# Oligo(cyclohexylidene) oximes and derivatives as probe molecules for long-range substituent effects on $^{13}C$ NMR chemical shifts

**Frans J. Hoogesteger,[a] David M. Grove,[b] Leonardus W. Jenneskens,*[,a] Theodorus J. M. de Bruin[a] and Bart A. J. Jansen[a]**

[a] *Debye Institute, Department of Physical Organic Chemistry, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands*

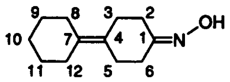
[b] *Debye Institute, Department of Metal-Mediated Synthesis, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands*

**For a series of rodlike aliphatic oximes (1–4) the influence of the oxime substituent on the $^{13}C$ NMR chemical shifts has been studied. Various 2D NMR techniques were applied for the unequivocal assignment of their $^{1}H$ and $^{13}C$ resonances. For bicyclohexylidene oximes 1–2 long-range substituent effects on the $^{13}C$ NMR chemical shifts of aliphatic carbon atoms of the six-membered rings due to the presence of the oxime group are discernible up to positions six carbon–carbon bonds distant from the iminyl carbon! The $^{13}C$ NMR data obtained for bicyclohexyl oximes 3–4 reveal that in this series the effect is limited to carbon atoms which are five bonds distant from the iminyl carbon. The observed differences between the two series is attributed to the presence of an olefinic double bond in 1–2, whch becomes polarized by the electric field of the oxime substituent.**

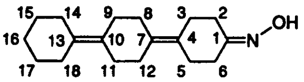
## Introduction

Both ketoximes and aldoximes have been the subject of $^{13}C$ NMR studies in connection with the topic of *syn–anti* stereochemistry around the C=N bond.[1–7] Considerable differences in chemical shifts are found for the carbon atoms positioned α (Cα) to the iminyl carbon atom.† It has been shown that $C\alpha_{syn}$ always resonates at higher field than $C\alpha_{anti}$ and this effect has been attributed to steric factors. Similar effects, but of a lesser magnitude, have been found for the β and γ carbon atoms.[1–2,8] Since ketoximes derived from unsymmetrical ketones, *i.e.* ketones lacking a twofold symmetry axis, occur in two isomeric forms, the chemical shift difference $\Delta\delta(C\alpha_{syn} - C\alpha_{anti})$ [$=\Delta\delta(sa)$, *vide infra*] has been applied for their stereochemical assignment.

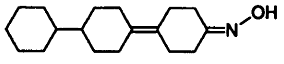
Formally, the occurrence of long-range substituent effects on the $^{13}C$ NMR chemical shift values of carbon atoms positioned β, γ, δ, ε, *etc.* can be verified using ketoximes derived from symmetrical ketones, such as cyclohexanone oxime, if distinct chemical shifts are present for carbon atoms which only differ in their position (*syn*/*anti*) with respect to the oxime functionality. To address this issue we report in this paper $^{13}C$ NMR data of a series of linear, rodlike hydrocarbons functionalized with an oxime group (compounds 1–4). It is shown for compounds 1 and 2 that a long-range substituent effect of the oxime group on their $^{13}C$ NMR chemical shifts is discernible up to carbon atoms C-9 and C-11, *i.e.* positions that are separated from the iminyl carbon atom by as much as six carbon–carbon bonds (distance *ca.* 7 Å)! The (end-functionalized) oligo(cyclohexylidene) oximes and oligo(cyclohexyl) oximes 1–4 represent an analogous series which differs with respect to the number and position of olefinic double bonds; the most prominent feature in 1–2 being the exocyclic double bond on the oxime-bearing cyclohexane-type ring. They have been used previously for the formation of ordered monolayers (Langmuir–Blodgett films),[9] hydrogen bonded supramolecular structures[10] and the preparation of micro-crystals on silicon wafers by spin-coating.[11] To illustrate their use as probes for the detection of long-range effects of the oxime substituent, compound **1b** is a representative example. The aliphatic carbon atoms (except C-16) are either *syn* or *anti* positioned with regard to the oxime substituent. Thus, carbon atoms C-2 (*syn*) and C-6 (*anti*) will possess different $^{13}C$ NMR chemical shifts. The same applies for the other *syn*/*anti* pairs of carbon atoms (C-3/C-5, C-8/C-12, C-9/C-11, C-14/C-18 and C-15/C-17). It is expected that the difference in $^{13}C$ chemical shift between related *syn* and *anti* positioned carbon atoms will decrease with increasing distance from the oxime substituent. Hence, the $^{13}C$ NMR data of compounds 1–4 will probe to which positions the influence of the oxime substituent reaches and to what extent this phenomenon is affected by the nature of the bond connecting the cyclohexane-type rings. The results indicate that primarily through-space electric field effects are responsible for the observed long-range substituent effect.



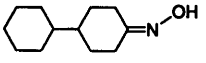
**1a**



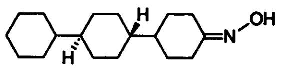
**1b**



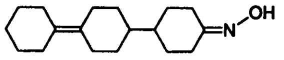
**2**



**3a**



**3b**



**4**

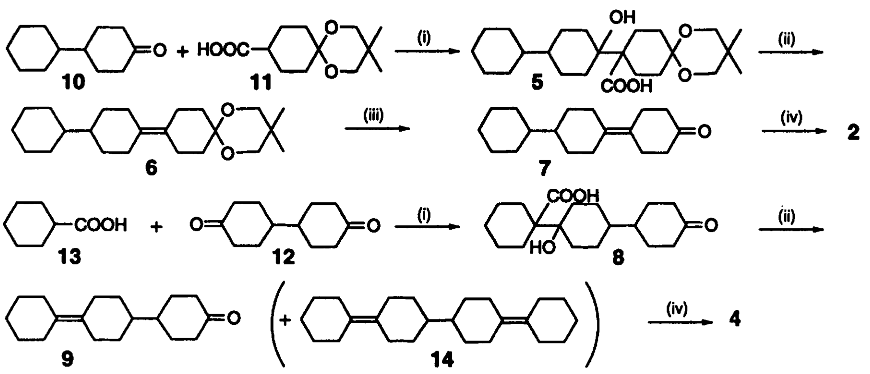
## Results

### Synthesis

Oximes 1–4 were synthesized in good to reasonable yields from the corresponding ketones by treatment with hydroxylamine

---

† The *syn* and *anti* notations refer to the carbon positions with respect to the hydroxy group.



**Scheme 1** Synthetic scheme for oximes **2** and **4**. Reagents (i) BuLi, $(Pr^i)_2NH$, THF; (ii) $Me_2NCH(OCH_2CMe_3)_2$, $CH_3CN$; (iii) $H_3O^+$, THF; (iv) $NH_2OH$, HCl, $C_5H_5N$, EtOH.

**Table 1** $^1$H and $^{13}$C NMR data for cyclohexanone oxime[a]

| Position | $\delta$ $^{13}$C | $\delta$ $^1$H | INADEQUATE[b] |
|---|---|---|---|
| C-1 | 160.00 | — | C-2 (38.9); C-6 (46.2) |
| C-2 | 24.17 | 2.45 (t, $^3J_{HH}$ 6.2, 2 H) | C-1 (38.9); C-3 (32.0) |
| C-3 | 25.26 | 1.40–1.18 (m, 6 H, H-3, H-4, H-5) | C-2 (32.0); C-4[c] |
| C-4 | 25.50 | 1.40–1.18 (m, 6 H, H-3, H-4, H-5) | C-3[c]; C-5 (32.9) |
| C-5 | 26.57 | 1.40–1.18 (m, 6 H, H-3, H-4, H-5) | C-4 (32.9); C-6 (31.8) |
| C-6 | 31.64 | 2.11 (t, $^3J_{HH}$ 6.2, 2 H) | C-5 (31.8); C-1 (46.2) |

[a] All spectra recorded in $CDCl_3$ at 298 K. [b] $^1J_{CC}$ Coupling constants (Hz) in parentheses (values ±0.2 Hz). [c] $^1J_{CC}$ Coupling constants not resolved.

hydrochloride in the presence of pyridine as a base; they are obtained as white crystalline solids. Oxime **1a** and the precursor ketone for **1b** were available from previous studies.[10,12] The precursor ketones for **3a–b** were obtained by catalytic hydrogenation of the corresponding unsaturated ketones (see Experimental).[12] The synthesis of oximes **2** and **4** and their precursor ketones **7** and **9** is shown in Scheme 1. Ketone **7** was obtained by alkylation of the dianion of carboxylic acid **11** giving β-hydroxy acid **5**, followed by dehydration and decarboxylation, and finally hydrolysis of the resulting acetal **6**. Mono-alkylation of diketone **12** yielded β-hydroxy acid **8** which gave ketone **9** upon dehydration and decarboxylation.‡ Whereas **1a** and **3a** possess good solubility in common organic solvents, the longer (tercyclic) compounds **1b**, **2**, **3b** and **4** are only sparingly soluble. Single-crystal X-ray investigations revealed dimer formation in the solid state for **1a** and **2**.[9,10] It should be noted, that oximes **2**, **3a–b** and **4** are axially dissymmetric since they possess two non-equivalent substituents at either position 4 or 10. Hence, they are chiral compounds.[13,14] Racemic mixtures were used in all NMR experiments.

### $^{13}$C NMR spectral assignment of cyclohexanone oxime

Since cyclohexanone oxime is the archetype of compounds **1–4**, the unequivocal assignment of its $^{13}$C NMR resonances is of major importance for our analysis. Unfortunately, its reported $^{13}$C NMR chemical shift assignment is ambiguous.[1-3,5,15] Therefore, we started our investigation with the unambiguous assignment of its $^{13}$C NMR chemical shifts using INADEQUATE 2D $^{13}$C–$^{13}$C correlation experiments.[16] The INADEQUATE (incredible natural abundance double quantum transfer experiment) technique allows the determination of carbon–carbon connectivities. An additional INADEQUATE 1D experiment was carried out to provide $^1J_{CC}$ coupling constants with a resolution of 0.2 Hz/point. The results corroborate the spectral assignment by Fraser *et al.*, based on lanthanide-induced shift (LIS) data.[6] The $^1$H resonances were readily assigned using $^1$H–$^{13}$C correlation data (Table 1).

The values of the carbon–carbon coupling constants ($^1J_{CC}$) between the iminyl carbon and the α carbon atoms depend on the position of the α carbons with respect to the iminyl function: values of 38.9 and 46.2 Hz were found for $C\alpha_{syn}$ and $C\alpha_{anti}$, respectively. These values agree well with those reported previously for cyclohexanone oxime (38.7 and 46.2 Hz) and other aliphatic oxime derivatives ($C\alpha_{syn}$ range: 38.7–41.5 Hz; $C\alpha_{anti}$ range: 45.7–49.3 Hz).[17] A comparison of $^1J_{CC}$ coupling constant values of oximes with those found for their related ketones shows that $^1J_{CC}$ for the $C\alpha_{syn}$ position is similar for both classes, whereas $^1J_{CC}$ for the $C\alpha_{anti}$ position is *ca.* 8–11 Hz larger in the oximes. This has been attributed to the close proximity of the nitrogen lone pair to $C\alpha_{anti}$.[17]

### $^1$H and $^{13}$C NMR spectral assignment of 1,1′-bicyclohexyliden-4-one oxime (1a)

The $^1$H spectrum of **1a** contains multiplets which all integrate for multiples of two protons. To differentiate between protons of the two distinct six-membered rings, a $^1$H–$^1$H COSY spectrum was recorded. No $^3J_{HH}$ vicinal couplings were observed between protons resonating at $\delta > 2$ ppm and those resonating at $\delta < 2$ ppm. Since the former set integrates for a total of eight protons, they were assigned to the oxime-functionalized six-membered ring, while the resonances at $\delta < 2$ ppm, which integrate for a total of 10 protons, represent those of the cyclohexylidene ring.

The $^{13}$C NMR spectrum of **1a** (solvent $C_6D_6$) contains 12 distinct resonances; one can be readily assigned to the iminyl carbon atom ($\delta$ = 159.90 ppm), two to the olefinic carbon atoms ($\delta$ = 132.18 and 125.66 ppm) and the other nine to the aliphatic carbon atoms [range $\delta$ = 31.06–25.77 ppm, Fig. 1(*a*)]. No solvent dependency was found; similar sets of resonances were observed in $C_6D_6$, $CDCl_3$, $CD_3OD$ and $(CD_3)_2SO$, respectively.

In order to assign the $^1$H and $^{13}$C resonances of **1a** unequivocally, 2D NMR techniques were applied and the results are summarized in Table 2. According to $^1$H–$^{13}$C correlation data, each aliphatic carbon atom correlates with one multiplet in the $^1$H spectrum. Hence, the two protons at each carbon atom are isochronous at room temperature (*vide infra*). The $^{13}$C resonances were assigned using INADEQUATE 2D $^{13}$C–$^{13}$C correlation experiments. Starting from the iminyl carbon atom the assignment of the carbon framework was straightforward. With the exception

---

‡ 4,4′-Bis(cyclohexylidene-1,1′-bicyclohexyl) (**14**) was isolated as a side product. It results from alkylation of both ketone functions of **12** (see Scheme 1 and Experimental).

Table 2 $^1H$ and $^{13}C$ NMR data for 1,1′-bicyclohexylidene-4-one oxime (**1a**)[a]

| Position | $\delta$ $^{13}C$ | $\delta$ $^1H$ | INADEQUATE[b] |
|---|---|---|---|
| C-1 | 159.90 | — | C-2 (42.0); C-6 (48.5) |
| C-2 | 25.77 | 2.60 (t, $^3J_{HH}$ 6.7, 2 H) | C-1 (42.0); C-3[c] |
| C-3 | 25.87 | 2.11 (t, $^3J_{HH}$ 6.7, 2 H) | C-2[c]; C-4 (45.2) |
| C-4 | 125.66 | — | C-3 (45.2); C-5 (41.8) C-7[d] |
| C-5 | 27.98 | 2.13 (t, $^3J_{HH}$ 7.2, 2 H) | C-6 (31.5); C-4 (41.8) |
| C-6 | 31.06 | 2.26 (t, $^3J_{HH}$ 7.2, 2 H) | C-5 (31.5); C-1 (48.5) |
| C-7 | 132.18 | — | C-8 (43.4); C-12 (43.4) C-4[d] |
| C-8 | 30.39 | 1.96 (t, $^3J_{HH}$ 5.9, 2 H) | C-7 (43.4); C-9 (31.5) |
| C-9 | 28.41 | 1.36 (m, 4 H; H-9, H-11) | C-8 (31.5); C-10 (33.7) |
| C-10 | 27.32 | 1.42 (m, 2 H) | C-9 (33.7); C-11 (33.7) |
| C-11 | 28.69 | 1.36 (m, 4 H; H-9, H-11) | C-10 (33.7); C-12 (30.8) |
| C-12 | 30.47 | 1.99 (t, $^3J_{HH}$ 5.9, 2 H) | C-11 (30.8); C-7 (43.4) |

[a] All spectra recorded in $C_6D_6$ at 298 K. [b] $^1J_{CC}$ Coupling constants (Hz) in parentheses (values ± 0.2 Hz). [c] $^1J_{CC}$ Coupling constants not resolved. [d] No coupling observed under the experimental conditions (*cf.* Text).

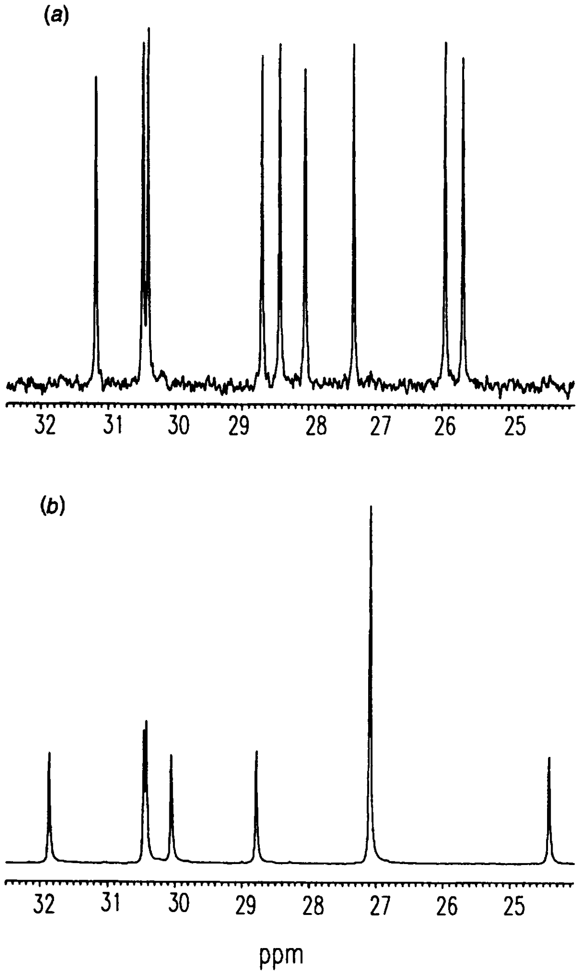


Fig. 1 Aliphatic part of the $^{13}C$ NMR spectra of **1a** (*a*) and **3a** (*b*)

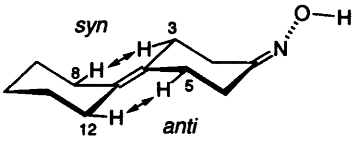


Fig. 2 Proposed dipolar interactions in **1a**

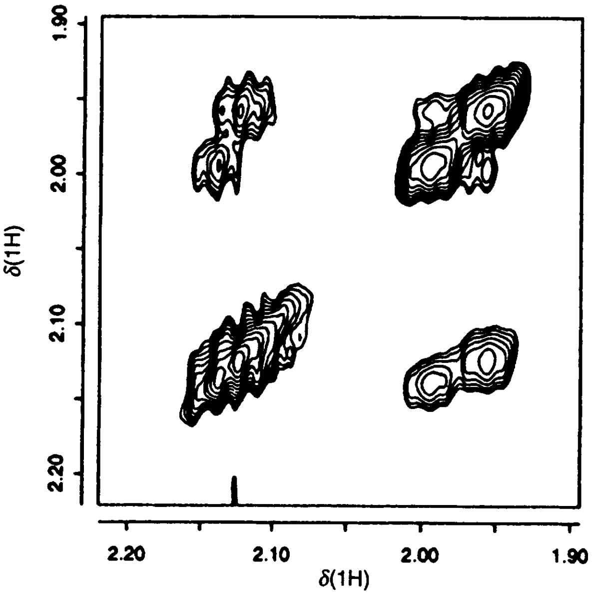


Fig. 3 Part of the ROESY spectrum of **1a**

of the $C_{olefinic}$–$C_{olefinic}$ coupling, for which no correlation was found, all connectivities could be determined. The absence of a signal for the $C_{olefinic}$–$C_{olefinic}$ coupling is attributed to the fact that the INADEQUATE 2D experiment was optimized for a $^1J_{CC}$ of 33 Hz, which is a typical value for $sp^3$–$sp^3$ C–C bonds. The value of $^1J_{CC}$ for olefinic carbons is *ca.* 75 Hz.[15] However, since all the $C_{aliphatic}$–$C_{aliphatic}$ and $C_{aliphatic}$–$C_{olefinic}$ connectivities were clear, this posed no problems for the further assignment. The $^1J_{CC}$ coupling constants were determined by taking cross-sections in the f2 direction of the 2D spectrum (Table 2). The $^1J_{CC}$ coupling constants between the iminyl carbon (C-1) and $C\alpha_{syn}$ (C-2) and $C\alpha_{anti}$ (C-6) [42.0 and 48.5 Hz, respectively] are slightly larger than the corresponding $^1J_{CC}$ coupling constants in cyclohexanone oxime (38.9 and 46.2 Hz, Table 1).

Based on the INADEQUATE 2D results the only ambiguity is the absolute numbering of the carbon atoms positioned *syn* and *anti* within the distant cyclohexylidene ring. More specifically, it has to be confirmed that the $^{13}C$ NMR resonances assigned to C-8 and C-9 belong to carbon atoms positioned on the *syn* side of the molecule while those assigned to C-11 and C-12 belong to carbon atoms located on the *anti* side. From the structure of **1a** it is expected that protons attached to allylic carbon atoms C-3, C-5, C-8 and C-12 will display a strong dipolar interaction if these carbon atoms are *cis* positioned with respect to the double bond (Fig. 2). To assess this problem a ROESY (rotating frame nuclear overhauser effect spectroscopy)[18] experiment was performed. ROESY cross peaks were found between protons resonating at $\delta = 1.96$ and $\delta = 2.11$ ppm and between protons resonating at $\delta = 1.99$ and $\delta = 2.13$ ppm (Fig. 3). From their correlations with C-8, C-3, C-12 and C-5, respectively, the assignment of both the $^1H$ and $^{13}C$ NMR spectra of **1a** was unequivocal.

**Table 3** $^1H$ and $^{13}C$ NMR data for 1,1′-bicyclohexyl-4-one oxime (**3a**)

| Position | $\delta\,^{13}C$[a] | $\delta\,^1H$[a,b] | INADEQUATE[c,d] |
|---|---|---|---|
| C-1 | 160.04 | — | — |
| C-2 | 24.41 | 1.58 (m, 1 H, ax); 3.50 (d, $^2J_{HH}$ −14.1, 1 H, eq) | C-3 (31.5) |
| C-3 | 28.78 | 1.0 (m, 1 H, ax); 1.6 (m, 1 H, eq) | C-2 (31.5); C-4 (33.6) |
| C-4 | 42.74 | 0.97 (m, 1 H) | C-3 (33.6); C-5 (33.6); C-7[e] |
| C-5 | 30.04 | 1.0 (m, 1 H, ax); 1.6 (m, 1 H, eq) | C-4 (33.6); C-6 (31.9) |
| C-6 | 31.85 | 1.87 (dd, $^2J_{HH}$ *ca.* −14, $^3J_{HH}$ *ca.* 14, 1 H, ax); 2.51 (d, $^2J_{HH}$ *ca.* −14, 1 H, eq) | C-5 (31.9) |
| C-7 | 42.61 | 0.87 (d, $^3J_{HH}$ *ca.* 13.5, 1 H) | C-4[e]; C-8 (33.3); C-12 (33.3) |
| C-8 | 30.41 | 0.82 (m, 1 H, ax); 1.45 (d, $^2J_{HH}$ *ca.* −12, 1 H, eq) | C-7 (33.3); C-9 (*ca.* 33) |
| C-9 | 27.08 | 1.1 (m, 1 H, ax); 1.6 (m, 1 H, eq) | C-8 (*ca.* 33) |
| C-10 | 27.08 | 1.1 (m, 1 H, ax); 1.6 (m, 1 H, eq) | — |
| C-11 | 27.08 | 1.1 (m, 1 H, ax); 1.6 (m, 1 H, eq) | C-12 (*ca.* 33) |
| C-12 | 30.45 | 0.82 (m, 1 H, ax); 1.45 (d, $^2J_{HH}$ *ca.* −12 Hz, 1 H, eq) | C-7 (33.3); C-11 (*ca.* 33) |

[a] All spectra recorded in $C_6D_6$ at 298 K. [b] Additional fine coupling present on all apparent 'doublets' and 'triplets'. [c] For viscosity reasons recorded in $CDCl_3$ (298 K); $^{13}C$ chemical shifts for **3a** in $CDCl_3$ are tabulated in Table 4. [d] $^1J_{CC}$ Coupling constants (Hz) in parentheses (values ± 0.2 Hz); only $C_{allphatic}$–$C_{allphatic}$ couplings were determined. [e] $^1J_{CC}$ Coupling constants not resolved.

**Table 4** $^{13}C$ NMR data for oximes **1**–**4**[a,b]

| Compound | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | C-7 | C-8 | C-9 | C-10 | C-11 | C-12 | C-13 | C-14/C-18 | C-15/C-17 | C-16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | 161.19 | 25.23 | 25.59 | 124.80 | 27.62 | 30.89 | 132.66 | 30.19 | 28.13 | 26.95 | 28.38 | 30.27 | — | — | — | — |
| **1b** | 161.50 | 24.80 | 25.65 | 125.75 | 27.73 | 30.63 | 131.45 | 29.47 | 28.69 | 127.35 | 28.98 | 29.51 | 130.75 | 30.15 | 28.41 | 27.14 |
| **2** | 161.73 | 24.98 | 25.74 | 124.70 | 27.79 | 30.93 | 132.67 | 29.75 | 31.19 | 42.90§ | 31.44 | 29.83 | 43.59§ | 30.35 | 26.83 | 26.83 |
| **3a** | 160.88 | 24.02 | 28.52 | 42.58 | 29.74 | 31.64 | 42.36 | 30.19 | 26.67 | 26.67 | 26.67 | 30.22 | — | — | — | — |
| **3b** | 161.31 | 23.90 | 28.74 | 42.60 | 29.95 | 31.75 | 42.56 | 30.38 | 30.14 | 43.33¶ | 30.14 | 30.43 | 43.48¶ | 30.28 | 26.87 | 26.87 |
| **4** | 160.00 | 23.82 | 28.43 | 42.78$ | 30.03 | 31.81 | 42.23$ | 31.72 | 30.16 | 128.81 | 30.16 | 31.75 | 129.68 | 29.42 | 28.65 | 27.23 |

[a] All spectra recorded in $CDCl_3$ at 298 K. [b] Assignments with identical labels (§, ¶, $) may be interchanged.

### $^1H$ and $^{13}C$ NMR spectral assignment of 1,1′-bicyclohexyl-4-one oxime (3a)

The $^{13}C$ NMR spectrum of **3a** (solvent $C_6D_6$) contains only ten resonances; one can be assigned to the iminyl carbon ($\delta = 160.04$ ppm), two to the tertiary carbons ($\delta = 42.74$ and 42.61 ppm) and seven to the aliphatic carbon atoms [range $\delta = 31.85$–24.41 ppm, Fig. 1(*b*)]. Assignment of all aliphatic $^{13}C$ resonances was established with an INADEQUATE 2D experiment (Table 3). The $^1H$ spectrum of **3a** is considerably more complex than that of **1a**. Three well separated multiplets between $\delta$ 3.50 and $\delta$ 1.87 ppm and several overlapping multiplets in the region $\delta$ 1.70–0.70 ppm are observed. The $^1H$ assignments were confirmed by a COSY experiment (Table 3). The $^1H$–$^{13}C$ correlation spectrum shows a correlation of each aliphatic carbon atom with two distinct protons. Hence, in the case of **3a** the protons attached to the same carbon atoms are not isochronous.

### $^{13}C$ NMR spectral assignments of compounds 1b, 2, 3b and 4

The $^{13}C$ resonances of **1b** and **2** were assigned using $^{13}C$ NMR data of oxime **1a** and the unfunctionalized parent compounds 1,1′:4′,1″-tercyclohexylidene[12] and 4-cyclohexyl-1,1′-bicyclohexylidene (**17**), respectively. In the case of compounds **3b** and **4**, $^{13}C$ NMR data of **3a** and the unfunctionalized parent compounds *trans*-1,1′:4′,1″-tercyclohexyl[19] and 4-cyclohexyl-1,1′-bicyclohexylidene (**17**), respectively, were used. The results are presented in Table 4.

## Discussion

### Conformational properties of oximes 1–4

Remarkably, the $^{13}C$ NMR spectrum of 1,1′-bicyclohexyliden-4-one oxime **1a** displays nine resonances in the aliphatic region while its saturated analogue **3a** provides only seven resonances for the corresponding carbon atoms. These data indicate that neither rotation around the C=N bond nor inversion at the oxime nitrogen atom occur for both **1a** and **3a** at room temperature. Note that upon heating **1a** to 100 °C [solvent $(CD_3)_2SO$] no coalescence of the $^{13}C$ signals was found. This is in agreement with the results of the theoretical calculations which showed a high activation barrier ($\Delta H^\ddagger$ 46.4 kcal $mol^{-1}$; 1 cal = 4.184 J)) for nitrogen inversion in the case of **1a**.[10] Due to this high activation barrier, oximes of which the corresponding ketones lack a two-fold symmetry axis give distinct sets of $^{13}C$ NMR signals for the *E* and *Z* isomers.§[1,3,4]

As shown by their $^1H$ NMR spectra a profound difference between 1,1′-bicyclohexyliden-4-one oxime (**1a**) and 1,1′-bicyclohexyl-4-one oxime [**3a**] is found. This is in line with the effect of incorporation of $sp^2$ hybridized carbon atoms.[20] The $^1H$ NMR spectrum of **3a** shows distinct chemical shfits for the axial and equatorial protons of the α carbon atoms.[21] In $C_6D_6$, $H_{eq\ syn}$ is found at $\delta = 3.50$ ppm, $H_{ax\ syn}$ at $\delta = 1.58$ ppm, $H_{eq\ anti}$ at $\delta = 2.51$ ppm and $H_{ax\ anti}$ at $\delta = 1.87$ ppm (Table 3). For **1a** the *syn* and *anti* α protons are positioned as triplets at $\delta = 2.60$ ppm and $\delta = 2.26$ ppm, respectively (Table 2). These chemical shifts are close to the time-averaged values of the corresponding protons in **3a** (2.54 and 2.19 ppm, respectively). The equatorial α protons of **3a** occur as an apparent doublet due to the large value of the geminal coupling constant ($^2J_{HH}$) compared to the vicinal coupling constants ($^3J_{HH}$) $J_{ae}$, $J_{ee}$ and $J_{aa}$ ($J_{ae}$: vicinal coupling constant between an axially and an equatorially oriented proton; $J_{ee}$: between two equatotially oriented protons; $J_{aa}$: between two axially oriented protons). Typical values for cyclohexane derivatives in their chair conformation are $J_{ae}$ 2–5 Hz, $J_{ee}$ 2–5 Hz and $J_{aa}$ 10–13 Hz.[22] The axial α protons **3a** should provide doublet of doublets resonance patterns but, due to the similar magnitude of $^2J_{HH}$ and $J_{aa}$, in combination with the relatively small value of $J_{ae}$, they appear as triplets.

As found for **3a**, the $^1H$ NMR spectra of **3b** and **4** reveal distinguishable $^1H$ chemical shifts for the axial and equatorial α protons, while for **1b** and **2** which contain an exocyclic double bond, the two protons at each carbon atom are isochronous in analogy to **1a**.

---

§ The high activation barrier to oxime nitrogen inversion is also a prerequisite for the occurrence of axial dissymmetry in compounds **2**, **3a**–**b** and **4**.[13]

### Influence of the oxime substituent on $^{13}C$ NMR chemical shifts

The polar oxime group in **1a–b** and **2** has a marked influence on the chemical shifts of the sp$^2$ carbon atoms C-4 and C-7. Compared with the parent compound 1,1′-bicyclohexylidene ($\delta$ $C_{olefin}$ = 129.42 ppm; $CDCl_3$)[12] compound **1a** shows an upfield shift for C-4 ($\Delta\delta = -4.62$ ppm) and a downfield shift for C-7 ($\Delta\delta = 3.24$ ppm, Table 4). This is attributed to $\pi$-polarization of the double bond by the polar substituent inducing a redistribution of electron density in the $\pi$-bond and, consequently, different magnetic shieldings for C-4 and C-7.[23] An inspection of the $^{13}C$ NMR data of **3a** shows that C-4 resonates downfield from C-7 (Table 3). Seidman *et al.* have shown that although the effect of a dipole on the $^{13}C$ chemical shifts of an ethylene-type system can be rationalized by bond polarization, a similar explanation does not hold for ethane-type systems.[24] In contrast, the chemical shift difference between C-4 [$\delta$ = 42.74 ppm ($C_6D_6$)] and C-7 [$\delta$ = 42.61 ppm ($C_6D_6$)] in **3a** is best attributed to the deshielding effect of the induced magnetic field of the oxime group on carbon nuclei C-4 and C-7. As a consequence of the closer proximity of C-4 to the oxime functionality it will resonate at a slightly lower field than C-7.

The observation of nine resonances for the aliphatic carbon atoms of oxime **1a** is remarkable. It indicates that the oxime group displays an effect on the $^{13}C$ NMR chemical shift up to carbon atoms C-9 and C-11. Long-range substituent effects of the oxime group of a similar magnitude are discernible in **1b** and **2** (Table 4).¶ Compound **1a** is the archetype for all bicyclohexylidene oximes; the influence of the oxime group on the $^{13}C$ NMR chemical shifts reaches up to positions six bonds distant from the iminyl carbon atom (distance *ca.* 7 Å). To our knowledge such a long-range substituent effect of the oxime group on $^{13}C$ NMR chemical shifts has not been reported before. The influence of the oxime substituent on the chemical shifts becomes negligible (at 75.47 MHz) at positions which are more than six bonds distant from the iminyl carbon atom, as can be seen from the $^{13}C$ NMR chemical shifts obtained for **1b**; carbon atoms C-14 and C-18 possess identical chemical shifts ($\delta$ = 30.15 ppm, Table 4).

The saturated analogue **3a** displays a long-range substituent effect of the oxime group on the $^{13}C$ NMR chemical shifts too. Interestingly, the effect does not reach further than positions C-8 and C-12 (Table 3). Similar results were found for **3b** and **4** (Table 4). From a comparison of the data of bicyclohexylidene oximes **1** and **2** with those of bicyclohexyl oximes **3** and **4**, it can be concluded that in the former series the C-4–C-7 olefinic double bond must play an important role in the mediation of this long-range substituent effect.

The influence of an oxime functionality and related functional groups such as imines, hydrazones and oxime ethers on $^{13}C$ chemical shifts has been discussed mainly with respect to the large differences between the values of $C\alpha_{syn}$ and $C\alpha_{anti}$. For a series of relatively rigid cyclic ketoximes Geneste *et al.* reported that the difference in chemical shift between $C\alpha_{syn}$ and $C\alpha_{anti}$ [$\Delta\delta(sa)$] depends largely on the dihedral angle $\theta$ between the C=N and the $C_\alpha$-H bond ($\theta < 90°$). The largest $\Delta\delta(sa)$ value was found for $\theta = 0°$. This dependence of $\Delta\delta(sa)$ on $\theta$ has been attributed to steric compression effects.[2–3,25] However, due to their structural similarity, compounds **1–4** show only a marginal variation in $\theta$ (MMX[26] optimized structures: $\theta$ range 2.3–9.9 °). Moreover, no long-range substituent effect is expected as a result of steric effects on the α carbon atoms.

A more appealing explanation for the long-range substituent effect exerted by the oxime substituent is a through-space electric field effect.[2,27] As a consequence of the presence of the polar oxime functionality an electric field is present which will affect the charge distribution in the molecule. The N–O bond of the oxime group is oriented almost diagonally with respect to the long molecular axis of compounds **1–4** and its electric field is invoked to rationalize the observed differences in $^{13}C$ NMR chemical shifts between carbon atoms located on the *syn* and *anti* side of the molecules. Since the electric field effect will be primarily operative on unsaturated bonds ($\pi$-electrons), it is proposed that polarization of the olefinic bond plays an important role for the propagation of the electric field anisotropy of the oxime group into the second cyclohexylidene ring in the case of **1** and **2**. In the absence of a double bond (**3** and **4**) the unsymmetrical charge distribution results only from the direct electric field of the oxime group and consequently becomes negligible [$\Delta\delta(sa) = 0$] earlier than in the case of **1** and **2** where a second (induced) dipole is present.

Other potential contributing interactions are through-bond orbital interactions.[28] However, in a recent publication,[29] their effect on $^{13}C$ NMR chemical shifts has been questioned. Nevertheless, for **1a** different $^1J_{CC}$ values between C-4 and C-3 (45.2 Hz) and C-4 and C-5 (41.8 Hz) are found, whereas in the case of **3a** both coupling constants possess an identical value (33.6 Hz) in **3a** (Tables 2 and 3). Since the magnitude of $^1J_{CC}$ will be mainly determined by the hybridization of the coupling nuclei, and to a lesser extent by substitution, ring size and substituent orientation, the different $^1J_{CC}$ values in the case of **1a** suggest the occurrence of electron density reorganization presumably *via* orbital interactions between the oxime group in **1a** and the exocyclic double bond.||

Finally, it should be realized that apart from the electronic effect of the exocyclic double bonds of **1** and **2** their presence also induces conformational mobility (*vide supra*). The present investigations cannot rule out that the difference in rigidity between bicyclohexylidene derivatives **1–2** and bicyclohexyl derivatives **3–4** affects the electronic charge distribution. For instance, the carbon skeleton may be positioned (time-averaged) more effectively in the electric field of the oxime functionality during ring-inversions.

## Conclusions

$^{13}C$ NMR spectroscopy unequivocally reveals that in the bicyclohexylidene oximes **1–2** the oxime functionality affects the chemical shift of carbon atoms that are six carbon–carbon bonds distant from the iminyl carbon atom (distance *ca.* 7 Å). For related bicyclohexyl oximes **3–4** the long-range substituent effect is limited to carbon atoms which are five carbon–carbon bonds distant from the iminyl carbon atom. The more pronounced effect for **1–2** is attributed to an electric field effect of the conformationally locked oxime substituent on the olefinic double bond in these compounds. Nevertheless, a comparison of $^1J_{CC}$ coupling constants of **1a** and **3a** indicates that through-bond interactions may play an additional role. To shed light on the latter high level theoretical calculations to determine magnetic shieldings will be necessary.

## Experimental

### General

All reactions were carried out under a dry $N_2$ atmosphere. Solvents were dried using standard procedures. 4-Cyclohexylcyclohexanone (**10**) and 1,1′-bicyclohexyl-4,4′-dione (**12**) were obtained by catalytic hydrogenation of 1,1′-bicyclohexyliden-4-one[12] and 1,1′-bicyclohexylidene-4,4′-dione,[12] respectively (ethyl acetate; 10% Pd/C; 4 atm $H_2$) in a Parr apparatus. Routine NMR spectra were recorded in $CDCl_3$ at 300.13 MHz for $^1H$ NMR and 75.47 MHz for $^{13}C$ NMR. Infrared spectra were recorded on a Mattson Galaxy Series FTIR 5000 spectro-

---

¶ Similar effects are discernible for other end-functionalized oligo(cyclohexylidene) oximes.[9]

|| It has been shown that $^1J_{CC}$ values of aromatic hydrocarbons possess a significant dependence on $\pi$-bond order.[15]

photometer using a diffuse reflectance accessory; samples were diluted with optically pure KBr. For column chromatography silica (Merck kieselgel 60, 230–400 mesh ASTM) was used. Elemental analyses were carried out by H. Kolbe Mikroanalytisches Laboratorium, Müheim a.d. Ruhr, Germany.

### NMR Spectroscopy

All measurements were carried out at 298 K using 5 mm NMR tubes and either $C_6D_6$ or $CDCl_3$ as a solvent, unless stated otherwise. One-dimensional $^1$H and $^{13}$C NMR spectra were acquired using standard conditions on a Bruker AMX 500 spectrometer operating at 500.14 MHz for $^1$H, and a Bruker AC 300 spectrometer operating at 300.13 MHz for $^1$H and 75.47 MHz for $^{13}$C. 2D $^{13}$C–$^1$H and $^1$H–$^1$H COSY spectra were recorded on a Bruker AC300 spectrometer using standard pulse sequences. Chemical shifts are given in ppm relative to external $SiMe_4$. ROESY experiments[18] were performed on a Bruker AMX-500 spectrometer with 400 ms spin lock (mixing) and the pulse sequence ROESYFSTP. INADEQUATE 2D $^{13}$C–$^{13}$C correlation spectra were recorded on a Bruker WP200 spectrometer operating at 50.3 MHz for $^{13}$C using a standard pulse sequence INAD2D. 10 mm NMR tubes were used containing 1 g of **1a** or **3a** in 2 ml solvent. Acquisition parameters were optimized for $^1J_{CC}$ 33 Hz (typical aliphatic value[15]). Typical acquisition parameters of 2 K data points and 256 or 128 experiments afforded after standard data processing 2D spectra with a resolution of typically 10–24 Hz/point in f1 and 0.7–6 Hz/point in f2. For cyclohexanone oxime an additional INADEQUATE 1D experiment was carried out to provide $^1J_{CC}$ coupling constants with a resolution of 0.2 Hz/point.

### 1,1′-Bicyclohexyliden-4-one oxime (1a)

The synthesis of compound **1a** has been described elsewhere.[10]

### 1,1′:4′,1″-Tercyclohexyliden-4-one oxime (1b)

A mixture of 1,1′:4′,1″-tercyclohexyliden-4-one[12] (132 mg, 0.51 mmol), hydroxylamine hydrochloride (194 mg, 2.79 mmol) and pyridine (245 mg, 3.11 mmol) in ethanol (35 ml) was heated at reflux overnight. After solvent removal *in vacuo* a white solid was obtained which was dissolved in dichloromethane (100 ml) and washed with water. The solution was dried ($MgSO_4$) and concentrated under reduced pressure to give pure **1b** (120 mg, 0.44 mmol, 86%): mp 210 °C decomp.; $\delta_H$ (300.13 MHz, $CDCl_3$) 2.55 (m, 2 H), 2.36 (m, 6 H), 2.25 (m, 8 H), 2.18 (m, 4 H) and 1.55 (m, 6 H); $\delta_C$(75.47 MHz, $CDCl_3$) see Table 4; $\nu_{max}$(KBr)/cm$^{-1}$ 3300–3000, 2978, 2922, 2866, 2840, 1678, 1461, 1445, 1430, 967, 937 and 759. Found: C, 78.96; H, 10.02; N, 5.10; O, 5.89. Calc. for $C_{18}H_{27}NO$: C, 79.07; H, 9.95; N, 5.12; O, 5.85.

### 9-(4-Cyclohexyl-1-hydroxycyclohexanyl)-3,3-dimethyl-1,5-dioxaspiro[5.5]undecane-9-carboxylic acid (5)

To a two-necked flask containing THF (40 ml) and diisopropylamine (1.47 g, 14.6 mmol) a solution of 1.4 mol dm$^{-3}$ butyllithium in hexane (10.4 ml, 14.6 mmol) was added at −40 °C. After stirring for 30 min solid 3,3-dimethyl-1,5-dioxaspiro[5.5]undecane-9-cyclohexanecarboxylic acid (**11**, 1.66 g, 7.28 mmol) was added at −40 °C. The reaction mixture was then stirred for 2 h at 50 °C and afterwards re-cooled to −40 °C. Subsequently, 1,1′-bicyclohexyl-4-one (**10**, 1.31 g, 7.28 mmol) (oil) was added to the reaction mixture and stirring was continued for another 2 h at 50 °C. After cooling to room temp. the reaction mixture was poured on ice (100 g) and washed with diethyl ether (3 × 25 ml). Upon acidification of the water layer to pH 1 (3 mol dm$^{-3}$ hydrochloric acid) a white solid precipitated which was filtered off. The solid was washed with water and dried *in vacuo* over KOH to yield **5** (1.11 g, 2.72 mmol, 37%) as a white powder: mp 205 °C decomp.; $\nu_{max}$(KBr)/cm$^{-1}$ 3381, 3367, 3200–2800, 1674, 1447 and 1115.

### 9-(4-Cyclohexylcyclohexylidene)-3,3-dimethyl-1,5-dioxaspiro[5.5]undecane (6)

To a suspension of β-hydroxy acid **5** (1.11 g, 2.72 mmol) in acetonitrile (60 ml) *N*,*N*-dimethylformamide dineopentyl acetal (1.26 g, 5.44 mmol) was added. After stirring for 1 h at room temp. the reaction mixture was heated at reflux overnight. The mixture was cooled to −20 °C and filtered. The residue was washed with cold acetonitrile and dried to yield **6** (0.65 g, 188 mmol, 69%) as a white solid: mp 165–167 °C; $\delta_H$(300.13 MHz, $CDCl_3$) 3.53 (s, 4 H), 2.71 (br d, $J_{HH}$ 13.2, 2 H), 2.24 (m, 4 H), 1.90–1.60 (m, 13 H) and 1.35–0.93 (m, 15 H); $\delta_C$(75.47 MHz, $CDCl_3$) 130.74, 126.87, 97.83, 70.06, 43.71, 42.93, 33.65, 31.61, 30.34, 30.21, 29.76, 26.82, 25.01 and 22.76; $\nu_{max}$(KBr)/cm$^{-1}$ 2982, 2944, 2913,2868, 1470, 1447, 1431 and 1109.

### 4′-Cyclohexyl-1,1′bicyclohexyliden-4-one (7)

Acetal **6** (623 mg, 1.80 mmol) was dissolved in THF (20 ml) and 2 mol dm$^{-3}$ hydrochloric acid (20 ml) was added. The mixture was heated at reflux for 1 h. After cooling to room temp. THF was removed *in vacuo* and the resulting white suspension was extracted with dichloromethane (3 × 25 ml). The combined organic extracts were subsequently washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$) and concentrated under reduced pressure. The product was obtained quantitatively as a white solid which was recrystallized from methanol–water (3:1 v/v): mp 78–80 °C (lit,[19] 81–81.5 °C); $\delta_H$(300.13 MHz, $CDCl_3$) 2.68 (br d, $J_{HH}$ 15.4, 2 H), 2.56 (m, 4 H), 2.39 (m, 4 H), 1.75 (m, 9 H) and 1.20–0.85 (m, 9 H); $\delta_C$(75.47 MHz, $CDCl_3$) 212.97, 133.70, 122.95, 43.48, 42.85, 40.88, 31.24, 30.32, 29.86, 26.79 and 26.61; $\nu_{max}$(KBr)/cm$^{-1}$ 2965, 2944, 2932, 2917, 2891, 2847, 1719, 1437 and 1406.

### 4′-Cyclohexyl-1,1′-bicyclohexyliden-4-one oxime (2)

A mixture of 4′-cyclohexyl-1,1′-bicyclohexyliden-4-one (**7**, 150 mg, 0.58 mmol), hydroxylamine hydrochloride (60.6 mg, 0.87 mmol) and pyridine (68.4 mg, 0.87 mmol) in ethanol (25 ml) was heated at reflux overnight. After cooling to room temp., **2** crystallized out as white needles which were filtered off (142 mg, 0.52 mmol, 89%): mp 170 °C; $\delta_H$(300.13 MHz, $CDCl_3$) 7.42 (s, 1 H), 2.68 (br t, $J_{HH}$ 13.4, 2 H), 2.55 (m, 2 H), 2.34 (m, 6 H), 1.90–1.55 (m, 9 H) and 1.35–0.90 (m, 9 H); $\delta_C$(75.47 MHz, $CDCl_3$) see Table 4; $\nu_{max}$(KBr)/cm$^{-1}$ 3500–3050, 2930, 2850, 1658, 1464, 1445, 1431, 984, 962, 928 and 760. Found: C, 78.56; H, 10.68; N, 5.03; O, 5.75. Calc. for $C_{18}H_{29}NO$: C, 78.49; H, 10.61; N, 5.09; O, 5.81.

### 4-Cyclohexylcyclohexanone oxime (3a)

To a solution of 4-cyclohexylcyclohexanone (**10**, 0.20 g, 1.11 mmol) in ethanol (50 ml) hydroxylamine hydrochloride (0.16 g, 2.30 mmol) and pyridine (1.82 mg, 2.30 mmol) were added. The reaction mixture was heated at reflux overnight and the solvent was removed under reduced pressure. The resulting solid was dissolved in dichloromethane (100 ml), washed with water, dried ($MgSO_4$) and after solvent removal *in vacuo* the product **3a** was obtained quantitatively as a white solid. After recrystallization from hexane **3a** was obtained analytically pure (126 mg, 0.65 mmol, 59%): mp 97 °C; $\delta_H$(300.13 MHz, $CDCl_3$) 3.30 (br d, $J_{HH}$ 13.0, 1 H), 2.55 (br d, $J_{HH}$ 13.0, 1 H), 2.12 (br t, $J_{HH}$ 13.0, 1 H), 2.00–1.50 (m, 8 H) and 1.50–0.90 (m, 9 H); $\delta_C$(75.47 MHz, $CDCl_3$) see Tables 3 and 4; $\nu_{max}$(KBr)/cm$^{-1}$ 3500–3000, 2952, 2921, 2894, 2851, 1676, 1446, 1439, 981, 969, 946, 937, 909 and 761. GC/MS: *m/z* 195 ($M^{\cdot+}$, 100%); 178 [$(M - OH)^+$, 71%].

### *trans*-1,1′:4′, 1″-Tercyclohexyl-4-one (15)

1,1′:4′,1″-Tercyclohexyliden-4-one[12] (300 mg, 1.16 mmol) in ethyl acetate (200 ml) was hydrogenated overnight in a Parr apparatus (4 atm $H_2$) using 50 mg 10% Pd/C as a catalyst. The reaction mixture was filtered over Celite and after solvent removal *in vacuo* a white solid was obtained, consisting of a mixture of (partly) hydrogenated products (NMR, GC). Column chromatography [5 ml fractions; silica; eluent ethyl acetate/hexane (1:1 v/v)] afforded ten fractions containing a compound with $R_f = 0.5$. These fractions were combined and after solvent removal a white solid was obtained which was recrystallized from methanol (50 ml). Yield: 92.9 mg (0.35 mmol, 30%): mp 117 °C (lit,[19] 121–122 °C); $\delta_H$(300.13 MHz, CDCl$_3$) 2.34 (m, 4 H), 2.05 (m, 2 H), 1.87–1.40 (m, 10 H) and 1.32–0.80 (m, 14 H); $\delta_C$(75.47 MHz, CDCl$_3$) 212.62, 43.39, 43.28, 42.06, 41.70, 41.14, 30.52, 30.26, 30.07, 29.86 and 26.84; $\nu_{max}$(KBr)/cm$^{-1}$ 2952, 2922, 2852, 1721 and 1447.

### *trans*-1,1′:4′,1″-Tercyclohexyl-4-one oxime (3b)

From *trans*-1,1′:4′,1″-tercyclohexyl-4-one (**15**, 32 mg, 0.123 mmol), hydroxylamine hydrochloride (34.6 mg, 0.50 mmol) and pyridine (39.5 mg, 0.50 mmol) in ethanol (25 ml) a white solid was obtained as described for **1b**. The solid was dissolved in dichloromethane (50 ml) and washed with water. The organic layer was dried (MgSO$_4$) and evaporated to dryness under reduced pressure to yield **3b** as a white solid (30.9 mg, 0.11 mmol, 91%): mp 178 °C decomp.; $\delta_H$(300.13 MHz, CDCl$_3$) 3.29 (br d, $J_{HH}$ 13.0, 1 H), 2.39 (br d, $J_{HH}$ 13.0, 1 H), 2.05 (td, $J_{HH}$ 13.0, $J_{HH}$ 3.0, 1 H), 1.85 (m, 2 H) 1.80–1.60 (m, 10 H) and 1.40–0.80 (m, 15 H); $\delta_C$(75.47 MHz, CDCl$_3$) see Table 4; $\nu_{max}$(KBr)/cm$^{-1}$ 3500–3100, 2947, 2933, 2914, 2884, 2847, 1682, 1435, 982, 960, 915 and 765. Found: C, 77.80; H, 11.17. Calc. for $C_{18}H_{31}NO$: C, 77.92; H, 11.26; N, 5.05; O, 5.77.

### 1-[4-(4-Oxocyclohexyl)-1-hydroxycyclohexanyl]cyclohexane carboxylic acid (8)

Coupling of 1,1′-bicyclohexyl-4,4′-dione (**12**, 3.06 g, 15.8 mmol) and cyclohexanecarboxylic acid (**13**, 2.02 g, 15.8 mmol) using 1.4 mol dm$^{-3}$ butyllithium in hexane (22.5 ml, 31.5 mmol) and diisopropylamine (3.19 g, 31.5 mmol) in THF (75 ml) as described for **5** afforded 2.57 g of a white solid: mp 220 °C decomp.; $\nu_{max}$(KBr)/cm$^{-1}$ 3418, 3402, 3380, 3200–2800, 1678 and 1454. According to the results of the next reaction step β-hydroxy acid **8** was contaminated with 4,4′-[bis-hydroxy-bis(cyclohex-1-yl carboxylic acid)]-1,1′-bicyclohexyl which results from coupling of both carbonyl groups with the acid.

### 4′-Cyclohexylidene-1,1′-bicyclohexyl-4-one (9)

To a suspension of β-hydroxy acid **8** (2.57 g) in acetonitrile (100 ml) *N*,*N*-dimethylformamide dineopentyl acetal (5.29 g, 22.8 mmol) was added and after stirring for 1 h at room temp. the reaction mixture was heated at reflux overnight. Upon cooling to −20 °C an off-white solid precipitated which was filtered off (0.77 g). The mother liquor was concentrated under reduced pressure to yield a yellow oil which was subsequently dissolved in diethyl ether (50 ml). The mixture was washed with brine and water, dried (MgSO$_4$) and after solvent removal *in vacuo* a white solid (1.31 g) was obtained. Recrystallization from methanol (20 ml) afforded **9** as a white solid (0.50 g, 1.92 mmol): mp 68–72 °C; $\delta_H$(300.13 MHz, CDCl$_3$) 2.75 (br d, $J_{HH}$ 13.5, 2 H), 231 (m, 4 H), 2.19 (m, 4 H), 2.01 (m, 2 H), 1.81 (m, 2 H), 1.65 (m, 2 H), 1.49 (m, 10 H) and 1.01 (m, 2 H); $\delta_C$(75.47 MHz, CDCl$_3$) 212.51, 129.81, 128.47, 42.25, 41.30, 41.07, 31.84, 30.11, 29.89, 29.31, 28.59 and 27.16; $\nu_{max}$(KBr)/cm$^{-1}$ 2978, 2944, 2930, 2920, 2882, 2847, 1721, 1447 and 1439. The initially formed off-white precipitate (0.77 g) was stirred in boiling hexane (250 ml) for 10 min, cooled to room temp. and filtered off yielding 4,4′-bis(cyclohexylidene-1,1′-bicyclohexyl) (**14**, 422 mg, 1.29 mmol): mp 212 °C; $\delta_H$(300 MHz, CDCl$_3$) 2.73 (br d, $J_{HH}$ 13.4, 4 H), 2.19 (m, 8 H), 1.79 (m, 4 H), 1.70–1.40 (m, 16 H), 1.27 (m, 2 H) and 0.97 (m, 4 H); $\delta_C$(75 MHz, CDCl$_3$) 129.34, 129.28, 43.36, 31.92, 30.15, 29.55, 28.67 and 27.26; $\nu_{max}$(KBr)/cm$^{-1}$ 2980, 2961, 2930, 2847, 1451, 1429 and 1003. Found: C, 88.17; H, 11.61. Calc. for $C_{24}H_{38}$: C, 88.27; H, 11.73.

### 4′-Cyclohexylidene-1,1′-bicyclohexyl-4-one oxime (4)

From 4′-cyclohexylidene-1,1′-bicyclohexyl-4-one (**9**, 200 mg, 0.77 mmol), hydroxylamine hydrochloride (80.8 mg, 1.15 mmol) and pyridine (91.2 mg, 1.15 mmol) in ethanol (25 ml) **4** was obtained as a white solid after work up as described for **2** (yield **4**: 141 mg, 0.51 mmol, 66%): mp 179 °C; $\delta_H$(300.13 MHz, CDCl$_3$) 3.30 (br d, $J_{HH}$ 14.2, 1 H), 2.74 (br d, $J_{HH}$ 13.2, 2 H), 2.40 (br d, $J_{HH}$ 14.0, 1 H), 2.20–2.00 (m, 5 H), 200–1.05 (m, 17 H) and 0.99 (m, 2 H); $\delta_C$(75.47 MHz, CDCl$_3$) see Table 4; $\nu_{max}$(KBr)/cm$^{-1}$ 3500–3050, 2986, 2918, 2886, 2849, 1684, 1464, 1445, 1431, 974, 916 and 760. Found: C, 78.36; H, 10.65; N, 5.06; O, 5.84. Calc. for $C_{18}H_{29}NO$: C, 78.49; H, 10.61; N, 5.09; O, 5.81.

### 1-(4-Cyclohexyl-1-hydroxycyclohexanyl)cyclohexanecarboxylic acid (16)

This compound was synthesized from 4-cyclohexylcyclohexanone (**10**, 0.93 g, 5.17 mmol) and cyclohexanecarboxylic acid (**13**, 0.66 g, 5.16 mmol) using 1.46 mol dm$^{-3}$ butyllithium in hexane (7.2 ml, 10.5 mmol) and diisopropyamine (1.06 g, 10.5 mmol) in THF (25 ml) as described for β-hydroxy acid **5**. Compound **16** was obtained as a white solid (yield 0.85 g, 2.76 mmol, 53%): mp 160 °C decomp.; $\nu_{max}$(KBr)/cm$^{-1}$ 3437, 3200–2800, 1680, 1452 and 1136.

### 4-Cyclohexyl-1,1′-bicyclohexylidene (17)

Starting from β-hydroxy acid **16** (0.82 g, 2.60 mmol) and *N*,*N*-dimethylformamide dineopentyl acetal (1.35 g, 5.83 mmol) in acetonitrile (20 ml) as described for **6**, compound **17** (0.25 g, 1.02 mmol, 39%) was obtained as a white solid: mp 102–103 °C; $\delta_H$(300.13 MHz, CDCl$_3$) 2.73 (br d, $J_{HH}$ 13.1, 2 H), 2.17 (m, 4 H), 1.79–1.45 (m, 15 H) and 1.23–0.90 (m, 9 H); $\delta_C$(75.47 MHz, CDCl$_3$) 129.41, 129.22, 43.83, 43.01, 31.73, 30.37, 30.15, 29.58, 28.67, 27.28 and 26.86; $\nu_{max}$(KBr)/cm$^{-1}$ 2916, 2849, 2835, 1448 and 1431.

## References

1 G. E. Hawkes, K. Herwig and J. D. Roberts, *J. Org. Chem.*, 1974, **39**, 1017.

2 P. Geneste, R. Durand, J.-M. Kamenka, H. Beierbeck, R. Martino and J. K. Saunders, *Can. J. Chem.*, 1978, **56**, 1940.

3 R. R. Fraser, J. Banville, F. Akiyama and N. Chuaqui-Offermans, *Can. J. Chem.*, 1981, **59**, 705.

4 C. A. Bunnel and P. L. Fuchs, *J. Org. Chem.*, 1977, **42**, 2614.

5 M. Allen and J. D. Roberts, *Can. J. Chem.*, 1981, **59**, 451.

6 R. R. Fraser, R. Capoor, J. W. Bovenkamp, B. V. Lacroix and J. Pagotto, *Can. J. Chem.*, 1984, **61**, 2616.

7 M. S. Gordon, S. A. Sojka and J. G. Krause, *J. Org. Chem.*, 1984, **49**, 97.

8 R. Knorr, K. Ferchland, J. Mehlstäubl, P. Böhrer, T. Phung Hoang and D. S. Stephenson, *Chem. Ber.*, 1992, **125**, 2033.

9 F. J. Hoogesteger, J. M. Kroon, L. W. Jenneskens, E. J. R. Sudhölter, T. de Bruin, J. W. Zwikker, E. ten Grotenhuis, C. H. M. Marée, N. Veldman and A. L. Spek, *Langmuir*, in the press.

10 F. J. Hoogesteger, L. W. Jenneskens, H. Kooijman, N. Veldman and A. L. Spek, *Tetrahedron*, 1996, **52**, 1773.

11 E. Ten Grotenhuis, J. P. van der Eerden, F. J. Hoogesteger and L. W. Jenneskens, *Chem. Phys. Lett.*, 1996, **250**, 549; *Adv. Mater.*, 1996, **8**, 666.

12 F. J. Hoogesteger, R. W. A. Havenith, J. W. Zwikker, L. W. Jenneskens, H. Kooijman, N. Veldman and A. L. Spek, *J. Org. Chem*, 1995, **60**, 4375.

13 E. L. Eliel, *Stereochemistry of Carbon Compounds*, McGraw-Hill, New York, 1962.

14 F. Toda and H. Akai, *J. Org. Chem.*, 1990, **55**, 4973.

15 H.-O. Kalinowski, S. Berger and S. Braun, *Carbon-13 NMR Spectroscopy*, Wiley, Chichester, UK, 1988.

16 For a review on 2D NMR techniques see: H. Kessler, M. Gehrke and M. Griesinger, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 490.

17 V. Wray, *Progr. NMR Spectrosc.*, 1979, **13**, 177; L. B. Krivdin, G. A. Kalabin, R. N. Nesterenko and B. A. Trofimov, *Tetrahedron Lett.*, 1984, **25**, 4817.

18 A. Bax and D. G. Davis, *J. Magn. Reson.*, 1985, **63**, 207.

19 E. G. Nidy, D. R. Graber, P. A. Spinelli, J. C. Sih and R. A. Johnson, *Synthesis*, 1990, 1053.

20 J. T. Gerig, *J. Am. Chem. Soc.*, 1968, **90**, 1065; F. R. Jensen and B. H. Beck, *J. Am. Chem. Soc.*, 1968, **90**, 1066.

21 W. F. Trager and A. C. Huitric, *Tetrahedron Lett.*, 1966, 825.

22 M. Hesse, H. Meier and B. Zeeh, *Spektroskopischen Methoden in der organischen Chemie*, 4. Aufl, Thieme, Stuttgart, 1991.

23 J. Bromilow, R. T. C. Brownlee, D. J. Craik, P. R. Fiske, J. E. Rowe and M. Sadek, *J. Chem. Soc., Perkin Trans. 2.*, 1981, 753; R. T. C. Brownlee and D. J. Craik, *J. Chem. Soc., Perkin Trans. 2*, 1981, 760; E. A. Hill and H. E. Günther, *Org. Magn. Reson.*, 1981, **16**, 177.

24 J. G. Batchelor, *J. Am. Chem. Soc.*, 1975, **97**, 3410; K. Seidman and G. E. Maciel, *J. Am. Chem. Soc.*, 1977, **99**, 3254.

25 R. Durand, P. Geneste, M. Moreau and A. A. Pavia, *Org. Magn. Reson.*, 1974, **6**, 73.

26 The MMX force field as implemented in PCMODEL 4.0, Serena Software, Bloomington, In., USA 1990 was used.

27 H.-J. Schneider and W. J. Freitag, *J. Am. Chem. Soc.*, 1977, **99**, 8363.

28 R. Hoffmann, *Acc. Chem. Res*, 1971, **4**, 1.

29 M. N. Paddon-Row, *Tetrahedron*, 1994, **50**, 10813.

*Paper* 6/03175G
*Received* 7*th May* 1996
*Accepted* 19*th June* 1996