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Synthesis of bicyclo[3.1.0]hexanones via 1,3-dipolar cycloaddition of diazoalkanes to homochiral α-sulfinyl-2-cyclopentenones

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ABSTRACT

The reactions of diazomethane, diazoethane, and (trimethylsilyl)diazomethane with (*S*)-2-*p*-tolylsulfinylcyclopent-2-en-1-one have been studied. The sulfinyl group increases the reactivity and controls the π-facial and *endo*/*exo* selectivities. The π-facial selectivity can be inverted in the presence of $Yb(OTf)_3$, which makes possible the stereodivergent synthesis of both diastereoisomeric pyrazolines. Completely stereoselective denitrogenation of optically pure pyrazolines into cyclopropanes was achieved under substoichiometric $Yb(OTf)_3$ catalysis.

1. Introduction

Bicyclo[3.1.0]hexanones are relevant structural moieties because of the biomedical properties associated to such a skeleton,[1] as well as their use in the flavor and fragrance industry,[2] or as synthetic intermediates.[3] This interest is reflected in the numerous methods for their asymmetric synthesis reported in the last years. Many of them are based on the intramolecular cyclopropanation of diazoderivatives. Thus Lahuerta et al. reported the preparation of bicyclo[3.1.0]hexanones from diazoketones bearing a double bond at the δ position employing chiral dirhodium(II) complexes,[4] whereas Nakada et al. used the reaction of α-diazo-β-ketosulfones with CuOTf and chiral ligands.[5] Optically active metallo-Salen complexes have shown to be efficient catalysts for the cyclization of phenyl alkenyl α-diazoketones,[6] and chincona alkaloids were used in the first enantioselective organocatalytic cyclopropanation.[7] On the other hand, Marquez et al. have used the enzymatic resolution of the racemic bicycle obtained by cyclopropanation of the inexpensive α-diazo β-ketoesters.[8] Other methodology widely used in the construction of the enantiomerically enriched bicyclo[3.1.0]hexanones is based on the reaction of cyclopentenones with ylides, with the chiral auxiliary supported by any of the reagents.[9] The stereoselective epoxidation of suitable substituted cyclopentenes, followed by an intramolecular epoxide ring opening, has also been used in the synthesis of some fluorinated derivatives containing the desired skeleton.[10]

In the course of our studies on the influence of the sulfinyl group on the asymmetric 1,3-dipolar cycloadditions with diazoalkanes[11] we have recently reported that reactions of these dipoles with (*S*)-3-*p*-tolylsulfinylfuran-2(5*H*)-ones proceed with high yields and excellent stereoselectivity.[12] Moreover, the stereoselective extrusion of nitrogen from the resulting $^1\Delta$-pyrazolines under $Yb(OTf)_3$ catalysis provides an excellent method for the synthesis of enantiomerically pure 3-oxabicyclo[3.1.0]hexanones.[13] Taking into account that bicyclo[3.1.0]hexanones could be obtained from cycloalkenones following a similar sequence, we decided to study the behavior of sulfinyl derivative **1** (it had previously shown to be efficient as a chiral dienophile[14] and dipolarophile[15]) in their reactions with diazoalkanes. The results obtained in this study as well as those observed in denitrogenation of the resulting $^1\Delta$-pyrazolines are reported in this paper.

2. Results and discussion

We first studied the reaction of α-sulfinylcyclopentenone **1**[16] with diazomethane under different conditions (Table 1). The addition of an ethereal solution of diazomethane over sulfinylcyclopentenone **1** dissolved in Et_2O produced, almost instantaneously, a mixture of only two $^1\Delta$-pyrazolines, **2A** (major) and **2B**, in almost quantitative combined yield. As expected, the facial selectivity increased and the reaction times were longer when the temperature became lower (Table 1, entries 1–3). The use of THF as the solvent provided similar results (Table 1, entries 4–6). Chromatographic separation of both isomers afforded major **2A** (>95% de) in 83% yield (entry 6).

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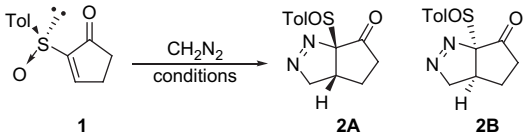
Table 1
Reactions of compound **1** with diazomethane



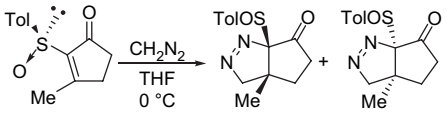
1 **2A** **2B**

Entry	Solvent	T (°C)	Lewis acid (equiv)	Time	Ratio[a] **2A**/**2B**	Yield[b] (%)
1	Et_2O	0	—	5 min	91/9	>95 (**2**)
2	Et_2O	−40	—	3 h	92/7	>95 (**2**)
3	Et_2O	−78	—	12 h	95/5	>95 (**2**)
4	THF	0	—	5 min	88/12	63 (**2A**)
5	THF	−40	—	30 min	90/10	80 (**2A**)
6	**THF**	**−78**	—	**9 h**	**96/4**	**83** (**2A**)
7	**THF**	**−78**	**$Yb(OTf)_3$ (0.5)**	**5 min**	**21/79**	**63** (**2B**)

[a] Determined by ^{1}H NMR from the reaction crude.
[b] Isolated yield.

The reaction was then performed in the presence of $Yb(OTf)_3$ (Table 1, entry 7), which inverted the π-facial selectivity determining the predominance of isomer **2B**, which could be obtained in 63% isolated yield in the conditions of entry 7.[17] Taking into account that the opening of the tetrahydrofuran ring by reaction with diazoalkane/boron trifluoride etherate had been reported[18] and it also takes place under $Yb(OTf)_3$ catalysis, as we could demonstrate the formation of the pyrazolines under the conditions used in entry 7 can only be explained as the consequence of the high reactivity of sulfinylcyclopentenone **1** toward diazomethane.[19]

We have also studied the reaction of (*S*)-3-methyl-2-(*p*-tolylsulfinyl)cyclopent-2-enone (**3**)[16] with diazomethane. As expected, it proved to be much less reactive than **1**, yielding a 69/31 mixture of **4A**/**4B** after 10 h at 0 °C (Scheme 1), which precluded the use of lower temperatures.



3 **4A** **4B**

Scheme 1. Reaction of cyclopentenone **3** with diazomethane.

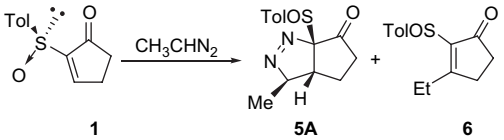
When reaction was conducted in the presence of $Yb(OTf)_3$ the isolation of pyrazolines is very difficult, because reactions of diazomethane with THF and with the C=O bond competed with the slower cycloaddition to the C=C of **3**.

We next studied reactions of compound **1** with diazoethane. Under thermal conditions, they were very fast, and afforded mixtures of compounds **5A** and **6** (Table 2). Olefin **6** could result from the extrusion of nitrogen from pyrazolines **5A** or **5B**. However, as compound **5A** dissolved in THF at 0 °C is stable for hours without significant decomposition, compound **6** obtained in the absence of acids (entries 1–4, Table 2) must derive from **5B** (not shown), which must be much less stable than **5A**. Therefore, the ratio **5A**/**6** indicated in Table 2 could be considered as a measure of the facial selectivity.

The proportion of **5A** increased when the temperature became lower (entries 1–4, Table 2) with the best isolated yield (67%) having been obtained at −78 °C (entry 4). In the presence of $Yb(OTf)_3$ compound **6** was exclusively formed, even at −78 °C. Cyclopropanes derived from **5A** or **5B** were not detected in any case.

The low reactivity of trimethylsilyldiazomethane determined that its reaction with **1** required higher temperature and longer

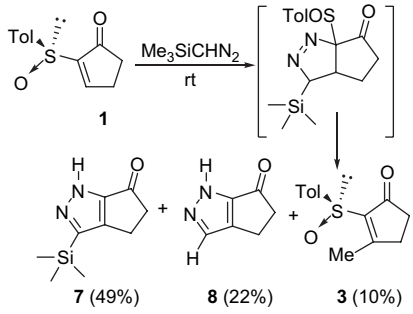
Table 2
Reactions of compound **1** with diazoethane



1 **5A** **6**

Entry	Solvent	T (°C)	Time	Ratio **5A**/**5B**/**6** (yield, %)
1	THF	0	5 min	68/—/32
2	THF	−20	5 min	75/—/25
3	THF	−40	50 min	83 (55)/—/17
4	**THF**	**−78**	**4 h**	**90** (**67**)/—/**10**
5	Et_2O	−40	2 h	81/8/11

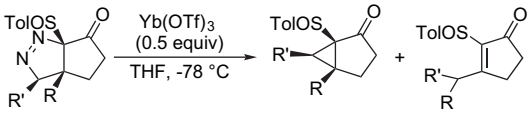
reaction time than the reactions with diazomethane and diazoethane. Additionally, trimethylsilylpyrazoline was neither isolated nor characterized, since spontaneously evolved into 3-(trimethylsilyl)cyclopenta[*c*]pyrazol **7**, 3-methylcyclopentanone **3**, and pyrazol **8** (Scheme 2), which were isolated by column chromatography.[20]



1 **7** (49%) **8** (22%) **3** (10%)

Scheme 2. Reaction of sulfinylcyclopentenone **1** with (trimethylsilyl)-diazomethane.

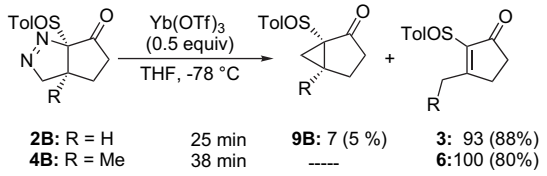
In order to obtain bicyclo[3.1.0]hexan-2-ones, we studied the reactions of the previously obtained pyrazolines **2A**, **2B**, **4A**, **4B**, and **5A** with $Yb(OTf)_3$ in the best conditions (0.5 equiv of the acid at −78 °C) that had allowed the formation of cyclopropane derivatives from the $^1\Delta$-pyrazoline ring of the furo[3,4-*c*]pyrazolones.[13] Pyrazoline **2A** only needed 20 min to be quantitatively transformed into an 88/12 mixture of **9A** and **3** (Scheme 3). A similar behavior was observed for the pyrazoline **4A** but, in this case, cyclopropane **10A** was obtained as the only product. By contrast, the formation of olefin **6** was clearly favored starting from **5A** and only a small amount of cyclopropane **11A** could be detected by NMR.



2A: R' = R = H 20 min **9A**: 88 (87%) 3: 12
4A: R' = H, R =Me 30 min **10A**:100 (78%) ----
5A: R' = Me, R = H 15 min **11A**: 5 6: 95

Scheme 3. Denitrogenation of pyrazolines **A** under $Yb(OTf)_3$ catalysis.

Pyrazolines **2B** and **4B** exhibited lower tendency to the formation of cyclopropane rings than their corresponding **2A** and **4A** diastereoisomers. Only a small amount of cyclopropane **9B** was formed from **2B**, and olefin **6** was the only product detected in the reaction crude from **4B** (Scheme 4).



Scheme 4. Denitrogenation of pyrazolines **B** under $Yb(OTf)_3$ catalysis.

Finally, in order to clarify the effect of the sulfinyl group on the reactivity of the sulfinylcyclopentenone **1** with diazoalkanes, we have studied the reactions of diazomethane with cyclopent-2-enone (**12**) and its 2-(*p*-tolylsulfanyl) and 2-(*p*-tolylsulfonyl) derivatives **13**[21] and **14**.[21] The results are collected in Table 3. The sulfinyl group strongly increased the reactivity of the double bond (compare entries 1 and 3). Moreover, the presence of the sulfinyl group stabilized the adduct (**15** completely decomposed after 2 days at −20 °C whereas **2A** can be stored for over two weeks under similar conditions). Sulfone **14** exhibited a reactivity even larger than that of sulfoxide **1** (entry 4), whereas thioether **13** did not react with diazomethane after 2 days at room temperature (entry 2), which are the expected results according to the electronic effects of the substituents.

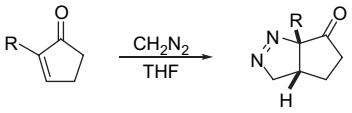
3. Structural and configurational assignments

Significant NMR parameters of the obtained pyrazolines are depicted in Table 4. The regiochemistry of compounds **2A**, **2B**, and **5A** could be easily deduced from the value of the coupling constant between the protons at C-3a and C-3. The structure is also supported by the $\delta_{C\text{-}6a}$ value observed for these compounds. Regiochemistry of compounds **4A** and **4B** (lacking of the protons at C-3a) must be identical ($\delta_{C\text{-}3a}$ and $\delta_{C\text{-}6a}$ are very similar for both isomers) and the same applies for pyrazolines **2A** and **2B** (similar values of $\delta_{C\text{-}6a}$ and $\delta_{C\text{-}3a}$).

The different $J_{3,3a}$ values observed for the protons at C-3 allows to differentiate H_{endo} and H_{exo} in compounds **2A** and **2B** (see Table 4). The $J_{3,3a}$ value (3.6 Hz) in compound **5A** suggests that they are in a *trans* relationship, which means that the Me group at C-3 occupies an *exo* position.

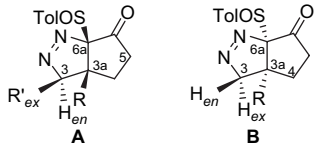
The absolute configuration of C_{3a} and C_{6a} in compounds **2A** and **2B** was tentatively assigned from the very different values of δ-H_{3exo} in both compounds. Taking into account the *S* configuration of the sulfinyl group in these compounds, the presumably most stable conformations for the two possible diastereoisomers (**A** and **B**) are depicted in Figure 1. As we can see, H_{exo} must be shielded by the tolyl group in **B**, but not in **A**. Compound **2A**, with the highest value of δ-H_{3exo} (4.84 ppm) must be assigned as **A**, whereas **2B** (δ-H_{3exo}=3.23 ppm) must be assigned as **B**. The same criteria should be valid for the assignment of compounds **4A** (larger δ-H_{3exo}) and **4B** (lower δ-H_{3exo}). In these cases the $\Delta\delta$ values are not so marked

Table 3
Reactivity of cyclopentenone and sulfur derivatives with diazomethane



Entry	R	Starting material	*T* (°C)	Time	Adduct
1	H	**12**	0	3 days	**15**
2	Tol-S	**13**	25	2 days	—
3	Tol-SO	**1**	−78	9 h	**2A**
4	Tol-SO_2	**14**	−78	0.5 min	**16**

Table 4
^1H and ^{13}C NMR data of pyrazolines



Pyrazoline			Chemical shifts					Coupling constant	
No.	R	R′	H_{3endo}	H_{3exo}	H_{3a}	C_{3a}	C_{6a}	$J_{3exo,3a}$	$J_{3endo,3a}$
2A	H	H	4.57	4.84	3.00	30.4	125.1	8.7	3.2
2B	H	H	4.37	3.23	2.97	31.0	124.6	8.1	2.1
4A	Me	H	4.51 and 4.81		—	36.9	121.3	—	—
4B	Me	H	4.61 and 4.05		—	37.2	118.0	—	—
5A	H	Me	4.60	—	2.56	37.5	125.3	—	3.6

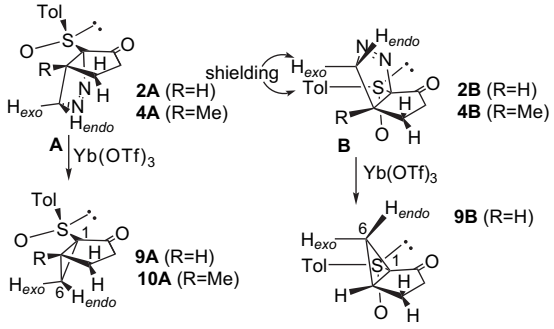


Figure 1. Assignation of the **A** or **B** stereoisomer.

because of the quasi 1,3-*syndiaxial* interaction Tol/R (R=Me), which would destabilize the conformation of diastereoisomer **B** shown in Figure 1, provoking conformational changes decreasing the shielding effect of the tolyl group at H_{exo}. The stereochemical model proposed to explain the experimental results (see later) also supports this assignment.[22]

The stereochemical assignments of cyclopropanes **9A**, **9B**, and **10A** can be easily made taking into account that the extrusion of the nitrogen from the corresponding pyrazolines does not affect any bond at C-3a and therefore configuration of C-5 at cyclopropane must be the same than that of C-3a in the pyrazoline precursor (see Fig. 1).

4. Stereochemical model

The π-facial selectivity of these reactions can be explained by assuming that the sulfinyl group at compounds **1** and **3** mainly adopts conformation **I**, with the oxygen and C=C in an *s-cis* arrangement, thus minimizing its electrostatic repulsion with the carbonyl oxygen. The orientation of the *p*-tolyl group at this conformation determines the favored approach of the dipole (Fig. 2a).

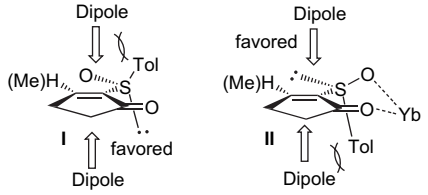


Figure 2. Rationalization of the π-facial selectivity of the cycloadditions.

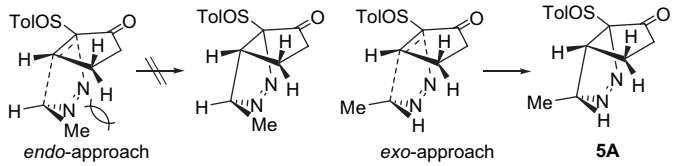


Figure 3. Rationalization of the *endo*/*exo*-selectivity in reactions of **1** with diazoethane.

As the conformational preference must be less marked for compound **3** because of the $(Me/O)_{1,3\text{-}syndiaxial}$ interaction, the facial selectivity in the absence of catalyst is lower (compare entry 4 in Table 1 with Scheme 1).

The influence of $Yb(OTf)_3$ can be rationalized by assuming the formation of a chelated species **II** involving the two oxygens (Fig. 2b). It arranges the *p*-tolyl group in the opposite face to that occupied in **I** (compare Fig. 2a and b), thus explaining the inversion of stereoselectivity produced by this catalyst.

The complete *exo*-selectivity observed in the reaction of diazoethane with **1** can be explained on the basis of the steric interactions of the methyl group at the dipole with the substituents at C-3 of **1**. They are stronger for the *endo* approach (Fig. 3) and therefore the *exo* adduct **5A** was exclusively formed.

Finally, the formation of the cyclopropyl rings in the reactions of bicyclic pyrazolines **2A**, **4A**, and **5A** with substoichiometric amounts of $Yb(OTf)_3$ and the low tendency of pyrazolines **2B** and **4B** to form these cycles, thus preferring the formation of the olefins, can be rationalized on the basis of the same stereochemical model proposed for the synthesis of the 3-oxabicyclo[3.1.0]hexanones.[13]

5. Conclusions

In summary, we have demonstrated that the sulfinyl group at cyclopentenones is able to control the π-facial and *endo*/*exo* selectivities of their 1,3-dipolar reactions with diazoalkanes. The reaction of some of the obtained pyrazolines with $Yb(OTf)_3$ provides an efficient procedure for preparing bicyclo[3.1.0]hexanone derivatives in their optically pure form.

6. Experimental section

6.1. General methods

THF and diethyl ether were distilled from sodium benzophenone under argon. Lewis acids are commercially available and were used without further purification. Flash chromatography was carried out with silica gel Merck 60 (230–400 mesh ASTM). NMR spectra were determined in $CDCl_3$ solutions at 300 and 75 MHz for ^1H and ^{13}C NMR, respectively; *J* values are given in hertz. Melting points were measured using a Gallenkamp apparatus in open capillary tubes and are uncorrected. The optical rotations were measured at room temperature (20–23 °C) using a Perkin–Elmer 241MC polarimeter (concentration in g/100 mL). Compounds **1**,[16] **3**,[16] **13**,[21] and **14**[21] were synthesized and purified following the reported procedures.

6.2. 1,3-Dipolar cycloadditions of diazomethane or diazoethane

Method A. To a solution of cyclopent-2-enones **1**, **3**, **12**, **13**, or **14** (1 mmol) in the appropriate solvent cooled at the indicated temperature (see Tables 1 or 2 and Schemes 1 or 2), was added a solution of diazoalkane in Et_2O. The resulting mixture was stirred under the conditions shown in tables and schemes and evaporated. The residue was analyzed by ^1H NMR and purified as indicated in each case.

Method B. To a stirred solution of Lewis acid (amounts indicated in Table 1) in THF at room temperature was added a solution of sulfinylcyclopentenone **1** or **3** (0.5 mmol) in THF. The mixture was stirred for 1 h, cooled at the temperature indicated in Table 1, then was added the solution of diazoalkane in Et_2O. The reaction mixture was stirred for the time indicated in Table 1. The reaction was quenched at the indicated temperature with a saturated solution of potassium sodium tartrate and extracted with ethyl acetate (3×8 mL). The organic layer was washed with brine (7 mL) and dried ($MgSO_4$). The solvent was removed under vacuum. The resulting residue was analyzed by ^1H NMR.

*6.2.1. (3aR, 6aR, S_S)-6a-[(4-Methylphenyl)sulfinyl]-3a,4,5,6a-tetrahydrocyclopenta[c]pyrazol-6(3H)-one (**2A**)*

It was obtained from (+)-(*S*)-2-(*p*-tolylsulfinyl)cyclopent-2-enone (**1**) and diazomethane in ether or THF (see Table 1) following method A. It was isolated by dissolving the crude reaction in AcOEt and further precipitation with Et_2O/hexane. White solid, mp: 92–94 °C. $[\alpha]_D$ +277.0 (*c* 1, acetone). IR (KBr) 1700, 1491, 1429. ^1H NMR δ 7.48 and 7.33 (AA′BB′ system, 4H), 4.84 (dd, 1H, *J*=8.7 and 18.8), 4.57 (dd, 1H, *J*=3.2 and 18.8), 3.00 (m, 1H), 2.40 (s, 3H), 2.01 (m, 1H), 1.65 (m, 1H), 1.43 (m, 1H), 1.24 (m, 1H). ^{13}C NMR δ 202.3, 143.1, 134.8, 130.2, 125.1, 87.3, 37.6, 30.4, 24.8, 21.4. Anal. Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; S, 12.22. Found: C, 59.64; H, 5.52; N, 10.76; S, 12.18.

*6.2.2. (3aS, 6aS, S_S)-6a-[(4-Methylphenyl)sulfinyl]-3a,4,5,6a-tetrahydrocyclopenta[c]pyrazol-6(3H)-one (**2B**)*

It was obtained from (+)-(*S*)-2-(*p*-tolylsulfinyl)cyclopent-2-enone (**1**) and diazomethane in THF at −78 °C following method B. It was isolated by dissolving the crude reaction in AcOEt and further precipitation with hexane. Yellow solid, mp: 68–70 °C. $[\alpha]_D$ +68 (*c* 1, $CHCl_3$). IR (film) 1708, 1475, 1425. ^1H NMR δ 7.47 and 7.30 (AA′BB′ system, 4H), 4.37 (dd, 1H, *J*=2.1 and 18.8), 3.23 (dd, 1H, *J*=8.1 and 18.8), 2.97 (m, 1H), 2.35 (s, 3H), 1.98 (m, 1H), 1.65 (m, 1H), 1.42 (m, 1H), 1.22 (m, 1H). ^{13}C NMR δ 202.3, 142.9, 134.8, 130.2, 125.1, 124.6, 86.1, 37.6, 31.0, 25.5, 21.4. Anal. Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; S, 12.22. Found: C, 59.38; H, 5.45; N, 10.82; S, 12.05.

*6.2.3. (3aR, 6aR, S_S)-3a-Methyl-6a-[(4-methylphenyl)sulfinyl]-3a,4,5,6a-tetrahydrocyclopenta[c]pyrazol-6(3H)-one (**4A**)*

It was obtained from (+)-(*S*)-3-methyl-2-(*p*-tolylsulfinyl)cyclopent-2-enone (**3**) and diazomethane in THF at 0 °C following method A. It was isolated by dissolving the crude reaction in AcOEt and further precipitation with Et_2O/hexane. White solid, mp: 85–86 °C. $[\alpha]_D$ +210.0 (*c* 1, $CHCl_3$). IR (film) 1718, 1502, 1421. ^1H NMR δ 7.62 and 7.35 (AA′BB′ system, 4H), 4.81 and 4.51 (AB system, 2H, *J*=18.3), 2.43 (s, 3H), 2.31–1.81(m, 4H), 1.67 (s, 3H). ^{13}C NMR δ 202.0, 143.5, 134.4, 129.8, 125.0, 121.3, 86.8, 36.9, 31.2, 26.3, 25.4, 21.4. Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14; S, 11.60. Found: C, 60.59; H, 6.08; N, 10.24; S, 11.82.

*6.2.4. (3aS, 6aS, S_S)-3a-Methyl-6a-[(4-methylphenyl)sulfinyl]-3a,4,5,6a-tetrahydrocyclopenta[c]pyrazol-6(3H)-one (**4B**)*

It was obtained from (+)-(*S*)-3-methyl-2-(*p*-tolylsulfinyl)cyclopent-2-enone (**3**) and diazomethane in THF at 0 °C following method A. It was isolated by dissolving the crude reaction in AcOEt and further precipitation with hexane. Yellow solid, mp: 75–78 °C. $[\alpha]_D$ +61.0 (*c* 1, $CHCl_3$). IR (film) 1704, 1492, 1412. ^1H NMR δ 7.61 and 7.31 (AA′BB′ system, 4H), 4.61 and 4.05 (AB system, 2H, *J*=18.3), 2.40 (s, 3H), 2.28–1.80 (m, 4H), 1.49 (s, 3H). ^{13}C NMR δ 202.3, 143.7, 134.4, 129.6, 125.2, 118.0, 85.9, 37.2, 32.0, 26.9, 24.8, 21.3. Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14; S, 11.60. Found: C, 60.71; H, 5.72; N, 10.34; S, 11.75.

*6.2.5. (3aR, 6aR, 3R, S_S)-3-Methyl-6a-[(4-methylphenyl)sulfinyl]-3a,4,5,6a-tetrahydrocyclopenta [c]pyazol-6(3H)-one (**5A**)*

It was obtained from (+)-(*S*)-2-(*p*-tolylsulfinyl)cyclopent-2-enone (**1**) with diazoethane (see Table 2) following method A. White solid, mp: 89–91 °C. $[\alpha]^{20}_D$ +620.0 (*c*=1, $CHCl_3$). IR (KBr) 1737, 1455, 1405. ^{1}H NMR δ 7.34 and 7.53 (AA′BB′ system, 4H), 4.60 (cd, 1H, *J*=3.6 and 7.5), 2.56 (m, 1H), 2.43 (s, 3H), 2.05 (m, 2H), 1.61 (d, 3H, *J*=7.5), 1.49 (m, 2H). ^{13}C NMR δ 202.4, 142.9, 134.7, 130.1, 125.3, 124.9, 95.6, 37.5, 37.2, 23.8, 21.3, 18.1. Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14; S, 11.60. Found: C, 60.52; H 5.59; N, 9.97; S, 11.84.

*6.2.6. (±)-3a,4,5,6a-Tetrahydrocyclopentapyrazol-6(3H)-one (**15**)*

It was obtained from 2-cyclopenten-1-one (500 mg, 6.09 mmol) and diazomethane in THF (15 mL) at 0 °C following method A. The residue was analyzed by ^{1}H NMR (46% conversion) and purified by flash chromatography (AcOEt/hexane, 1/1). Colorless oil (35% yield). ^{1}H NMR δ 4.92–4.87 (m, 1H), 4.51–4.46 (m, 2H), 2.76–2.64 (m, 1H), 2.15–1.82 (m, 3H), 1.26–1.12 (m, 1H). ^{13}C NMR δ 207.6, 99.0, 85.6, 36.1, 31.3, 25.8.

*6.2.7. (±)-6a-[(4-Methylphenyl)sulfonyl]-3a,4,5,6a-tetrahydrocyclopentapyrazol-6(3H)-one (**16**)*

It was obtained from 2-(4-methylphenyl)sulfonylcyclopent-2-en-1-one (**14**) (500 mg, 6.09 mmol) and diazomethane in THF at 0 °C following method A. ^{1}H NMR δ 7.77 and 7.42 (AA′BB′ system, 4H), 4.91 (dd, 1H, *J*=7.2 and 18.7), 4.83 (dd, 1H, *J*=3.3 and 18.7), 3.54 (m, 1H), 2.65 (m, 1H), 2.50 (s, 3H), 2.38 (m, 2H), 1.26 (m, 1H). ^{13}C NMR δ 199.4, 146.2, 131.9, 130.7, 129.5, 119.1, 86.9, 38.1, 35.0, 24.9, 21.7.

6.3. Addition of (trimethylsilyl)diazomethane to (S_S)-2-(4-methylphenyl)sulfinylcyclopent-2-enone (1)

To a solution of 252 mg (1.145 mmol) of **1** in Et_2O (24 mL) was added at room temperature 0.356 mL of 2 M $TMSCHN_2$ in hexane (1.5 equiv, 1.718 mmol). After 30 h the solvent was removed under reduced pressure and the resulting oil purified by column chromatography (AcOEt/hexane, 3/1) to afford 108 mg (49% yield) of 3-trimethylsilylcyclopentan[1,2-*c*]pyrazol-6-one (**7**), 14 mg of the cyclopenta[1,2-*c*]pyrazol(3)-6-one (**8**) (22% yield), and 59 mg (10% yield) of cyclopentenone **3**.

*6.3.1. 3-(Trimethylsilyl)-4,5-dihydrocyclopenta[c] pyrazol-6(1H)-one (**7**)*

White solid, mp: 128 °C. IR (KBr) 1718. ^{1}H NMR δ 3.03 (m, 4H), 0.36 (s, 9H). ^{13}C NMR δ 197.4, 153.4, 148.2, 140.2, 42.8, 18.8, −1.5. Anal. Calcd for $C_9H_{14}N_2OSi$: C, 55.63; H, 7.26; N, 14.42. Found: C, 55.68; H, 7.19; N, 13.99.

*6.3.2. 4,5-Dihydrocyclopenta[c]-pyrazol-6(1H)-one (**8**)*

Yellow solid, mp: 134 °C. IR (KBr) 3355, 3106, 1708. ^{1}H NMR δ 7.58 (s, 1H), 3.0 (m, 4H). ^{13}C NMR δ 195.0, 149.7, 142.5, 130.2, 42.8, 18.2.

6.4. Nitrogen extrusion reaction

To a stirred solution of pyrazolines **2**, **4** or **5** in THF (0.1 M) cooled at −78 °C was added a solution of $Yb(OTf)_3$ (0.5 equiv) in THF (0.1 M). The mixture was stirred for the time indicated in Scheme 3 or 4. The reaction was quenched at the indicated temperature with a saturated solution of potassium sodium tartrate and extracted with ethyl acetate (3×8 mL). The organic extracts were washed with brine (7 mL) and dried ($MgSO_4$). The solvent was removed under vacuum. The resulting residue was analyzed by ^{1}H NMR.

*6.4.1. (1R, 5R, S_S)-1-[(4-Methylphenyl)sulfinyl]bicyclo[3.1.0]hexan-2-one (**9A**)*

It was obtained from **2A** and purified by flash chromatography (AcOEt/hexane, 1/5). White solid, mp: 84–86 °C. $[\alpha]_D$ −36.2 (*c* 0.505, acetone). IR (KBr) 1722. ^{1}H NMR δ 7.47 and 7.28 (AA′BB′ system, 4H), 2.36 (s, 3H), 2.12 (m, 6H), 1.45 (t, 1H, *J*=5.5). ^{13}C NMR δ 204.8, 142.3, 139.8, 128.9, 125.4, 54.6, 33.1, 26.3, 21.4, 20.9, 17.9. Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02; S, 13.68. Found: C, 66.58; H, 6.20; S, 13.97.

*6.4.2. (1S, 5S, S_S)-1-[(4-Methylphenyl)sulfinyl]bicyclo[3.1.0] hexan-2-one (**9B**)*

It was obtained from **2B** and purified by flash chromatography (AcOEt/hexane, 1/5). White solid, mp: 64–61 °C. $[\alpha]_D$ +131.1 (*c* 1.1, acetone).[9d] IR (film) 1714. ^{1}H NMR δ 7.45 and 7.27 (system AA′BB′, 4H), 2.34 (s, 3H), 2.21–2.03 (m, 6H), 0.82 (t, 1H, *J*=5.3). ^{13}C NMR δ 203.4, 142.1, 139.2, 129.4, 125.2, 54.1, 33.0, 25.9, 21.3, 20.7, 18.4. HRMS (EI): $C_{13}H_{14}O_2S$ requires 234.0715. Found: 234.0713.

*6.4.3. (1R, 5R, S_S)-5-Methyl-1-[(4-methylphenyl)-sulfinyl]bicyclo[3.1.0]hexan-2-one (**10A**)*

It was obtained from **4A** and purified by flash chromatography (AcOEt/hexane, 1/2). White solid, mp: 121–123 °C. $[\alpha]_D$ −2.9 (*c* 0.14, $CHCl_3$). IR (KBr) 3050, 1723. ^{1}H NMR δ 7.56–7.27 (AA′BB′ system, 4H), 2.37 (s, 3H), 2.14–1.87 (m, 4H), 1.89 and 1.48 (AB system, 2H, *J*=5.5), 1.41 (s, 3H). ^{13}C NMR δ 207.1, 141.3, 139.2, 129.6, 124.9, 55.7, 33.2, 31.2, 28.2, 24.2, 21.4, 18.1. Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49; S, 12.91. Found: C, 67.53; H, 6.35; S, 13.12.

*6.4.4. (S_S)-3-Ethyl-2-[(4-methylphenyl)sulfinyl]cyclopent-2-en-1-one (**6**)*

It was obtained from **5A** and purified by flash chromatography (AcOEt/hexane, 2/1). White solid, mp: 108–110 °C. $[\alpha]_D$ +18.0 (*c* 1, acetone). IR (KBr) 1693. ^{1}H NMR δ 7.61 and 7.28 (AA′BB′ system, 4H), 3.08–2.87 (m, 2H), 2.72–2.66 (m, 2H), 2.42–2.37 (m, 2H), 2.39 (s, 3H), 1.20 (t, 3H, *J*=7.5). ^{13}C NMR δ 202.6, 186.4, 141.1, 140.7, 139.7, 129.8, 124.4, 34.3, 30.3, 24.0, 21.3, 12.1. Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49; S, 12.91. Found: C, 67.64; H, 6.29; S, 13.24.

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