Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 2969

www.rsc.org/obc

PAPER

Reactivity of *endo*-3-bromocamphor with sulfur-centered nucleophiles by an electron transfer mechanism. Electrophilic behaviour of the 3-camphoryl radical†

Jorge G. Uranga and Ana N. Santiago*

Received 2nd December 2010, Accepted 12th January 2011
DOI: 10.1039/c0ob01108h

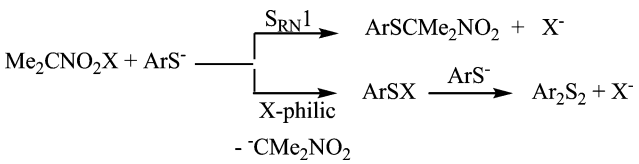
The photostimulated reaction of arylthiolate ions with *endo*-3-bromocamphor produced both reduction and substitution products. The pK_a and proton affinities of the conjugated acids were found to be good indicators of the reactivity.

Introduction

α-Halocarbonyl compounds such as *endo*-3-bromocamphor (**1**) are potential substrates for substitution by a radical nucleophilic substitution ($S_{RN}1$) mechanism[1] which involves an intermolecular electron transfer step (inter-ET). It is known that the presence of a carbonyl group in aliphatic substrates facilitates an inter-ET reaction pathway, since these π-electron acceptors decrease the energy of the LUMO of the substrate.[2] Consequently, the oxo-group may enhance the initiation steps by redox catalysis, allowing the formation of radicals. On the other hand, we have described the reactivity of 3-camphoryl radicals with diverse nucleophiles[3] and showed that those conjugated radicals can delay the coupling reactions due to their stability.[3]

Other examples involving conjugated radicals have been reported. For instance, *p*-nitro-1,1-dimethylphenacyl chloride afforded substitution products with 2-nitropropane, diethyl malonate or diethyl methylmalonate anions *via* the $S_{RN}1$ process, whereas classical substitutions were observed when PhS^- or *p*-$MeC_6H_4SO_2^-$ ions were used.[4]

On the other hand, α-substituted nitroalkanes ($XR^1R^2CNO_2$), such as 2-bromonitropropane,[5] are some of the most extensively studied in $S_{RN}1$ reactions at an sp^3 carbon.[6] Different substituents (R) have been reported, including cyclic, heterocyclic, and alkyl groups functionalized by –OH, –CN, and $–CO_2Me$, which react with a large variety of nucleophiles. In particular, with ArS^- anions these reactions could proceed by ET or X-philic[7] mechanisms (Scheme 1) depending on the nucleophile,[8] leaving group[8a] and solvent.[9] The substitution reaction is favored by weak nucleophilic ArS^- anions and the polar reaction is facilitated by strong nucleophilic ArS^- anions. Therefore, *p*-$O_2NC_6H_4S^-$ and 1,3-benzothiazol-2-yl thiolate give only the $S_{RN}1$-nitrosulfide product, while the phenyl, tolyl, and benzyl thiolate yield the disulfide redox product.[7] The X-philic mechanism has also been reported with *gem*-bromonitroalkanes and aliphatic thiolates such as *t*-BuS^-.[10]



Scheme 1

Additionally, other reports on α-keto radicals have been studied.[11] α-Keto radicals react with a double bond by an intramolecular path, giving cyclization adducts which are interesting synthetic products.[12] Further, α-keto radicals generated from α-halo ketones have an electrophilic radical-like behavior.[13] However, Markó *et al.* have reported an unexpected nucleophilic behaviour for these radicals during addition reactions with alkenes.[14] A study on the reactivity of radicals towards nucleophilic or electrophilic reactions suggests that nucleophilicity and electrophilicity are inversely related. This study has shown that *tert*-butoxycarbonylmethyl radicals (α-keto) are sometimes both weak nucleophiles and weak electrophiles (dual behavior), depending on their tendency to attack sites with relatively higher or lower electron density.[15]

The main goal of this study was to evaluate the reactivity of the 3-camphoryl radicals with sulfur-centered nucleophiles. Additionally, theoretical calculations were performed to fully understand the reactivity.

Results and discussion

The photostimulated reaction of **1** with ArS^- ions afforded substitution products together with a reduction product in good yields with DMSO as solvent (reaction 1). Thus, different ArS^- ions, such as benzenethiolate (**2**), 4-methoxybenzenethiolate (**3**),

INFIQC, Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria, Córdoba, 5000, Argentina. E-mail: santiago@fcq.unc.edu.ar; Fax: +54 351 4334170

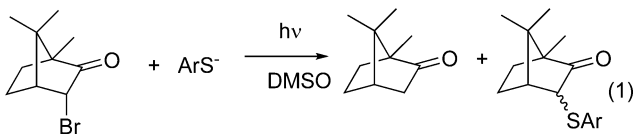
† Electronic supplementary information (ESI) available: Experimental details, characterization of products, computational procedures and cartesian coordinates. See DOI: 10.1039/c0ob01108h

Table 1 Reactions of *endo*-3-bromocamphor with arylthiolate ions, duration 270 min[a]

	ArS^- (M)	Conditions	Yield of products[b]		Ratio *endo*/*exo*[c]
1	**2** (0.5)	DMSO *hν*	**7**, 27	**8**, 61	**8**, 4.7
2	**2** (0.5)	DMSO	—	—	—
3	**3** (0.5)	DMSO *hν*	**7**, 22	**9**, 72	**9**, 4.4
4	**3** (0.5)	DMSO	—	—	—
5	**4** (0.5)	DMSO *hν*	**7**, 24	**10**, 68	**10**, 4.5
6	**4** (0.5)	DMSO	—	—	—
7	**5** (0.5)	DMSO *hν*	**7**, 28	**11**, 58	**11**, 6.2
8	**6** (0.5)	DMSO *hν*	**7**, 35	**12**, 38[d]	**12**, *endo*-isomer

[a] 0.1 M of substrate was used. [b] Yields quantified by GLC using the internal standard method. [c] Ratio measured by GLC. [d] Dicamphor was found as product with 5% yield.

4-methylbenzenethiolate (**4**), 2-naphtalenethiolate (**5**) or pyridin-2-thiolate (**6**) ions were used as nucleophiles (Table 1).

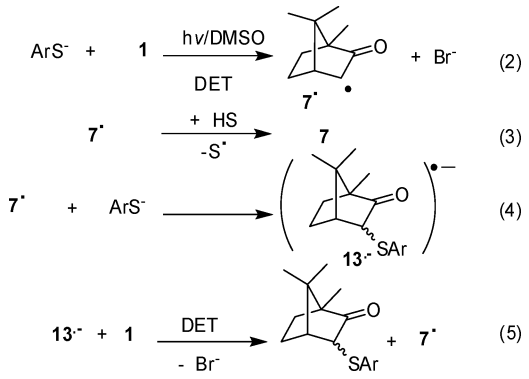


	2	**7**, 27%	**8**, 61%
1, BrCam	**3**	22%	**9**, 72 %
	4	24%	**10**, 68 %
	5	28%	**11**, 58 %
	6	35%	**12**, 38 %

When PhS^- ions were used, **1** reacted yielding both *endo*- and *exo*-3-camphorylphenylsulfide (**8**) (61% yield, *exo*/*endo* = 4.7) (Table 1, entry 1). In the dark, however, this reaction did not occur (Table 1, entry 2). The absence of reaction in the dark and the light catalysis indicate that no polar mechanism is involved. The S_N2 path is unlikely due to the steric hindrance on the camphor moiety. Furthermore, an X-philic mechanism could be excluded considering both the lack of reactivity in the dark and the reactivity order shown, which is contrary to what is expected under this process.[7] Similar results have been found when **3–6** were used as nucleophiles (Table 1, entries 3–8).

It is interesting to observe the presence of the substrate dimer (dicamphor) as well as poor yield of the substitution product during the reaction of **1** with **6** (Table 1, entry 8). These results show that the coupling reaction of 3-camphoryl radicals with **6** is slower than those corresponding to other nucleophiles studied. The formation of this dimer also confirms a radical mechanism with camphoryl radicals as intermediates.

Finally, considering that these reactions are catalyzed by light, in addition to the formation of substitution products as well as the production of dicamphor during slow coupling reactions, we propose that these reactions occur by the $S_{RN}1$ mechanism, as shown in Scheme 2. When **1** receives one electron from the nucleophile, a dissociative inter-molecular electron transfer takes place (inter-DET) and radical **7**$^\bullet$ is formed by fragmentation of the C–Br bond (Scheme 2, reaction 2). Radical **7**$^\bullet$ could either be reduced to form camphor (**7**) or afford radical anion **13**$^{\bullet-}$ by reaction with the nucleophile (Scheme 2, reactions 3 and 4). This radical anion intermediate finally affords the substitution products in addition to a new radical **7**$^\bullet$ (Scheme 2, reaction 5), which can continue the propagation steps in the chain reaction. The formation of the reduction product **7** also indicates that the

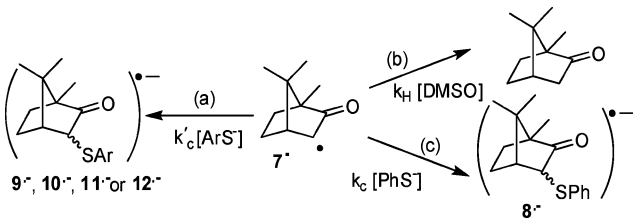


Scheme 2

coupling reaction of **7**$^\bullet$ with sulfur-centered nucleophiles is not efficient, probably due to the stability of this radical.

Considering that the proposed $S_{RN}1$ mechanism includes several steps, namely initiation, propagation and termination, it was interesting to evaluate the relative reactivity of ArS^- toward **7**$^\bullet$ in competitive experiments.[16] In these competitive reactions, the ratio of products depends on the relative rate of the coupling between them. Thus, we selected **2** as a reference to evaluate the relative reactivity in separate competitive reactions.

Three competitive reaction pathways can occur from the intermediate 3-camphoryl radicals, outlined in Scheme 3: (a) coupling with anions **3**, **4**, **5**, or **6** to yield the substitution product (**9**, **10**, **11** or **12**) after electron transfer; (b) hydrogen abstraction from the solvent (DMSO) to afford reduction product **7**; (c) coupling with **2** to give substitution product **8** by electron transfer.



Scheme 3

Thus, by determining the products distribution in the competing reactions we were able to calculate the relative reactivity using eqn (1).

$$\frac{k'_c}{k_c} = \frac{[\mathrm{ArSCam}]_t\ [\mathrm{PhS}^-]_0}{[\mathrm{PhSCam}]_t\ [\mathrm{ArS}^-]_0} \quad (1)$$

In eqn (1), $[PhS^-]_0$ and $[ArS^-]_0$ are the initial concentrations of both nucleophiles, while $[PhSCam]_t$ and $[ArSCam]_t$ are the concentrations of the substitution products at time t.[17]

As evaluated from the competitive experiments (Table 2), the relative reactivity, established for the coupling reaction of different anions with 3-camphoryl radicals, is **3** > **4** > **2** > **5** > **6**. Table 2 also shows that the ratios between substitution and reduction products are close to 3 in all cases.

To further understand our current experimental results, we carried out theoretical calculations by employing the B3LYP functional at the 6-31+G* level and LANL2DZ (for sulfur atoms), as implemented in Gaussian 03.[18] First, geometries were optimized for anions **2–6**. Subsequently, Mulliken population analyses were

Table 2 Competition experiments of different anions with **1** under irradiation for 270 min in DMSO

Expt	Nucleophiles, M		**1**, M	Yield of Products[a]		$k'_c/k_{cl} \pm 0.1$ (average)	$k'_c + k_c/k_H$
1	**2**, 0.5	**3**, 0.50	0.10	**8**, 16	**9**, 59	3.69	3.10
2	**2**, 0.5	**4**, 0.50	0.10	**8**, 23	**10**, 45	1.95	2.97
3	**2**, 0.5	**5**, 0.50	0.10	**8**, 35	**11**, 31	0.89	2.95
4	**2**, 0.5	**6**, 1.00	0.10	**8**, 52	**12**, 12	0.11	2.64

[a] From duplicated experiments: average error ≤10%. The product yields were quantified by GLC using the internal standard method.

achieved to obtain the charge density on the sulfur atom (Fig. 1). The calculated charge density on the sulfur could indicate the reactivity these anions may have toward **7**$^{\bullet}$. If radical **7**$^{\bullet}$ reacts with high-charge density species, these theoretical results predict the following reactivity order: **3** > **4** > **2** > **5** > **6** (Fig. 1), in full agreement with the experimental trend observed during this work. This reactivity order clearly indicates that, under the conditions studied, this α-keto radical shows an electrophilic behavior and is more likely to attack electron-rich sites.

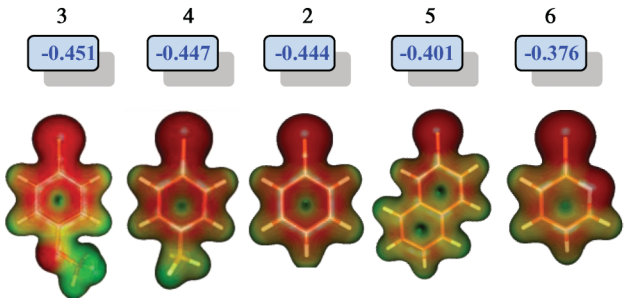


Fig. 1 The charge density on sulfur calculated using the B3LYP functional for anions **2**–**6**.

Moreover, one could employ experimental pK_a values for the conjugated acids to predict the relative reactivity of the corresponding nucleophiles. Bordwell and Hughes used this approach to determine the nucleophilicity order by using S_N2 reactions[19] and electron donor capacity by using ET reactions.[20] The rationale is that the lower the pK_a value for the conjugated acid, the higher the stability of its conjugated base, and consequently, the lower reactivity during the coupling reaction. The pK_a values for the conjugated acids of the nucleophiles studied in this work are listed in Table 3. To the extent of our knowledge, there are no published reports on pK_a values for arenethiols **5** and **6**, however, the trend observed for the rest of the nucleophiles is in agreement with experiments. Furthermore, the pK_a of the nucleophile's phenolic analogues in DMSO has been reported, which are also included in Table 3. The trend in pK_a values is in excellent agreement with the experimental results reported here, assuming that the trend in the pK_a values in the phenolic analogs mirrors the sulfur series used in this work. Therefore, it seems that the acidity of the anion's conjugated acid is a good indicator of its reactivity in this type of reaction.

Considering frontier orbitals, the most important interaction in this coupling reaction is found between the HOMO of the nucleophile and the SOMO of the substitution product. It has been shown that the $\Delta E\pi$ (HOMO–SOMO) predicts the reactivity of aromatic[21] and vinyl[22] radicals with enolate ions. On the contrary, the aryl thiolates studied have significantly different charge distribution making them unsuitable to compare their HOMOs energy without considering the solvent effect owing to their different solvation. Additionally, small energetic changes, associated with the substitution product's electronic properties (SOMO) do not determine the reactivity.[23] So far, previously presented arguments preclude the use of the frontier orbitals theory to predict the reactivity in these systems.

Table 3 pK_a values in DMSO from the literature and proton affinities calculated for arenethiolate compounds

Compound		**3**	**4**	**2**	**5**	**6**
pK_a	X═S	11.35[a]	10.82[a]	10.28[a]	—	—
	X═O	19.1[b]	18.9[b]	18[b]	17.2[c]	15.7[c]
PA[d] kcal mol^{-1} = ArS^- + $H_3O^+ \rightarrow ArSH + H_2O$		−43.99	−43.75	−43.29	−42.92	−41.71

[a] Ref. 28. [b] Ref. 29. [c] http://www.chem.wisc.edu/areas/reich/pKatable/. [d] Calculated with B3LYP/6-31+G* employing the model IEFPCM and acetonitrile as polar solvent, all values are zero point corrected at 6-31+G* level.

A more representative theoretical measure, representing the reagents' stability, could be their proton affinities (PA). Therefore we calculated the PA corresponding to the different anions, including consideration of the solvent (Table 3). As can be seen, the pK_a and the estimated PA values of the conjugated acids follow the same trend and are good indicators of the reactivity, since both can reasonably predict experimental results. Finally, in the studied system the coupling reactions depend on the stability of reagents rather than the stability of the radical anions of the substitution product.

Conclusions

In conclusion, we report the reactivity and theoretical calculations of *endo*-3-bromocamphor (**1**) with sulfur-centered nucleophiles by the $S_{RN}1$ mechanism. Under these conditions, **1** afforded good yields of both substitution and reduction products using DMSO as solvent. The experimentally determined relative reactivity of the nucleophiles, with respect to 3-camphoryl radicals, was **3** > **4** > **2** > **5** > **6**. Theoretical calculations of the charge density, in addition to pK_a and PA values of the conjugated acid involved, allowed a detailed understanding of the experimental reactivity observed. It is interesting to note that the pK_a and PA values of the conjugated acids are good indicators of the anions' reactivity. Additionally, these results predict the electrophilic behavior for α-keto radicals, in contrast with reactions observed with alkenes.[5] They are also

relevant to understand the behavior of conjugated radicals toward the $S_{RN}1$ reaction mechanism.

To the extent of our knowledge, this is the first study on the behavior of α-keto radicals toward nucleophiles.

Experimental

General methods

Irradiation was conducted in a reactor equipped with two 400-W UV lamps emitting maximally at 350 nm (Philips Model HPT, water-refrigerated). ^{1}H and ^{13}C-NMR spectra were recorded on a High Resolution Spectrometer Avance 400 (working frequency 400 MHz and 100 MHz, respectively), at ambient temperature in $CDCl_3$ (Aldrich).

Materials

endo-3-bromocamphor, ArSH (**2**, **3**, **4**, **5** and **6**) and potassium *t*-butoxide were commercially available and used as received. DMSO was distilled under vacuum and stored under molecular sieves (4 Å).

Photostimulated reactions of *endo*-3-bromocamphor with ArS^- ions in DMSO

The following procedure is representative. To 5 mL of dry and degassed DMSO under nitrogen *t*-BuOK (5.1 mmol), and PhSH (5 mmol) were added. After 15 min, *endo*-3-bromocamphor (1.0 mmol) was added and the reaction mixture was irradiated. The reaction was quenched with an excess of methyl iodide. The residue was dissolved with water and extracted with diethyl ether. Finally, HNO_3 was added to the aqueous phase up to pH = 5–6. The aqueous phase was then extracted with diethyl ether. The products were isolated by column chromatography. In similar experiments the products were quantified by GC using the internal standard method.

Competition experiments

The experiments were carried out in 5 mL of dry and degassed DMSO under nitrogen adding 2.5 mmol of ArSH, 2.5 mmol of PhSH and *t*-BuOK (5.1 mmol). After 15 min, *endo*-3-bromocamphor (1.0 mmol) was added and the reaction mixture was irradiated. The reaction was quenched with an excess of methyl iodide and the work-up for individual nucleophiles was similar to the above mentioned. The reactivity ratio was performed in duplicate.

Reactions in the dark

The procedure was similar to that of the previous reaction, except that the reaction flask was wrapped with aluminium foil prior to substrate addition.

Isolation and characterization

1,7,7-trimethyl-3-(phenylthio)bicyclo[2.2.1]heptan-2-one (8). The ether layer was dried over $MgSO_4$ and evaporated under reduced pressure to afford a colourless oil. The desired product was purified by column chromatography employing ethylic ether : petroleum ether (2 : 98).

***exo*-8** GC/MS (EI$^+$) *m*/*z* (%): 260.15 (M$^+$) (34.6); 232 (4.64); 149 (100); 123.2 (35.18); 116.15 (16.14); 83.1 (8.24); 81.1 (11.64). ***endo*-8** GC/MS (EI+) *m*/*z* (%): 260 (44), 232 (6), 150 (11), 149 (100), 147 (11), 134 (5), 123 (37), 116 (16), 115 (10), 109 (6), 81 (12), 65 (6), 55 (12).

***endo*-8** ^{1}H-NMR: δ: 0.92 (s, 3H), 0,96 (s, 3H), 1.03 (s, 3H), 1.73 (m, 3H), 2.03 (m, 1H), 2.28 (m, 1H), 3.92 (d, 1H), 7.33–7.17 (m, 3H), 7.43–7.56 (m, 2H). ^{13}C-NMR δ: 9.70, 19.39, 19.71, 21.47, 30.82, 46.03, 48.7, 56.69, 58.6, 126.9, 129.01 (2C), 130.93 (2C), 135.73, 215.91. ***exo*-8** ^{1}H-NMR δ: 0.96 (s, 3H), 0.98 (s, 3H), 1.02 (s, 3H), 1.71 (m, 3H), 2.02 (m, 1H), 2.28 (m, 1H), 3.33 (d, 1H), 7.17–7.33 (m, 3H), 7.43–7,56 (m, 2H). ^{13}C-NMR δ: 9.57, 19.4, 19.83, 21.51, 30.91, 46.74, 51.32, 57.70, 58.11, 126.59, 129.02 (2C), 130.10 (2C), 135.84, 216.90. HRMS: (MH+) exact mass calcd for $C_{16}H_{20}OS$ 261.1313 found: 261.1308.

3-(4-methoxyphenylthio)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (9). The ether layer was dried over $MgSO_4$ and evaporated under reduced pressure to afford a colourless oil. The desired product was purified by column chromatography employing ethylic ether : petroleum ether (5 : 95).

***endo*-9** GC/MS (EI+) *m*/*z* (%): 292 (4), 291 (13), 290 (55), 180 (13), 179 (100), 177 (8), 147 (9), 146 (41), 139 (11), 123 (17), 81 (11), 55 (13). ***exo*-9** GC/MS (EI$^+$) *m*/*z* (%): 292 (4), 291 (11), 290 (51), 180 (12), 179 (100), 177 (7), 147 (9), 146 (41), 139 (11), 123 (19), 81 (12), 55 (13).

***endo*-9** ^{1}H-NMR δ: 0.86 (s, 3H), 0.94 (s, 3H), 1.00 (s, 3H), 1.40–1.51 (m, 1H), 1.60–1.86 (m, 2H), 1.99–2.11 (m, 1H), 2.19 (t, J = 1.3, 1H), 3.76 (dd, J_1 = 1.8, J_2 = 4.6 1H), 3.79 (s, 3H), 6.81–6.87 (m, 2H), 7.47–7.53 (m, 2H). ^{13}C-NMR δ: 9.69, 19.38, 19.63, 21.26, 30.77, 45.93, 48.52, 55.34, 58.25, 58.66, 114.59 (2C), 125.6, 134.58 (2C), 159.46, 216.14. ***exo*-9** ^{1}H δ: 0.95 (s, 3H), 0.96 (s, 3H), 1.01 (s, 3H), 1.35–1.53 (m, 1H), 1.58–1.88 (m, 2H), 1.97–2.08 (m, 1H), 2.26 (d, J = 4.3, 1H), 3.16 (s, 1H), 3.80 (s, 3H), 6.81–6.87 (m, 2H), 7.47–7.53 (m, 2H). ^{13}C δ: 9.57, 19.85, 21.59, 28.62, 29.08, 46.69, 51.19, 55.34, 58.66, 59.60, 114.59 (2C), 127.87, 133.96 (2C), 159.28, 217.32. HRMS: (MH+) exact mass calcd. for $C_{17}H_{22}O_2S$ 291.1419 found: 291.1418.

1,7,7-trimethyl-3-(4-methylphenylthio)bicyclo[2.2.1]heptan-2-one (10). The ether layer was dried over $MgSO_4$ and evaporated under reduced pressure to afford a colourless oil. The desired product was purified by column chromatography employing ethylic ether : petroleum ether (2 : 98).

***endo*-10** ^{1}H-NMR δ: 0.896 (s, 3H), 0.96 (s, 3H), 1.03 (s, 3H), 1.40–1.51 (m, 2H), 1.64–1.88 (m, 2H), 2.01–2.11 (m, 1H), 2.24 (t, J = 4.32, 1H), 2.33(s, 3H), 3.84 (dd, J = 1.94, J = 4.4, 1H), 7.1–7.14 (m, 2H), 7.42–7.46 (m, 2H). ^{13}C-NMR: δ 9.69, 19.39, 19.65, 21,1, 21.41, 30.80, 45.97, 48.60, 57.37, 58.64, 129.76 (2C), 131.76 (2C), 133.09, 137.17, 216.01. ***exo*-10** ^{1}H δ: 0.96 (s, 3H), 0.97 (s, 3H), 1.01 (s, 3H), 1.39–1.55 (m, 1H), 1.58–1.84 (m, 2H), 1.97–2.10 (m, 1H), 2.28 (d, J = 4.24, 1H), 2.33 (s, 3H), 2.42 (s,1H), 3.27 (s, 1H), 7.09–7.14 (m, 2H). 7.39–7.43 (m, 2H). ^{13}C δ: 9.57, 19.85, 21.04, 21.54, 28.71, 29.1, 46.7, 51.26, 58.06, 58.54, 130.96 (2C), 131.83 (2C), 133.89

136.86, 217.07. HRMS: (MH+) exact mass calcd. for $C_{17}H_{23}OS$ 275.1464 found 275.1468.

1,7,7-trimethyl-3-(naphthalen-2-ylthio)bicyclo[2.2.1]heptan-2-one (11). The ether layer was dried over $MgSO_4$ and evaporated under reduced pressure to afford a colourless oil. The desired product was purified by column chromatography employing ethylic ether : petroleum ether (5 : 95).

***endo*-11** GC/MS (EI^+) *m/z* (%): 312(4), 311 (14), 310 (58), 200(15), 199(100), 197(8), 166(40), 165(24), 123(18), 115(21), 81(9), 55(12). ***exo*-11** GC/MS (EI^+) *m/z* (%): 312 (4), 311 (13), 310 (55), 200 (14), 199 (100), 197 (8), 166 (39), 165 (25), 123 (19), 115 (21), 81 (11), 55 (12).

***endo*-11** ^{1}H-NMR δ: 0.94 (s, 3H), 0.98 (s, 3H), 1.04 (s, 3H), 1.40–1.51 (m, 2H), 1.79–1.89 (m, 1H), 2.05–2.15 (m, 1H), 2.31 (t, J = 4.3, 1H), 4.04 (dd, J = 1.6, J = 4.6, 1H), 7.47 (ddd, J_1 = 14, J_2 = 4.8, J_3 = 1.6, 2H), 7.59 (dd, J_1 = 8.8, J_2 = 1.6, 1H), 7.75–7.82 (m, 3H), 7.98 (d, J = 1.2, 1H). ^{13}C-NMR: δ 9.71, 19.40, 19.73, 21.52, 30.86, 46.10, 48.66, 56.84, 58.70, 126.07, 126.57, 127.38, 127.70, 128.54, 128.74, 129.53, 132.19, 133.02, 133.68, 215.99. ***exo*-11** ^{1}H δ: 0.92 (s, 3H), 1.01 (s, 3H), 1.06 (s, 3H), 1.67–1.78 (m, 2H), 1.79–1.89 (m, 1H), 2.01–2.15 (m, 1H), 2.35 (d, J = 4.1, 1H), 3. 64 (s, 1H), 7.42–7.52 (m, 2H), 7.56–7–62 (m, 1H), 7.73–7.86 (m, 3H), 7.92 (d, J = 1.2, 1H). ^{13}C δ: 9.69, 19.40, 19.86, 21.60, 23.00, 23.74, 28.93, 51.26, 57.85, 126.07, 126.57, 127.36, 128.21, 128.40, 128.81, 129.60, 132.03, 132.54, 133.69, 217.49. HRMS: (MH+) exact mass calcd for $C_{20}H_{22}OS$ 311.1469 found: 311.1470.

***endo*-1,7,7-trimethyl-3-(2-piridynthio)bicyclo[2.2.1]heptan-2-one (12).** The ether layer was dried over $MgSO_4$ and evaporated under reduced pressure to afford a colourless oil. The desired product was purified by column chromatography employing ethylic ether : petroleum ether (20 : 80).

GC/MS (EI+) *m/z* (%): 262 (16), 261 (98), 233 (47), 228 (13), 219 (14), 218 (100), 201 (21), 200 (35), 190 (32), 186 (21), 162 (17), 158 (16), 152 (32), 151 (45), 150 (90), 136 (29), 123 (19), 117 (19), 112 (64), 111 (63), 107 (22), 95 (19), 93 (19), 91 (20), 82 (22), 81 (23), 79 (34), 78 (42).

^{1}H-NMR δ: 0.98 (s, 3H), 1.05 (s, 3H), 1.07 (s, 3H), 1.36–1.47 (m, 1H), 1.70–1.79 (m, 1H), 1.79–1.97 (m, 2H), 2.39 (t, 1H), 5.04 (d, 1H), 6.99 (ddd, J_1 = 7, J_2 = 5, J_3 = 0.8, 1H), 7.24 (dd, J_1 = 8, J_2 = 0.8, 1H), 7.47 (ddd, J_1 = 8, J_2 = 7, J_3 = 1, 1H), 8.38 (dd, J_1 = 5, J_2 = 1, 1H) ^{13}C-NMR δ: 9.71, 19.45, 19.84, 22.36, 31.04, 46.26, 48.59, 51.59, 52.16, 58.74, 119.87, 122.48, 136.03, 149.33, 157.57, 216.41. HRMS: (MH+) exact mass calcd. for $C_{15}H_{19}NOS$ 262.1266 found 262.1267.

Dicamphor. Isolated by column chromatography in the reaction involving nucleophile **6** and identified by comparison with the literature.[24]

Computational procedures

These calculations were performed with Gaussian 03.[25] The characterization of stationary points was performed by Hessian matrix calculations. The exploration of the potential surface was carried out within the functional B3LYP[26] at 6-31+G* level and LANL2DZ for sulfur atoms. The charge distribution was obtained by Mulliken Population Analysis from the anion optimized structures. The themochemical study was carried out with full optimization using acetonitrile solvent according to the polarized continuum model IEFPCM.[27]

Acknowledgements

This work was supported in part by Córdoba Ciencia (ACC), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), SECYT, Universidad Nac. de Córdoba and Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT).

Notes and references

1 R. A. Rossi, A. B. Pierini and A. B. Peñéñory, *Chem. Rev.*, 2003, **103**, 71.
2 (*a*) A. N. Santiago, D. G. Morris and R. A. Rossi, *J. Chem. Soc., Chem. Commun.*, 1988, 220; (*b*) A. N. Santiago, S. V. Iyer, W. Adcock and R. A. Rossi, *J. Org. Chem.*, 1988, **53**, 3016; (*c*) A. E. Lukach, D. G. Morris, A. N. Santiago and R. A. Rossi, *J. Org. Chem.*, 1995, **60**, 1000; (*d*) A. N. Santiago, K. Takeuchi, Y. Ohga, M. Nishida and R. A. Rossi, *J. Org. Chem.*, 1991, **56**, 1581.
3 J. G. Uranga and A. N. Santiago, *New J. Chem.*, 2010, **34**, 2006.
4 (*a*) G. A. Russell and F. Ros, *J. Am. Chem. Soc.*, 1982, **104**, 7349; (*b*) G. A. Russell and F. Ros, *J. Am. Chem. Soc.*, 1985, **107**, 2506.
5 G. A. Russell and W. C. Danen, *J. Am. Chem. Soc.*, 1966, **88**, 5663.
6 W. R. Bowman, *Chem. Soc. Rev.*, 1988, **17**, 283.
7 N. S. Zefirov and D. I. Markhonkov, *Chem. Rev.*, 1982, **82**, 615.
8 (*a*) W. R. Bowman and G. D. Richardson, *Tetrahedron Lett.*, 1981, **22**, 1551; (*b*) W. R. Bowman and G. D. Richardson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1407.
9 I. Suleiman, S. I. Al-Khalil and W. R. Bowman, *Tetrahedron Lett.*, 1984, **25**, 461.
10 A. A. Madjdabadi, R. Beugelmans and A. Lechevallier, *Tetrahedron Lett.*, 1987, **28**, 4525.
11 J. Iqbal, B. Bathia and N. K. Nayyar, *Chem. Rev.*, 1994, **94**, 519.
12 (*a*) C.-K. Sha, F.-K. Lee and C.-J. Chang, *J. Am. Chem. Soc.*, 1999, **121**, 9875; (*b*) C.-K. Sha, H.-W. Liao, P.-C. Cheng and S.-C. Yen, *J. Org. Chem.*, 2003, **68**, 8704.
13 M. B. Smith and J. March, *March's Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, Wiley & Sons, Inc., 6ta ed. 2007.
14 C. De Dobbeleer, J. Pospíil, F. De Vleeschouwer, F. De Proft and I. E. Markó, *Chem. Commun.*, 2009, 2142.
15 F. Vleeschouwer, V. Speybroeck, M. Waroquier and F. De Proft, *Org. Lett.*, 2007, **9**, 2721.
16 J. F. Bunnett, In *Investigation of Rates and Mechanisms of Reactions*, 3rd ed., E. S. Lewis, Ed., Wiley, New York, 1974, part 1, p 159.
17 The equations suppose first order reactions and constant concentrations during the reactions.
18 See ESI† for more details.
19 F. Bordwell and D. L. Hughes, *J. Org. Chem.*, 1980, **45**, 3314.
20 (*a*) F. G. Bordwell and X. Zhang, *Acc. Chem. Res.*, 1993, **26**, 510; (*b*) F. G. Bordwell, X. Zhang and R. Filler, *J. Org. Chem.*, 1993, **58**, 6067.
21 (*a*) G. L. Borosky, A. B. Pierini and R. A. Rossi, *J. Org. Chem.*, 1992, **57**, 247; (*b*) M. T. Baumgartner, A. B. Pierini and R. A. Rossi, *J. Org. Chem.*, 1993, **58**, 2593.
22 C. Galli, P. Gentili and Z. Rappoport, *J. Org. Chem.*, 1994, **59**, 6786.
23 See ESI† for more details.
24 S. E. Boiadjiev and D. A. Lightner, *Collect. Czech. Chem. Commun.*, 2000, **65**, 477.
25 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz,

I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, *GAUSSIAN 03 (Revision B.02)*, Gaussian, Inc., Wallingford, CT, 2004.
26 (*a*) C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785; (*b*) A. D. Becke, *Phys. Rev. A: At., Mol., Opt. Phys.*, 1988, **38**, 3098; (*c*) E. Miehlich, A. Savin, H. Stoll and H. Preuss, *Chem. Phys. Lett.*, 1989, **157**, 200.
27 (*a*) D. M. Chipman, *J. Chem. Phys.*, 2000, **112**, 5558; (*b*) M. T. Cances, B. Mennucci and J. Tomasi, *J. Chem. Phys.*, 1997, **107**, 3032.
28 F. Bordwell and D. L. Hughes, *J. Org. Chem.*, 1982, **47**, 3324.
29 F. Bordwell and D. L. Hughes, *J. Org. Chem.*, 1984, **49**, 1424.

