5, acetone); IR (KBr) ν_{max} 1706, 1282, 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.54 (d, 1H, J = 6.3 Hz), 1.89−2.07 (m, 3H), 2.39 (s, 3H), 2.57−2.62 (m, 1H), 7.27 and 7.65 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.6, 18.5, 21.3, 21.4, 25.6, 47.1, 65.9, 126.1, 129.6, 140.3, 142.4, 166.9; EIMS *m*/*z* 264 (74%, M^+), 216 (8), 140 (45), 125 (100), 92 (41), 79 (24), 67(24), 41 (25); HRMS (FAB^+) *m*/*z* calcd for $C_{14}H_{17}O_3S$ [M + 1] 265.0898, found 265.0895.

(1*S*,6*S*,7*S*,*S*$_S$)-7-Methyl-1-[(4-methylphenyl)sulfinyl]-3-oxabicyclo[4.1.0]heptan-2-one (11). Compound **11** was obtained from **7**-*exo* (entry 14 in Table 3) and was purified by flash chromatography (ethyl acetate−hexane 80:20): white crystals (35% yield), mp 184−186 °C; $[\alpha]^{20}_D$ +53.8 (*c* 0.5, acetone); IR (KBr) ν_{max} 1706, 1277, 1137, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.04 (d, 3H, J = 6.3 Hz), 2.06−2.14 (m, 2H), 2.17−2.25 (m, 1H), 2.29 (q, 1H, J = 6.6 Hz), 2.40 (s, 3H), 4.13 (dt, 1H, J = 3.9 and 12.0 Hz), 4.24−4.31 (m, 1H), 7.28 and 7.78 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.3, 20.2, 21.3, 26.2, 46.4, 65.6, 125.4, 129.5, 139.3, 140.7, 167.8; EIMS *m*/*z* 264 (70%, M^+), 216 (7), 140 (50), 125 (100), 92 (42), 79 (21), 67 (30), 41 (26); HRMS (FAB^+) *m*/*z* calcd for $C_{14}H_{17}O_3S$ [M + 1] 265.0898, found 265.0899.

C. Reaction of Pyrazolines 4−7-*exo* with *m*-CPBA. Method A. To a solution of pyrazoline **4** or **5** (0.05 g, 0.18 mmol) in 5 mL of CH_2Cl_2 at 0 °C was added a solution of *m*-CPBA (0.062 g 0.36 mmol) in 5 mL of CH_2Cl_2. The mixture was stirred at 0 °C for 24 h. Then a 10% solution of Na_2CO_3 was added, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were dried with Na_2SO_4 and concentrated. The residue was dissolved in THF (5 mL), and $Yb(OTf)_3$ (0.039 g, 0.063 mmol) was added. The mixture was stirred at room temperature for 5 min, quenched with aqueous saturated potassium sodium tartrate, and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were dried with Na_2SO_4, concentrated, and purified by crystallization from Et_2O.

Method B. To a solution of pyrazoline **6**-*exo* (0.037 g, 0.13 mmol) or **7**-*exo* (0.025 g, 0.086 mmol) in 5 mL of CH_2Cl_2 at room temperature was added a solution of *m*-CPBA (2 equiv) in 4 mL of CH_2Cl_2. The mixture was stirred at room temperature for 19 h. Then a 10% solution of Na_2CO_3 was added, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were dried with Na_2SO_4 and concentrated. The residue was purified by flash chromatography (ethyl acetate−hexane 60:40).

(1*R*,6*R*)-1-[(4-Methylphenyl)sulfonyl]-3-oxabicyclo[4.1.0]heptan-2-one (16). Compound **16** was obtained from **4** by method A (entry 2 in Table 4): white solid (100% yield), mp 142 °C (d); $[\alpha]^{20}_D$ −42.8 (*c* 0.25, acetone); IR (KBr) ν_{max} 2931, 1727, 1302, 1154 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.87 (t, 1H, J = 6.6 Hz), 2.03−2.11 (m, 2H), 2.24−2.36 (m, 1H), 2.44 (s, 3H), 2.84−2.91 (m, 1H), 4.07 (dt, 1H, J = 3.6 and 12 Hz), 4.23−4.30 (m, 1H), 7.33 and 7.91 (AA′BB′ system, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.0, 20.7, 21.6, 22.5, 44.1, 64.9, 129.4, 129.6, 136.1, 144.9, 163.9; EIMS *m*/*z* 267 (1%, M^+), 202 (24), 187 (37), 157 (61), 143 (27), 91 (100), 65 (46), 53 (45), 41 (48); HRMS (FAB^+) *m*/*z* calcd for $C_{13}H_{15}O_4S$ [M + 1] 267.0691, found 267.0692.

(1*S*,6*S*)-1-[(4-Methylphenyl)sulfonyl]-3-oxabicyclo[4.1.0]heptan-2-one (*ent*-16). Compound *ent*-**16** was obtained from **5** by method A (entry 3 in Table 4): white solid (95% yield); $[\alpha]^{20}_D$ +40.4 (*c* 0.25, acetone). The spectroscopic data were identical to those compound **16**.

(1*R*,6*R*,7*R*)-7-Methyl-1-[(4-methylphenyl)sulfonyl]-3-oxabicyclo[4.1.0]heptan-2-one (17). Compound **17** was obtained from **6**-*exo* by method B (entry 4 in Table 4): white solid (65% yield), mp 137−139 °C; $[\alpha]^{20}_D$ −18.4 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2930, 1733, 1309, 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.60 (d, 3H, J = 6.6 Hz), 1.97 (dq, 1H, J = 6.3 and 6.6 Hz), 1.93−2.08 (m, 1H), 2.28 (ddd, 1H, J = 5.1, 9.6, and 19.5 Hz), 2.74−2.79 (m, 1H), 4.14 (ddd, 1H, J = 4.2, 9.0, and 11.7 Hz), 4.22−4.29 (m, 1H), 7.33 and 7.93 (AA′BB′ system, 4H); ^{13}C ($CDCl_3$, 75 MHz) δ 11.6, 21.6, 21.8, 48.1, 66.6, 129.3, 129.4, 136.9, 144.8, 164.3; EIMS *m*/*z* 281 (1%, M^+), 215 (23), 201 (71), 125 (100), 91 (40), 79 (26), 67 (25), 41 (24).

(1*S*,6*S*,7*S*)-7-Methyl-1-[(4-methylphenyl)sulfonyl]-3-oxabicyclo[4.1.0]heptan-2-one (*ent*-17). Compound *ent*-**17** was obtained from **7**-*exo* by method B (entry 5 in Table 4): white solid (65% yield); $[\alpha]^{20}_D$ +18.2 (*c* 0.5, $CHCl_3$). The spectroscopic data were identical to those compound **17**.

Conclusions

We have provided a new and efficient methodology for preparing enantiomerically pure 3-oxabicyclo[4.1.0]heptan-2-ones by almost complete stereoselective reactions of (*S*)-(+)-3-[(4-methylphenyl)sulfinyl]-5,6-dihydropyran-2-one (**3**) with diazoalkanes and subsequent treatment with $Yb(OTf)_3$. Sulfinyl pyrazolines afforded mixtures of cyclopropanes and olefins, whereas from sulfonyl pyrazolines, cyclopropanes are exclusively obtained in better yields. This behavior provides evidence for the relationship between the magnitude of the electron-withdrawing character of the substituents on the pyrazoline ring and the ease of the conversion thereof into cyclopropanes.

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Supporting Information Available: Experimental procedures and spectral data for compounds **12**−**15**, experimental procedure for the oxidation of cyclopropanes **8**−**11**, NMR spectra for all new compounds, and crystallographic data for compounds **8** and **10** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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