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The Lithium Amide Induced Rearrangement of Epoxysulfones Derived from Bicyclo[2.2.1]heptane System

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Abstract—Lithium amides induce rearrangement of the title compounds **1** to afford nortricyclanones **4** via a ketocarbene intermediate. Compounds **4** undergo hydride transfer reduction and imino aldol condensation to afford the other observed reaction products.

Oxiranes constitute an important family of strained small ring heterocyclic compounds widely recognized as being extremely useful synthetic intermediates.[1] Among functionalized epoxides, α,β-epoxysulfones have been proved to be versatile synthons in the presence of nucleophilic reagents.[2] However, the chemistry of bicyclic α,β-epoxysulfones such as **1** and in particular their reaction with organolithium bases remains unexplored.[3] In these cases the conformational rigidity of the bicyclic skeleton should permit a more accurate study of the reaction, because the evolution of the reactive intermediates would follow a predictable and well established reaction pathway. In this paper we wish to report our results concerning the reaction of α,β-epoxysulfones **1** with lithium amides as nucleophilic reagents.

Results and Discussion

The α,β-epoxysulfones **1** were prepared from the related vinylsulfones **2a**,[4] **2b**[5] and **2c**[6] by reaction with *t*-BuOOLi[7] (Scheme 1).

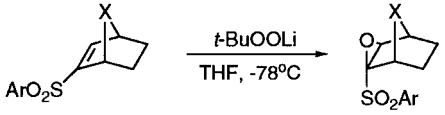
Reaction of **1** with LDA and lithium diethylamide in ether at −78°C afforded, after purification, a mixture of the related nortricyclanols **3**, nortricyclanones **4** and aldol adducts **5** in yields that can be reproduced fairly well (Scheme 2, Table 1).

In the cases of reaction of **1a** and **1b** with LDA, a more accurate distribution of products have been obtained when the reaction crudes were examined by coupled GLC–MS. The resulting data are collected in Table 2.

There is considerable evidence about the nature of the two first steps in the reaction of bicyclic epoxides with lithium amides. For instance, in the reaction of bicyclo[2.2.1]heptane-*exo*-oxide with lithium diethylamide Crandall and co-workers[8] showed that carbene **6** or its carbenoid equivalent[9] is a key intermediate formed via **7**, the metalated epoxide ring[10] (Scheme 3a). Further evidence arises from transannular insertion experiments[11] (Scheme 3b). Thus, compound **8** affords, by reaction with LDA, alcohol **9** in 82% yield. Similar results have been obtained for others bicyclic epoxides.[3] Formation of nortricyclanone **4a** or aldol adduct **5a** was not observed in these experiments.

Very different results have been obtained in the case of monosubstituted bicyclic epoxides. Thus, McDonald and co-workers[12] showed that the chloroepoxide **10** reacted with lithium diethylamide in ether–benzene to give a 10:1 mixture of **4a**:**3a**. No traces of aldols **5b** were observed. For these authors, the major compound **4a** arises from the generation of anion **11** followed by carbene insertion in **12**, whereas the origin of **3a** should be the lithium amide induced reduction of C_2–Cl bond to give anion **13** followed by evolution to carbene **14** (Scheme 4).

With these precedents in mind, we speculated with the possibility that in the case of the epoxysulfones **1**, the



2a-c **1a-c**

a X=CH_2, Ar=C_6H_5- 85 %
b X=O, Ar=C_6H_5- 98 %
c X=NBoc, Ar=p-CH_3-C_6H_4- 93 %

Scheme 1.

Keywords: bicyclic aliphatic compounds; carbenes and carbenoids; epoxides; lithium amides.

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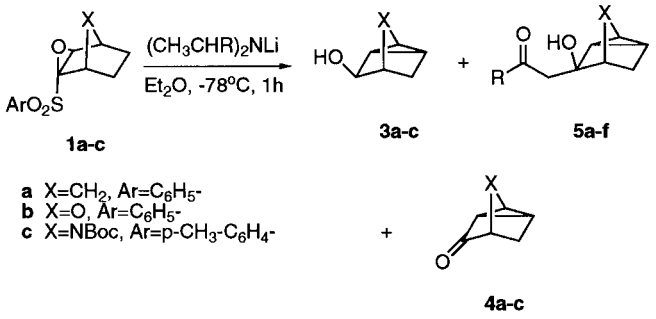


Scheme 2.

Table 1. Reaction of **1** with lithium amides

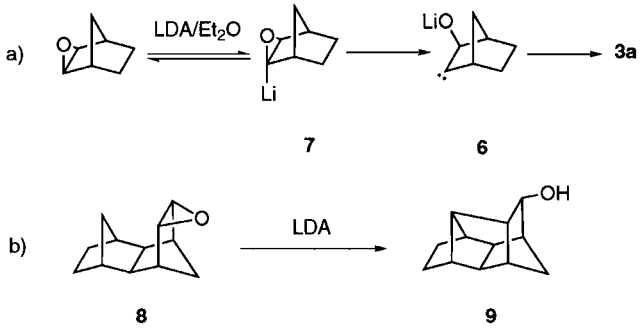
Starting material[a]	R	Compd	Yield (%)	Compd	Yield (%)	Compd	Yield (%)
1a	Me	**3a**	50–53[b]	**5a**	20–26[b]	**4a**	0[b]
1a	H	**3a**	43–50[c]	**5b**	20–25[c]	**4a**	0[c]
1b	Me	**3b**	49–55[b]	**5c**	7–8[b]	**4b**	7–11[b]
1b	H	**3b**	48–53[c]	**5d**	24–26[c]	**4b**	0[c]
1c	Me	**3c**	30–34[c]	**5e**	20–22[c]	**4c**	0[c]
1c	H	**3c**	32–37[c]	**5f**	10–16[c]	**4c**	0[c]

[a] All reactions were conducted in ether at −78°C. The ratio **1**: $(CH_3CHR)_2NLi$ was 1:5 equiv. in all cases. Concentrations of **1** were 0.1 M in ether with the exception of the 7-aza derivative **1c**, in which the concentrations used were 0.03 M due to the lower solubility of the starting material in ether.
[b] Isolated yields. The indicated yields are the average of three independent experiments.
[c] Isolated yields. The indicated yields are the average of two independent experiments.

Table 2. GLC–MS analysis of the crudes obtained from reaction of **1a** and **1b** with LDA

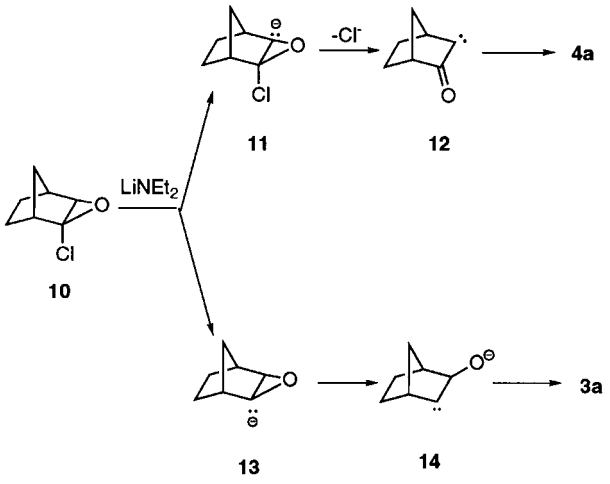
Reaction	Ratio of products (**3**:**4**:**5**)
1a+LDA	1: 0.13: 1.3[a]
1b+LDA	4.5: 1: 1.2[b,c]

[a] Ratio **3a**:**4a**:**5a**.
[b] Ratio **3b**:**4b**:**5c**.
[c] Traces of dimeric structure **19b** were also observed. See Scheme 7.



Scheme 3.

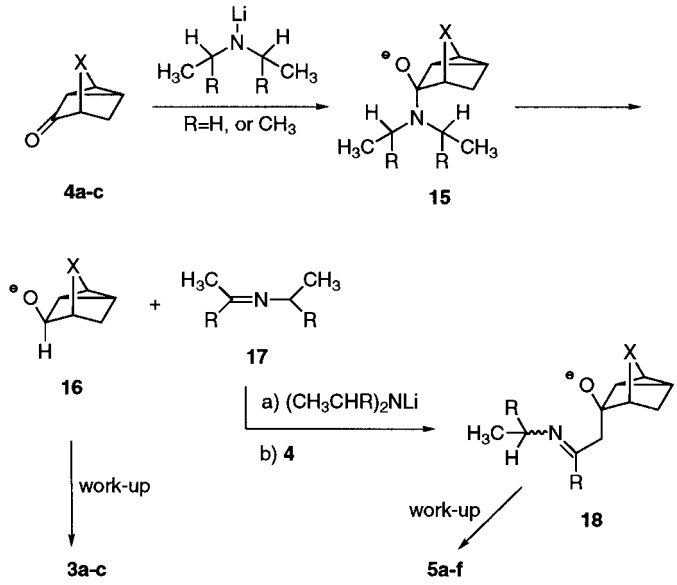
compounds **5** and, at least partially, **3** could arise from ketone **4**[13] (Scheme 5). Thus, nucleophilic addition of lithium amide to **4** gives **15** which undergoes β-hydride transfer reaction to **16** with concomitant formation of imine **17**. The iminoaldol reaction of **17** with ketone **4** promoted by lithium amide yields intermediate **18**. After



Scheme 4.

work-up, compounds **16** and **18** affords **3** and **5**, respectively.

It should be noted that LDA is known to be able to perform hydride transfer reduction of ketones,[14] although an electron transfer mechanism has also been proposed.[15] In this case, isolation of compounds **5** arising from the indicated reaction pathway seems to confirm the hydride transfer mechanism. On the other hand, it is known that the imine, resulted from hydride transfer, is deprotonated by the amide and the result anion can act as a nucleophile.[16] An alternative pathway should be the reduction of the C–S bond by the action of the lithium amide and further evolution of the epoxyanion



Scheme 5.

according to Crandall's mechanism[8a] (Scheme 3). However, although the reaction of sulfones with lithium naphthalenide has been proved to involve a desulfonylation process, the same reaction with lithium amides does not work in the same way.[17]

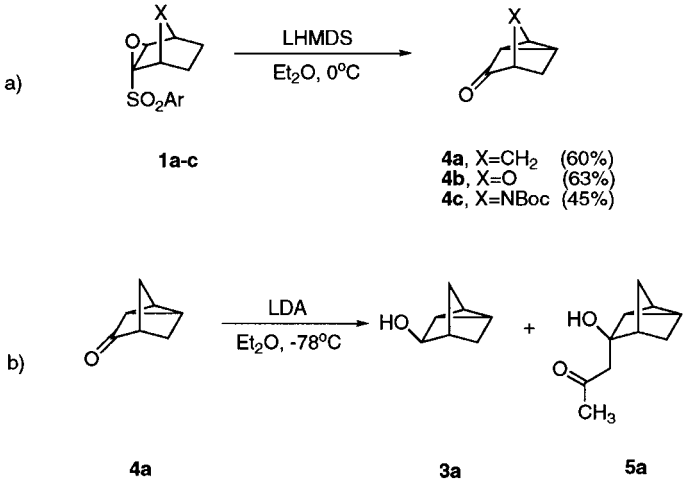
Two independent experiments gave further support for this hypothesis. Thus, reaction of epoxysulfone **1** with lithium bis(trimethylsilyl)-amide (LHMDS) afforded only the ketones **4** in moderate yields (Scheme 6a). With this base no hydride ion can be transferred to **4**. Considering that the remaining products obtained were always starting materials, we can conclude that nortricyclanols are not primary products in these processes, but products arising from the reduction of the related nortricyclanones **4**. Thus, a mechanism involving intermediates **13** and **14** (Scheme 4) can be ruled out in this case. The second experiment concerned the independent reaction of nortricyclanone **4a** with LDA under the same conditions of **1a**. In this case, products **3a** (47%) and **5a** (26%) were isolated (Scheme 6b).

The result of the reaction was also dependent on the temperature. Thus, when epoxysulfones **1** were treated with 5 equiv. of LDA in ether at −15 to 0°C, a new distribution of products was observed (Scheme 7, Table 3).

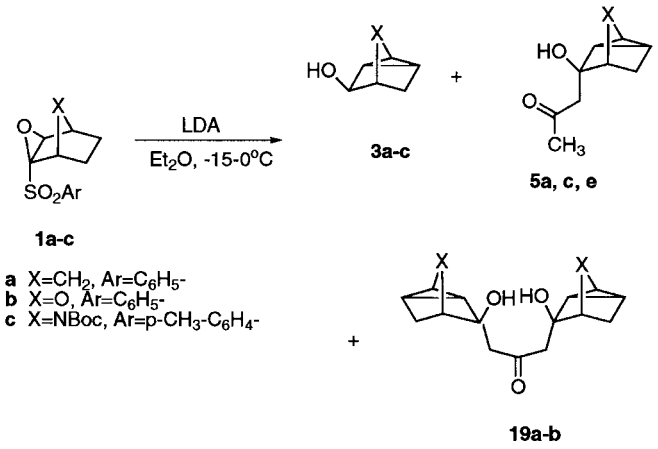
The formation of compounds **19** can be explained via an iminoaldol condensation between intermediate **18** (Scheme 5) and nortricyclanones **4** (Scheme 8).

Conclusions

The reaction of bicyclic epoxysulfones **1** with lithium amide derivatives shows a different behavior to other substituted bicyclic epoxides when treated with these reagents. From these results we can conclude that nortricyclanones **4** are the main products of the reaction being formed probably via ketocarbene intermediates. Nortricyclanones react concurrently with lithium amides via hydride transfer reduction to give the corresponding nortricyclanols. The other observed



Scheme 6.



Scheme 7.

Table 3. Reaction of epoxides **1** with LDA at −15 to 0°C. All reactions were conducted in ether at −15 to 0°C. The ratio **1**: LDA was 1:5 equiv. in all cases. Concentrations of **1** were 0.1 M in ether with the exception of the 7-aza derivative **1c**, in which the concentrations used were 0.03 M due to the lower solubility of the starting material in ether

Epoxide	Nortricyclanol (%) **3**	Aldol (%) **5**	Dimeric aldol (%) **19**
1a	23 (**3a**)	50 (**5a**)	20 (**19a**)
1b	20 (**3b**)	45 (**5c**)	8 (**19b**)
1c	11 (**3c**)	43 (**5e**)	Not observed

products arise from iminoaldol condensations of the proposed intermediates.

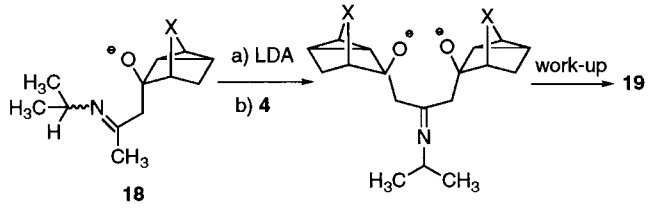
Experimental

General. Reagents and solvents were handled by using standard syringe techniques. Tetrahydrofuran and diethyl ether were distilled from sodium and benzophenone; methylene chloride, diethylamine and diisopropylamine from calcium hydride, all under argon. The remaining solvents and chemicals were commercial and used as received. All products were purified by flash chromatography using 230–400 mesh silica gel. Analytical TLC was carried out on silica gel plates. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. When peak multiplicities are reported, the following abbreviations are used: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets); dt (doublet of triplets). Chemical shifts (δ) are reported in ppm from $(CH_3)_4Si$ as internal standard and J values are given in hertz. IR spectra were recorded on a FT-IR spectrometer as thin films or KBr disks. GC–MS analyses were performed using a gas chromatograph coupled with a mass spectrometer with quadrupole filter. Elemental analyses were performed at the Universidad Complutense de Madrid.

General procedure for epoxidation of vinyl sulfones 2a–c.[7] A solution containing *t*-BuOOH (2.2 equiv.) in dry THF, was cooled at −78°C under argon. *n*-BuLi (2.2 equiv.) was added dropwise and the resulting solution was stirred at −78°C for 15 min. Then, 1 equiv. of **2** dissolved in THF was added dropwise. The reaction was warmed to rt and stirred overnight. The reaction mixture was quenched with brine, the organic layer was extracted with ether and dried over anhydrous magnesium sulfate. Evaporation of the solvent under reduced pressure followed by purification via flash chromatography eluting with an ethyl acetate:hexanes system of appropriate polarity, afforded the corresponding epoxysulfones (**1a–c**).

2-Phenylsulfonylbicyclo[2.2.1]hept-2-ene-*exo*-oxide (1a). mp: 71–72°C. IR (KBr): ν 2980, 1580, 1340, 1100 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.91 (dd, 2H, J=8.8, 1.9 Hz), 7.69–7.50 (m, 3H), 3.64 (s, 1H), 2.64 (d, 1H, J=1.5 Hz), 2.55 (d, 1H, J=1.5 Hz), 2.28 (td, 1H, J=8.9, 2.3 Hz), 1.64–1.55 (m, 2H), 1.40 (m, 1H), 1.36 (*br* s, 1H), 0.86 (dd, 1H, J=9.0, 1.2 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.7, 134.0, 129.1, 128.8, 72.5, 58.6, 38.7, 37.6, 29.9, 25.7, 23.3. Anal. Calcd for $C_{13}H_{14}O_3S$ (MW: 250): C, 62.40; H, 5.60. Found: C, 62.31; H, 5.56.

2-Phenylsulfonyl-7-oxabicyclo[2.2.1]hept-2-ene-*exo*-oxide (1b). IR (CCl_4): ν 2980, 1570, 1210, 860 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.93 (dd, 2H, J=8.4, 1.3 Hz), 7.73–7.55 (m, 3H), 4.57 (d, 1H, J=4.6 Hz), 4.50 (d, 1H, J=4.4 Hz), 3.87 (s, 1H), 2.55 (dd, 1H, J=10.2, 6.3 Hz),



Scheme 8.

1.85 (td, 1H, J=10.2, 4.6 Hz), 1.83–1.73 (m, 1H), 1.68–1.63 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 134.6, 129.4, 129.3, 128.7, 75.3, 74.9, 71.3, 57.6, 27.8, 25.0. Anal. Calcd for $C_{12}H_{12}O_4S$ (MW: 252): C, 57.14; H, 4.76. Found: C, 57.31; H, 4.63.

***N*-(*t*-Butyloxycarbonyl)-2-*p*-tolylsulfonyl-7-azabicyclo-[2.2.1]hept-2-ene-*exo*-oxide (1c).** mp: 148–149°C. IR (KBr): ν 3080, 1660, 1580, 1150 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.81 (d, 2H, J=5.5 Hz), 7.39 (d, 2H, J=5.5 Hz), 4.39 (d, 1H, J=3.3 Hz), 4.17 (d, 1H, J=2.8 Hz), 3.89 (s, 1H), 2.44 (s, 3H), 2.40–2.31 (m, 1H), 2.02–1.83 (m, 2H), 1.51 (ddd, 1H, J=7.0, 5.9, 2.8 Hz), 1.13 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.9, 129.9, 129.7, 128.6, 128.3, 80.1, 71.5, 58.4, 57.7, 27.9, 27.6, 26.8, 23.3, 21.5. Anal. Calcd for $C_{18}H_{23}O_5NS$ (MW: 365): C, 59.18; H, 6.30; N, 3.83. Found: C, 59.31; H, 6.22; N, 3.52.

General procedure for the reaction of epoxysulfones 1a–c with lithium diisopropylamide in ether[18]

Method A: at −78°C. A solution containing diisopropylamine (5 equiv.) in ether was cooled at −78°C under argon. Then, *n*-BuLi (5 equiv., 1.6 M solution in hexane) was added dropwise. After stirring for 20 min, **1a–c** (1 equiv.) dissolved in ether (see Table 1) was added under argon and the resulting yellow solution was stirred at −78°C for 1 h. The reaction was quenched with a saturated NaCl solution and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude was purified by silica gel chromatography eluting with an ethyl acetate:hexanes system of appropriate polarity to afford the title compounds shown in Table 1.

Method B: at −15 to 0°C. A solution of diisopropylamine (5 equiv.) in ether was placed in a flask previously cooled to −15°C. *n*-BuLi (5 equiv.) was injected by syringe over a period of 10 min with vigorous stirring. After 5 min, a solution of the appropriate epoxysulfone dissolved in ether (see Table 3) was added over a period of 10 min at −15°C. The flask was placed in an ice bath and the contents were stirred for 1 h. The reaction was quenched with ice water and the layers were allowed to separate. The aqueous layer was extracted with ether and the combined ether extracts were dried over $MgSO_4$ and filtered. The solvent was removed under vacuum and purification via flash-column chromatography on silica gel eluting with an ethyl acetate:hexanes system of appropriate polarity afforded the corresponding products (see Table 3).

General procedure for the reaction of epoxysulfones 1a–c with lithium diethylamide in ether

A solution containing diethylamine (5 equiv.) in ether was cooled at −78°C under argon. Then, *n*-BuLi (5 equiv., 1.6 M solution in hexane) was added dropwise. After stirring for 20 min, **1a–c** (1 equiv.) dissolved in ether (see Table 1) was added under argon and the resulting yellow solution was stirred at −78°C for 1 h. The reaction was quenched with a saturated NaCl solution and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude was purified by silica gel chromatography eluting with an ethyl acetate:hexanes system of appropriate polarity to afford the titled compounds shown in Table 1.

General procedure for the reaction of epoxysulfones 1a–c with lithium bis(trimethylsilyl)-amide (LHMDS) in ether[18]

A solution containing HMDS (5 equiv.) in ether (10 ml ether/mmol HMDS) was cooled at 0°C, *n*-BuLi (5 equiv., 1.6 M solution in hexane) was added dropwise. After stirring for 20 min, the appropriate epoxysulfone **1a–c** dissolved in ether was added and the solution was stirred at 0°C for 1 h. The reaction was quenched with a saturated NaCl solution and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude was purified by silica gel chromatography eluting with an ethyl acetate:hexanes system of appropriate polarity to afford the corresponding compounds (see Scheme 6a).

Tricyclo[2.2.1.0^{2,6}]heptan-3-ol (3a). mp: 111–112°C. IR (KBr): ν 3500–3300, 2860, 1120, 970 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.84 (s, 1H), 1.78 (d, 1H, J=10.8 Hz), 1.75 (s, 1H), 1.60 (s, 1H), 1.36 (dd, 1H, J=10.8, 1.2 Hz), 1.25–1.21 (m, 3H), 1.18 (s, 1H), 1.06 (td, 1H, J=5.1, 1.3 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 77.3, 35.7, 30.7, 29.4, 16.3, 13.7, 10.7. MS *m/z* 110 (M^+). Anal. Calcd for $C_7H_{10}O$ (MW: 110): C, 76.36; H, 9.09. Found: C, 76.41; H, 10.01.

7-Oxatricyclo[2.2.1.0^{2,6}]heptan-3-*exo*-ol (3b). IR (CCl_4): ν 3600, 2980, 1210, 1180 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.98 (t, 1H, J=4.1 Hz), 3.92 (d, 1H, J=1.9 Hz), 3.90 (dd, 1H, J=2.6, 1.9 Hz), 2.19–2.10 (m, 1H), 2.02 (dd, 1H, J=10.7, 0.7 Hz), 1.45 (t, 1H, J=4.1 Hz), 1.38 (dt, 1H, J=10.7, 1.8 Hz), 1.23 (td, 1H, J=4.1, 1.8 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 75.5, 71.8, 55.5, 29.1, 15.7, 11.8. MS *m/z* 112 (M^+). Anal. Calcd for $C_6H_8O_2$ (MW: 112): C, 64.28; H, 7.14. Found: C, 64.40; H, 7.19.

7-Oxatricyclo[2.2.1.0^{2,6}]heptan-3-one (4b). IR (CCl_4): ν 2990, 1710, 1210, 1150 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.95 (t, 1H, J=4.1 Hz), 3.93 (dd, 1H, J=2.2, 0.9 Hz), 2.27 (dd, 1H, J=10.7, 0.9 Hz), 1.48 (td, 1H, J=4.1, 1.0 Hz), 1.35 (dt, 1H, J=10.7, 2.2 Hz), 0.91 (t, 1H, J=4.1 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 216.7, 66.6, 54.9, 32.6, 29.5, 14.1. MS *m/z* 110 (M^+). Anal. Calcd for $C_6H_6O_2$ (MW: 110): C, 65.45; H, 5.45. Found: C, 65.38; H, 5.40.

(3-*exo*-Hydroxytricyclo[2.2.1.0^{2,6}]hept-3-yl)acetone (5a). IR (CCl_4): ν 3500, 1720, 1470, 1150 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.43 (s, 1H), 2.72 (d, 2H, J=2.5 Hz), 2.19 (s, 3H), 2.09 (dd, 1H, J=10.1, 1.3 Hz), 1.75 (s, 1H), 1.47 (dd, 1H, J=10.1, 1.2 Hz), 1.30 (s, 1H), 1.27–1.21 (m, 3H), 1.13 (td, 1H, J=4.7, 1.0 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 210.7, 82.0, 47.1, 38.4, 31.5, 31.4, 31.2, 19.8, 12.7, 11.8. MS *m/z* 166 (M^+). Anal. Calcd for $C_{10}H_{14}O_2$ (MW: 166): C, 72.29; H, 8.43. Found: C, 72.35; H, 8.50.

(3-*exo*-Hydroxytricyclo[2.2.1.0^{2,6}]hept-3-yl)acetaldehyde

(5b). IR (CCl_4): ν 3600, 2780, 1730, 1110 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.99 (s, 1H), 2.70 (d, 2H, J=1.8 Hz), 2.48 (d, 1H, J=2.9 Hz), 2.02 (dd, 1H, J=10.2, 1.2 Hz), 1.81 (s, 1H), 1.52 (dd, 1H, J=10.2, 1.3 Hz), 1.35 (s, 1H), 1.33–1.15 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 203.1, 82.3, 48.4, 38.8, 31.5, 31.3, 20.2, 12.1, 11.9. Anal. Calcd for $C_9H_{12}O_2$ (MW: 152): C, 71.05; H, 7.89. Found: C, 71.08; H, 7.93.

(3-*exo*-Hydroxy-7-oxatricyclo[2.2.1.0^{2,6}]hept-3-yl)acetone (5c). IR (CCl_4): ν 3500, 1710, 1470, 1150 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.83 (s, 1H), 3.75 (d, 1H, J=1.1 Hz), 2.81 (syst. AB, 2H, J_{AB}=12.2 Hz), 2.29 (d, 1H, J=7.2 Hz), 2.19 (s, 3H), 1.90 (*br* s, 1H), 1.41 (dd, 1H, J=7.2, 1.1 Hz), 1.26–1.24 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 211.4, 81.1, 74.3, 54.5, 45.5, 31.1, 30.2, 18.9, 12.8. MS *m/z* 169 (MH^+). Anal. Calcd for $C_9H_{12}O_3$ (MW: 168): C, 64.28; H, 7.14. Found: C, 64.36; H, 7.23.

(3-*exo*-Hydroxy-7-oxatricyclo[2.2.1.0^{2,6}]hept-3-yl)acetaldehyde (5d). IR (CCl_4): ν 3600–3300, 1710, 1200, 1180 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.98 (s, 1H), 3.94 (t, 1H, J=4.1 Hz), 3.79 (d, 1H, J=2.2 Hz), 2.86 (syst. AB, 2H, J_{AB}=18.0 Hz), 2.27 (d, 1H, J=10.7 Hz), 1.51 (m, 1H), 1.42 (dd, 1H, J=10.7, 2.2 Hz), 1.29–1.24 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 205.6, 74.4, 54.7, 47.0, 39.7, 30.2, 19.0, 12.9. Anal. Calcd for $C_8H_{10}O_3$ (MW: 154): C, 62.34; H, 6.49. Found: C, 62.26; H, 6.33.

(*N*-(*t*-Butyloxycarbonyl)-3-*exo*-hydroxy-7-azatricyclo-[2.2.1.0^{2,6}]hept-3-yl)acetone (5e). IR (CCl_4): ν 3500, 1730, 1650, 1200 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.91 (m, 1H), 3.81 (m, 1H), 3.54 (m, H), 2.73 (d, 1H, J=8.6 Hz), 2.42 (d, 1H, J=8.6 Hz), 2.23 (d, 1H, J=7.5 Hz), 2.19 (s, 3H), 1.99 (d, 1H, J=7.5 Hz), 1.59–1.57 (m, 2H), 1.45 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 205.6, 155.9, 80.0, 71.7, 60.9, 50.9, 45.2, 34.7, 31.3, 29.0, 28.4, 20.3. Anal. Calcd for $C_{14}H_{21}O_4N$ (MW: 267): C, 62.92; H, 7.86; N, 5.24. Found: C, 63.01; H, 7.93; N, 5.25.

(*N*-(*t*-Butyloxycarbonyl)-3-*exo*-hydroxy-7-azatricyclo-[2.2.1.0^{2,6}]hept-3-yl)acetaldehyde (5f). IR (CCl_4): ν 3300, 1730, 1640, 1380, 1180 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.53 (s, 1H), 3.85 (m, 1H), 3.75 (m, 1H), 3.48 (m, 1H), 2.67 (syst. AB, 2H, J_{AB}=11.2 Hz), 2.17 (d, 1H, J=7.0 Hz), 1.92 (d, 1H, J=7.0 Hz), 1.54–1.50 (m, 2H), 1.38 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 205.1, 156.7, 80.1, 75.2, 59.4, 48.6, 44.2, 35.1, 31.2, 28.7, 21.3. Anal. Calcd for $C_{13}H_{19}O_4N$ (MW: 253): C, 61.66; H, 7.51; N, 5.53. Found: C, 61.70; H, 7.39; N, 5.48.

1,3-bis-(3-*exo*-Hydroxytricyclo[2.2.1.0^{2,6}]hept-3-yl)acetone (19a). mp: 87–88°C. IR (KBr): ν 3600–3300, 1710, 1430, 1200 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.32 (s, 2H), 2.73 (d, 4H, J=2.6 Hz), 2.07 (d, 2H, J=10.0 Hz), 1.76 (s, 2H), 1.49 (d, 2H, J=10.0 Hz), 1.30 (d, 2H, J=1.2 Hz), 1.28–1.20 (m, 6H), 1.15 (td, 2H, J=4.6, 1.2 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 201.5, 82.4, 48.0, 38.6, 31.6, 31.3, 19.9, 12.9, 11.9. Anal. Calcd for $C_{17}H_{22}O_3$ (MW: 274): C, 74.45; H, 8.03. Found: C, 74.56; H, 7.93.

1,3-bis-(3-*exo*-Hydroxy-7-oxatricyclo[2.2.1.0^{2,6}]hept-3-yl)acetone (19b). IR (CCl_4): ν 3500–3200, 1710, 1460, 1180 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.99 (t, 2H, J=4.4 Hz), 3.95 (dd, 2H, J=4.1, 1.7 Hz), 2.58 (syst. AB, 2H, J_{AB}=15.8 Hz), 2.04 (d, 2H, J=10.2 Hz), 1.78–1.63 (m, 2H), 1.50 (t, 2H, J=4.4 Hz), 1.41 (dt, 2H, J=10.2, 1.7 Hz), 1.25–1.22 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 216.4, 75.6, 71.8, 55.6, 29.1, 15.7, 14.2, 13.0. MS *m/z* 276 (M^+-2). Anal. Calcd for $C_{15}H_{18}O_5$ (MW: 278): C, 64.75; H, 6.47. Found: C, 64.61; H, 6.30.

Reaction of nortricyclanone 4a with lithium diisopropylamide

To a solution containing 0.16 ml of diisopropylamine (1.1 mmol) in 1.5 ml of ether cooled at −78°C under argon, 0.74 ml of a 1.6 M *n*-BuLi solution in hexane (5 equiv.) was added dropwise. After stirring for 20 min, **4a** (25 mg, 0.23 mmol) dissolved in 2 ml of ether was added under argon and the resulting yellow solution was stirred at −78°C for 1 h. The reaction was quenched with a saturated NaCl solution and extracted with ether. The organic layer was dried over $MgSO_4$ and removal of the solvent under vacuum followed by silica gel chromatography (25:1, hexane:ethyl acetate) afforded 12 mg of **3a** (47%) and 10 mg of **5a** (26%).

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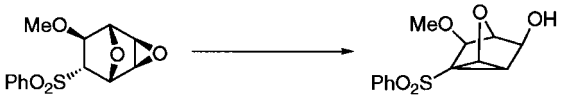
3. The reaction of bicyclic γ,δ-epoxysulfones with organolithium reagents has been previously considered. For instance, sulfone 20 (Scheme 9) reacts with *n*-BuLi (Toluene–CH_2Cl_2, −78°C, 70%) to give nortricyclanone derivative 21 (Aceña, J. L. PhD Thesis, 1996, Universidad Complutense de Madrid. Unpublished results).



20 21

Scheme 9.

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5. Vinyl sulfone **2b** was synthesized from bisulfone **22**, the Diels–Alder cycloadduct of furan and *E*-1,2-bis-phenylsulfonylethylene. Hydrogenation of the double bond in **22** using CH_3CN as solvent and further elimination of one of the phenylsulfonyl groups employing *t*-BuOK in equimolecular amount lead to **2b** in high yields (Scheme 10).

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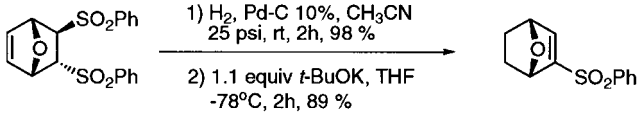

22 2b

Scheme 10.

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13. In comparative experiments with those reported by Crandall et al. (see Ref. 8a) and McDonald et al. (see Ref. 12a), we have observed that the unsubstituted bicyclo[2.2.1]hept-2-ene-*exo*-oxide reacts with LDA in the same conditions used in this work to give nortricyclanol **3a** in 88% yield. These conditions should be compared with those reported (reflux, ether–benzene, 50 h).

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