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STEREOSELECTIVE SYNTHESIS OF SOME *CIS* 2,3-DISUBSTITUTED CYCLANONES

RING SIZE INFLUENCE ON THE STEREOSELECTIVITY OF 2-SUBSTITUTED ENDOCYCLIC ENOLATES PROTONATION†

E. HATZIGRIGORIOU, L. WARTSKI* and J. SEYDEN-PENNE*
Laboratoire des Réactions Sélectives sur Supports, ERA 316 du CNRS Université Paris Sud, Bâtiment 410, 91405 Orsay Cedex, France

and

E. TOROMANOFF
ROUSSEL-UCLAF, Division Scientifique, B.P. No. 9, 93230 Romainville, France

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Abstract—Conjugate addition of carbanionic reagents formed from aryl- or phenyl-thioacetonitriles **1a–c** and **2** to 2-methyl and 2-phenyl 2-cyclohexenone or 2-methyl 2-cyclopentenone, followed by acidic quench, under kinetic control, leads to different ratios of *cis* and *trans* 2,3-disubstituted cyclanones according to ring size. From 2-methyl and 2-phenyl 2-cyclohexenone, the *cis* isomer is highly predominant (85 to 98%). From 2-methyl 2-cyclopentenone a *cis/trans* mixture is obtained: the *cis* isomer only predominates when a bulky reagent (**1c**) is used (80%); in the other cases a mixture of nearly 1:1 is obtained.

The stereochemistry of enolates protonation in acyclic series[1a] of 2-substituted enolates[1b] is well-documented. Contrarily in carbocyclic series there are only a few results in the literature[2–7] on the stereochemistry of the protonation of 2,3-disubstituted endocyclic enolates. Recently and simultaneously, Luchetti and Krief[2] and our group[3] have observed that by conjugate addition of lithiated carbanions to 2-methyl 2-cyclohexenone, followed by protonation, *cis* 2,3-disubstituted cyclohexanones were obtained with a high stereoselectivity. In the 6-membered ring series, Shea and Wada[4a] also observed a highly stereoselective protonation of a 2-methyl substituted enolate. Takano *et al.*[5] obtained stereoselectively disubstituted 5-membered ring lactones by protonation of the corresponding 2-substituted enolates. From all the work on conjugate addition to 2-substituted 2-cyclopentenones, mainly in the prostaglandin field,[6] the nearly exclusive obtention of *trans* 2,3-disubstituted cyclopentanones suffers only a few exceptions,[7] but the problem of kinetic control of protonation has only been raised in one case.[7b]

It therefore seemed interesting to test the extent of generality of our previous observations in order to delineate the influence of (a) ring size, (b) carbanionic reagent structure and (c) nature of the proton donor on the stereoselectivity of 2-methyl 3-substituted endocyclic enolates protonation in the cyclohexyl and cyclopentyl series.

Furthermore the reaction is extended to the 2-phenyl cyclohexenone. The carbanionic reagents were lithiated arylacetonitriles **1** according to their electronic distribution (**1a, b**) selected as benzoyl equivalents[8,9] and bulk (**1c**) and phenylthioacetonitrile **2** as the

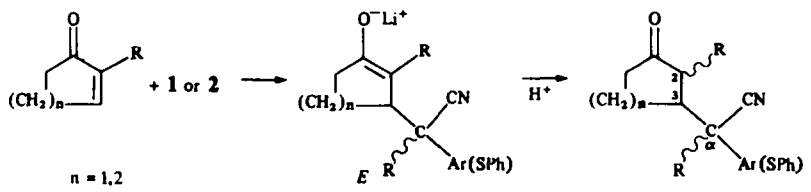
$[ArCHCN]^-Li^+$ $[C_6H_5C(CH_3)CN]^-Li^+$ $[C_6H_5SCHCN]^-Li^+$

1a Ar = $pCH_3OC_6H_4$ **1c** **2**
1b Ar = C_6H_5

precursor of acetonitrile.[10] As proton donors, we have chosen HCl, NH_4Cl, oxygen (acetic acid, methanol, phenol) or carbon (dimethylmalonate) acids.

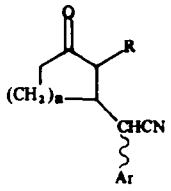
RESULTS

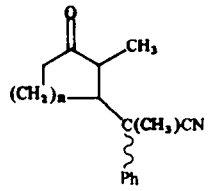
The following is the reaction scheme

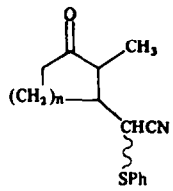


† A part of this paper has been communicated as a poster at the EUCHEM Conference, Louvain la Neuve, July 1982 and is taken from the Thèse de 3ème Cycle of E. Hatzigrigoriou, Orsay, June 1983.

The two expected *cis* diastereoisomers are







3c n = 1, Ar = C_6H_5 R = Me
4c n = 1, Ar = $pCH_3OC_6H_4$ R = Me
9c n = 2 R = Ar = C_6H_5

5c n = 2
6c n = 1

7c n = 2
8c n = 1

Their identification relies upon IR, ^{1}H-NMR and mass spectroscopy. The *cis* stereochemistry has been established by ^{1}H-NMR (250 or 400 MHz) using spin–spin decoupling as described in previous work[11] or by *cis–trans* equilibration of the reaction products. Moreover, the related *trans* diastereoisomers **3–6t**, obtained by conjugate addition of **1a–c** to 2-cyclopentenone or cyclohexenone followed by CH_3I trapping,[11] have also been characterised. In the case of compound **9c** the stereochemistry has been easily established after deuteriation in position 2 and comparison with **9t** obtained after equilibration.

The reactions were run in pure THF or in THF–4 molar equiv. HMPA at low temperature. Quenching of the reaction has been performed in two ways

Method A: Low temperature quench immediately followed by diethylether extraction.
Method B: Raising the reaction mixture temperature to room temperature before quenching and extraction.

From the results in Tables 1 and 2, it appears that in the 6-membered ring series, the highly stereoselective formation of the *cis* 2,3-disubstituted cyclanone is quite general. In the 5-membered ring system, a different behaviour is observed as, according to the reagent and the reaction conditions, various mixtures of *cis* and *trans* isomers or only *trans* isomers are formed. In nearly all cases, mixtures of diastereoisomers on C_α are obtained except in experiments 2, 3, 4 and 6 of Table 2 which lead to mixtures of one *cis* isomer and one *trans* isomer. The interpretation of these results necessitates further experiments to determine whether these reactions are under kinetic or thermodynamic control.

(a) *6-Membered ring*

The acidic equilibration of the *cis* compounds leads to the following mixtures, from **5c**: **5c**/**5t**: 40:60; from **7c** and **9c**: only *trans* isomers **7t** and **9t** were observed. Therefore reactions 1–5 of Table 1 are under kinetic control, as highly-predominant *cis* compounds are obtained. However partial equilibration probably takes place in one case (see footnote *a* of Table 1).

(b) *5-Membered ring*

The various *cis*/*trans* mixtures were equilibrated under acidic or basic conditions. In all cases, only the *trans* derivatives **3t**, **4t**, **6t** and **8t** were obtained. From **6** the equilibration is very fast, as it takes place in $CDCl_3$ at room temp in the NMR conditions.

Therefore, in all the experiments which lead to *cis*/*trans* mixtures, we had to check that no partial equilibration could occur, more particularly from **3c**, **4c** and **8c** which bear an acidic proton α to the CN group.

We have verified that **3** and **6** known *cis*/*trans* mixtures are recovered unchanged when treated by HCl in the conditions of method A; in the conditions of method B, only *trans* isomers are obtained. Furthermore, when the reaction of **1b** and 2-cyclopentenone which leads to a mixture of one diastereoisomer *cis* **3c** and one diastereoisomer *trans* **3t** (**3c**/**3t** = 30:70) is quenched by DCl/D_2O at low temperature, a **3c**(D)/**3t**(D) mixture is obtained in the same ratio as in entry 3, Table 2: the deuterium incorporation takes place in the 2-position exclusively, i.e. α to the CO group as determined by ^{1}H-NMR (250 MHz).

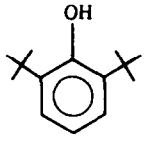
From all these experiments, it appears that the reaction process related to method B and protonation by MeOH (entries 5, 7, 15, Table 2) leading to *trans* isomers, is presumably under thermodynamic control. However, enolate protonation has a good opportunity to take place under kinetic control when method A is used with the other proton donors; its stereoselectivity is poorly sensitive to the nature of the protonating agent (Table 2). However, this stereoselectivity strongly depends on the bulk of the substituent in position 3: while from **1a**, **1b** and **2** a *cis*/*trans* mixture in the ratio

Table 1. Reactions of 2-substituted 2-cyclohexenone

Entry	Reagent	*R*	Solvent	Reaction conditions	Quenching	*cis*/*trans* ratio
1	**1c**	CH_3	THF/HMPA	3 min, −70° 40 min, −70° 2 hr 40 min, −70°	Method A, HCl	**5c**[b]/**5t** > 95:5
2			THF	10 min, −70°		**5c**[b]/**5t** > 95:5
3			THF/HMPA	40 min, −70°	Method B, HCl	**5c**[b]/**5t** > 95:5
4	**2**		THF	3 hr, −60°	Method A, NH_4Cl aq	**7c**[b]/**7t** > 95:5
5	**1b**	Ph	THF	40 min, −80°	Method A, DCl[a]	$\mathbf{9c_D}^b/\mathbf{9t_D}^b$ = 90:10

[a] When the reaction is run for 2 hr and quenched by aq NH_4Cl a 1:1 mixture of **9c**/**9t** is obtained.
[b] Mixture of two stereoisomers.

Table 2. Reactions of 2-methyl 2-cyclopentenone

Entry	Reagent	Solvent	Reaction conditions	Quenching	*cis/trans* ratio
1	1a	THF	10 min, −70° 40 min, −70° 3 min, −90°	Method A, HCl	4c[a]/4t[a] = 30:70
2	1a	THF/HMPA	5 min, −70° 30 min, −70°	Method A, HCl	4c[b]/4t[b] = 20:80
3	1b	THF	5 min, −80°	Method A, HCl	3c[b]/3t[b] = 30:70
4	1b	THF/HMPA	5 min, −70°	Method A, HCl	3c[b]/3t[b] = 30:70
5	1b	THF/HMPA	15 min, −70°	Method B, HCl	3c/3t[b] < 5:95
6	1b	THF	15 min, −80°	Method A, $CH_2(COOMe)_2$	3c[b]/3t[b] = 30:70
7	1b	THF	15 min, −80°	Method A, MeOH	3c[a]/t[a] = 8:92
8	1b	THF	15 min, −80°	Method A, AcOH	3c[a]/3t[a] = 30:70
9	1b	THF	15 min, −80°	Method A, 	3c[a]/t[a] = 30:70
10	1b	THF	15 min, −80°	Method A, NH_4Cl aq	3c[a]/3t[a] = 50:50
11	1b	THF/hexane	1 hr 30 min, −70°	Method A, NH_4Cl aq	3c[a]/3t[a] = 30:70
12	1c	THF	10 min, −70° 40 min, −70°	Method A, HCl	6c[a]/6t[a] = 80:20
13	1c	THF	15 min, −80°	Method A, NH_4Cl aq	6c[a]/6t[a] = 80:20
14	1c	THF/HMPA	5 min, −70° 15 min, −70°	Method A, HCl	6c[a]/6t[a] = 60:40
15	1c	THF	10 min, −80°	Method B, HCl	6c[a]/6t[a] < 5:95
16	2	THF/HMPA	1 hr 30 min, −70°	Method A, HCl	8c[a]/8t[a] = 35:65
17	2	THF/HMPA	1 hr 30 min, −70°	Method A, NH_4Cl aq	8c[a]/8t[a] = 35:65

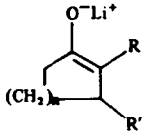
[a] Mixture of two stereoisomers.
[b] Only one single diastereoisomer.

30:70 is usually obtained, a high proportion of *cis* **6c** compound is formed from **1c** (**6c**/**6t**: 80:20) which is the bulkiest reagent. A similar stereoselectivity was obtained from bulky acyl equivalents **1** ($R = NMe_2$ or $OCH(CH_3)OCH_2CH_3$).[12]

DISCUSSION

In our discussion the lithium enolates will be considered as monomeric species which is "almost certainly an over simplification".[13] Kinetic protonation, without prejudice of its mechanism (primary O-protonation or direct C protonation)[4,14] of the six-membered ring 2-methyl and 2-phenyl-3-substituted enolates **10** ($n = 2$), takes place on the side of the molecule opposite to that of the 3-substituent R',[15] leading thus to highly predominant *cis* isomers.

However, for the 5-membered ring species, protonation takes place on both sides, the amount of *cis* isomers being larger when the substituent in position 3 is bulkier. This behaviour is different from the results obtained from trapping of enolates **11** by CH_3I, whatever the ring size ($n = 1$)[11] or ($n = 2$)[2,11] and the 3-substituent bulkiness, are only *trans* isomers formed under kinetic control; in these cases, the electrophile is always introduced on the side of the ring opposite to the substituent in position 3:



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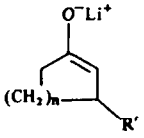

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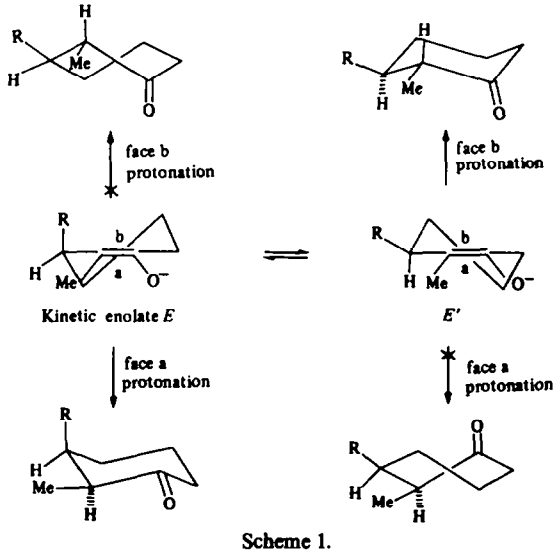
A general interpretation of the experimental results has been proposed by Toromanoff,[17] taking into account the steric interactions and the conformational interconversions which are much slower at low temperature in 6-membered ring series than in 5-membered ones.[18,19] As an example (Scheme 1), we consider the diffusion controlled protonation of the kinetic enolate *E* which is faster than its interconversion into enolate *E'*, at low temperature.

These results can be compared to those of Seebach *et al.*[1] in 5-membered ring heterocyclic enolates: while the



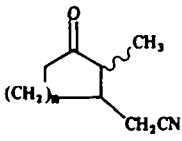
Scheme 1.

stereoselectivity of alkylation is always very high, that of the protonation is strongly dependent on the substrate nature.[16]

Synthetic applications

It is known that arylacetonitriles **1a, b** are benzoyl precursors.[8,9] Recently we have shown that *trans* 2-methyl 3-arylcyanomethyl cyclopentanones **3t, 4t** obtained via conjugate addition–methylation led after oxidative decyanation exclusively to *trans* 2-methyl 3-aroyl cyclopentanones.[20] The *trans* compounds **3t, 4t** obtained predominantly or exclusively from **1a, b** via conjugate addition–protonation could be used to prepare the above *trans* diketones in cyclopentane series.

On the other hand, the stereoselective synthesis of *cis* 2,3-disubstituted cyclopentanone **6c** obtained from the bulky reagent **1c** in the present work was extended in our laboratory. As quoted earlier, bulky acyl equivalents **1** ($R = NMe_2$ or $OCH(CH_3)OCH_2CH_3$) lead to precursors of *cis* 2-methyl 3-benzoyl cyclopentanones and cyclohexanones which were obtained after careful deprotection.[12] As we considered **7** and **8** as precursors of 3-cyanomethyl substituted cyclanones, we attempted Raney nickel desulfurisation of those compounds.[21] The pure *cis* compound **7c** formed from reagent **2** and 2-methyl 2-cyclohexenone was desulfurised in refluxing ethylacetate to yield the *cis* 2-methyl 3-cyanomethyl cyclohexanone **12c** accompanied by the isomer **12t** (**12c/12t** = 70:30). An attempt of purification on silica gel led to a *cis/trans* mixture **12c/12t**: 50:50. However, by adding boric acid to Raney nickel until neutral the desulfurisation process is more stereoselective as from *cis* compound **7c** a **12c/12t** mixture is obtained in a 90:10 ratio.



n = 2 **12**
n = 1 **13**

Furthermore, only **13t** was obtained by Raney nickel desulfurisation of a **8c/8t** (35:65) mixture.

Phenylsulfonylacetonitrile could also be used as acetonitrile precursor[22] but in the present case the conjugate addition to 2-methyl 2-cyclopentenone did not work.

CONCLUSION

From 2-methyl and 2-phenyl 2-cyclohexenone, carbanionic reagents **1** and **2** lead, after kinetic protonation, to *cis* 2,3-disubstituted cyclohexanones with a high stereoselectivity. From 2-methyl 2-cyclopentenone, the stereoselectivity of enolate *E* protonation, under kinetic control, does not depend on the nature of the proton donor; it depends upon the size of the introduced substituent in position 3: small reagents such as **1a, b** and **2** gave a nearly 30:70 *cis/trans* mixture while from bulky **1c** a 80:20 *cis/trans* mixture is obtained.

EXPERIMENTAL

The crude products were purified by thick layer chromatography on SiO_2 (diethyl ether/hexane = 70:30). The structures of all compounds were established by ^{1}H-NMR (Cameca 250 MHz and 400 MHz spectrometer by Mr. F. K. Kan's Service at IEF of Orsay) and mass spectrometry (on a AEIMS 30 spectrometer or Hewlett–Packard 5985 AGC/MS).[11] Gas chromatography (GC) was performed on an IGC 120 FB (column OV 17 3% on chromosorb WAW). The THF used was distilled over $LiAlH_4$ under N_2. 2-Methyl 2-cyclopentenone and 2-methyl 2-cyclohexenone were prepared according to the lit.[23,24] We thank Mr. Philippe Kahn for a gift of 2-methyl 2-cyclopentenone and Dr. Blanco for a gift of 2-phenyl 2-cyclohexenone.[25]

Enolate formation procedure

All reactions were run under argon at low temp maintained by a liquid N_2 bath. In a 100 ml three-necked flask equipped with a mechanical stirrer, a thermometer and a candlestick with N_2 and syringe entries previously flamed out, 5 mmol **1a–c** or **2** were dissolved in 25 ml dry THF or in a mixture of 20 ml THF and 5 ml HMPA. The soln was cooled to −70° and 1 equiv (3.6 ml) n-BuLi (1.6 M in hexane) was added dropwise via a syringe. After the addition was complete, the soln was stirred for 15 min and 5 mmol α-enone was added. After stirring for various times (Tables 1 and 2) the enolate was protonated.

Method A. At the reaction temp by adding excess of 10% HCl aq (entries 1, 2 Table 1, entries 1–4, 12, 14, 16 Table 2), sat NH_4Cl aq (entry 4 Table 1, entries 10, 11, 13, 17 Table 2), 5 mmol dimethylmalonate (entry 6 Table 2), 5.5 mmol methanol (entry 7 Table 2), 5.5 mmol AcOH dissolved in 2 ml THF (entry 8 Table 2) or 5 mmol di-t-butylphenol dissolved in 2 ml THF (entry 9 Table 2). The N_2 bath was removed and the mixture immediately extracted with three portions of diethyl ether; the organic phase was washed with sat NaCl aq and NH_4Cl until neutral and dried over $MgSO_4$. After solvent removal the crude product was purified and analysed as described above.

Method B. The mixture was allowed to warm to room temp before acidic quench, extraction and usual work up.

Determination of stereoisomers

The stereochemistry of all compounds has been established by spin–spin decoupling as described in previous work[11] or by *cis* → *trans* equilibration of the reaction products. The *cis/trans* ratio of stereoisomers was determined in all cases by integration of the different signals indicated below for each isomer (δ are given in ppm).

4c: 2 stereoisomers *cis* ^{1}H-NMR 400 MHz ($CDCl_3/C_6D_6$ = 80:20) $\delta(CH_3)$: 0.88 d and 1.7 d.

4t: 2 stereoisomers *trans* ^{1}H-NMR 400 MHz ($CDCl_3/C_6D_6$ = 80:20) $\delta(CH_3)$: 1 d and 1.8 d.

3c: 2 stereoisomers *cis* ^{1}H-NMR 250 MHz ($CDCl_3$) δ: 3.54 d and 3.9 d (H_α to nitrile group).

3t: 2 stereoisomers *trans* ^{1}H-NMR 250 MHz ($CDCl_3$) δ: 3.98 d and 4.18 d (H_α to nitrile group).

6c: 2 stereoisomers *cis* ^{1}H-NMR 250 MHz ($CDCl_3$) $\delta(CH_3)$: 0.97 d and 1.35 d.

6t: 2 stereoisomers *trans* ^{1}H-NMR 250 MHz ($CDCl_3$) $\delta(CH_3)$: 0.4 d and 1.3 d.

5c: 2 stereoisomers *cis* ^{1}H-NMR 250 MHz ($CDCl_3$) $\delta(CH_3)$: 1.1 d and 1.4 d.

5t: 2 stereoisomers *trans* ^{1}H-NMR 250 MHz ($CDCl_3$) $\delta(CH_3)$: 0.7 d and 1.2 d.

7c: 2 stereoisomers *cis* ^{1}H-NMR 90 MHz ($CDCl_3$) δ: 1 d (CH_3) and 1.02 d (CH_3); 3.57 2 d (H_α to nitrile group).

7t: 2 stereoisomers *trans* ^{1}H-NMR 90 MHz ($CDCl_3$) δ: 3.82 d and 3.9 d (H_α to nitrile group).

8c: 2 stereoisomers *cis* ^{1}H-NMR 250 MHz ($CDCl_3$) δ: 3.72 2 d (H_α to nitrile group).

8t: 2 stereoisomers *trans* ^{1}H-NMR 250 MHz ($CDCl_3$) δ: 3.97 d and 4.15 d (H_α to nitrile group).

Equilibration of **5c**. The *cis* compound (100 mg) was refluxed in 10 ml 10% HCl aq for 2 hr then extracted with diethyl ether. The ethereal soln was washed with sat $NaHCO_3$ aq and water until neutral and dried over $MgSO_4$. After solvent removal a mixture **5c/5t** (40:60) is obtained. The mixture **5c/5t** refluxed

for 6 hr, under the same reaction conditions has not been modified.

Equilibration of **7c**. The *cis* compound equilibrated under the same reaction conditions yields only the *trans* isomers **7t**.

Equilibration of **9c/9t**. The acidic equilibration of the *cis/trans* mixture (50:50) for 1 hr yields the *trans* isomers **9t**. In the same way the $\mathbf{9c_D/9t_D}$ mixture (90:10) equilibrated with 10% DCl in D_2O yield *trans* isomers $\mathbf{9t_D}$.

Equilibration of **4c/4t**. The *cis/trans* (30:70) mixture, 100 mg, was refluxed in 10 ml absolute ethanol containing a catalytic amount of sodium acetate for 12 hr. After diethyl ether extraction, the ethereal layer was washed with aqueous sodium chloride and dried over magnesium sulfate. After solvent removal only *trans* isomers **4t** were obtained.

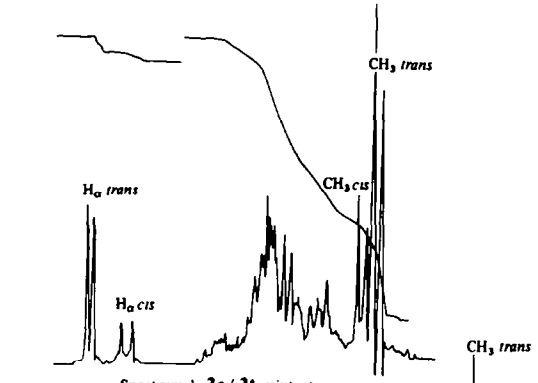
Equilibration of **3c/3t**. To a stirred solution of the *cis/trans* mixture (30:70), 100 mg, in 10 ml THF, 10 ml aqueous 10% HCl was added and the reaction mixture stirred for 10 min at room temp. After work up only *trans* isomer **3t** was obtained.

Equilibration of **8c/8t**. The *cis/trans* mixture (35:65) equilibrated as above with stirring for 30 min yields only *trans* isomers **8t**.

Equilibration of **6c/6t**. The *cis/trans* mixture (80:20) was equilibrated to the *trans* isomers **6t** by standing in $CHCl_3$ at room temp.

Preparation of **3c** (D)/**3t** (D) *mixture*

The experience described in method A for entry 3 Table 2, was performed but the reaction quench was realised by 10% DCl in D_2O. A mixture of **3c** (D)/**3t** (D) = 30:70 was obtained with the deuterium incorporation exclusively in position α to the carbonyl group, identified by comparing the ^{1}H-NMR spectrum at 250 MHz with that of the **3c/3t** mixture: in the region of H_α to the nitrile group ($CDCl_3$) δ ppm: 3.54 d and 3.98 d) no change was noted and in the region of the two doublets for methyl groups at δ ($CDCl_3$): 1.07 d and 1.2 d only two singlets were observed. Spectrum integration revealed the same stereoisomer ratio (spectra 1 and 2).



Spectrum 1 · **3c** / **3t** mixture

In this case a single diastereoisomer of **3c** and **3t** is observed

Spectrum 2 : **3c** (D) **3t** (D) mixture after DCl quench

Spectral characteristics of products **7**, **8** *and* **9**

7c: mixture of two diastereoisomers $\mathbf{7c_1/7c_2}$ = 65:35. SM: 259 (M^+, $C_{15}H_{17}NOS$). IR (neat) cm^{-1}: 2900, 2240, 1720. ^{1}H-NMR 90 MHz ($CDCl_3$) δ ppm: 1 d (3H, CH_3, **7c**$_2$), 1.02 d (3H, CH_3, **7c**$_1$), 1.35–2.5 m (7H, ring H), 2.5–3 m (1H, ring H), 3.57 2 d (1H, H_α, $^3J_{H_3H_\alpha}$ = 9 Hz **7c**$_1$, $^3J_{H_3H_\alpha}$ = 10 Hz **7c**$_2$), 7.27–7.65 m (5H, Ph).

7t: mixture of two diastereoisomers $\mathbf{7t_1/7t_2}$ = 60:40. IR (neat) cm^{-1}: 2900, 2240, 1720. ^{1}H-NMR 90 MHz ($CDCl_3$) δ ppm: 1 d (3H, CH_3), 1.5–2.75 m (8H, ring H), 3.82 d (1H, H_α, **7t**$_1$, $^3J_{H_3H_\alpha}$ = 3 Hz), 3.9 d (1H, H_α, **7t**$_2$, $^3J_{H_3H_\alpha}$ = 3 Hz), 7.28–7.65 m (5H, Ph).

8c/8t mixture: SM: 245 (M^+, $C_{14}H_{15}NOS$). IR (neat) cm^{-1}: 2900, 2400, 1740. ^{1}H-NMR 250 MHz ($CDCl_3$) δ ppm: 1.13 d (CH_3, **8c**, **8t**$_1$), 1.15 d (CH_3, **8t**$_2$), 1.9–2.8 m (6H, ring H), 3.72 2 d overlapped (H_α, $\mathbf{8c_1/8c_2}$ = 60:40, $^3J_{H_3H_\alpha}$ = 10 Hz **8c**$_1$, $^3J_{H_3H_\alpha}$ = 10 Hz **8c**$_2$), 3.97 d (H_α, **8t**$_2$, $^3J_{H_3H_\alpha}$ = 5 Hz), 4.15 d (H_α, **8t**$_2$, $^3J_{H_3H_\alpha}$ = 10 Hz), 7.3–7.75 m (5H, Ph). $\mathbf{8t_1/8t_2}$ ratio = 50:50 as determined by spectra integration.

9t: mixture of two diastereoisomers $\mathbf{9t_1/9t_2}$ = 55:45: SM: 289 (M^+, $C_{20}H_{19}NO$). IR (neat) cm^{-1}: 3050, 2950, 2250, 1710, 1600, 1495, 1450. ^{1}H-NMR 400 MHz ($CDCl_3$) δ ppm: **9t**: 0.7–2.46 m (7H, ring H), 2.25 m (H_3, **9t**$_2$), 2.75 m (H_3, **9t**$_1$), 3.16 d (H_2, **9t**$_1$, $^3J_{H_2H_3}$ = 11 Hz), 3.53 d (H_α, **9t**$_1$, $^3J_{H_3H_\alpha}$ = 3 Hz), 3.68 d (H_2, **9t**$_1$, $^3J_{H_2H_3}$ = 12 Hz), 3.73 d (H_α, **9t**$_2$, $^3J_{H_3H_\alpha}$ = 3 Hz), 7–7.46 m (10 H, Ph). **9c** (deduced from the spectrum of **9t/9c** mixture): mixture of two diastereoisomers $\mathbf{9c_1/9c_2}$ = 60:40. ^{1}H-NMR 400 MHz ($CDCl_3$) δ ppm: 0.61–2.7 m (8H, ring H), 3.15 d (H_α, **9c**$_2$, $^3J_{H_3H_\alpha}$ = 12 Hz), 3.35 d (H_2, **9c**$_2$, $^3J_{H_2H_3}$ = 6 Hz), 3.57 d (H_α, **9c**$_1$, $^3J_{H_3H_\alpha}$ = 9 Hz), 4.13 d (H_2, **9c**$_1$, $^3J_{H_2H_3}$ = 6 Hz), 7–7.46 m (10 H, Ph). H_2H_α assignments have been made by comparison with the spectrum of the products obtained after DCl quenching.

Desulfurisation procedure

Commercial Raney nickel (Prolabo) was suspended with vigorous shaking and transferred to a flask. The catalyst was allowed to settle and the water decanted. Following this, the catalyst was washed 9 times by stirring and decantation with absolute alcohol.

To a stirred solution of *cis* 2-methyl 3-phenylthiocyanomethyl cyclohexanone **7c** (130 mg) in 10 ml ethylacetate, 1 g of Raney nickel was added at 60°. The mixture was refluxed for 4 hr, filtrated and the residue was washed with hot EtOAc. The filtrate and the washings were combined and concentrated *in vacuo*. The crude product is composed of a *cis/trans* **12c/12t** mixture in a ratio of 70:30 as determined by GC and ^{1}H-NMR analysis. Purification on a silica gel column (ether/hexane, 45:55) led to 50 mg (60%) of a **12c/12t** mixture in a ratio of 50:50 determined by GC and ^{1}H-NMR. SM: 151 (M^+, $C_9H_{13}NO$). ^{1}H-NMR 90 MHz ($CDCl_3$) δ ppm: 1 d (3H, CH_3, **12c**), 1.02 d (3H, CH_3, **12t**), 1.7–2.25 m (9H, ring H + $C\underline{H}_2CN$).

The desulfurisation according to the usual procedure of a *cis/trans* 3-phenylthiocyanomethyl cyclopentanone mixture **8c/8t** = 35:65 yields a *cis/trans* **13c/13t** mixture in a ratio of 5:95 as determined by GC. This ratio is not modified by using acetone in place of ethylacetate for 1 hr. Attempts to desulfurise in ether at room temp for 12 hr leads only to starting materials. SM: 137 (M^+, $C_8H_{11}NO$). ^{1}H-NMR 90 MHz ($CDCl_3$) δ ppm: 1.04 d (3H, CH_3, **13t**), 1.58–2.75 m (8H, ring H + CH_2CN).

Desulfurisation in the presence of boric acid. To a stirred soln of *cis* **7c** (251 mg) in 20 ml EtOAc heated to 60° 2 g of Raney nickel was added. The mixture was neutralised by adding boric acid and the mixture was refluxed for 20 hr. The catalyst was removed by filtration, the filtrate washed with water, dried over $MgSO_4$ and concentrated. The crude product (120 mg) obtained with a yield of 80% is composed of a **12c/12t** mixture in a 90:10 ratio determined by GC and ^{1}H-NMR analysis.

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