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SUBSTITUENT EFFECTS IN ^{13}C NMR SPECTRA OF 6-*ENDO* SUBSTITUTED 9-THIABICYCLO[3.3.1]NON-2-ENES

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Abstract—A number of new 6-*endo*-X-9-thiabicyclo[3.3.1]non-2-enes have been synthesized (X = cyano, carbimino - methoxy, carbomethoxy, carboxylic acid, aminomethyl, tosylmethyl and methyl). The ^{13}C NMR spectra of six of these compounds were measured along with those of several known analogues with X = chloro, hydroxy, hydrogen and deuterium. Assignments were carried out with the aid of hetero (^{13}C-^{1}H) and homo (^{1}H-^{1}H) nuclear decoupling techniques. For the compounds with X = H and X = Cl our assignments differ from those published previously and hence result in different values of the substituent-induced chemical shifts (SIS-values) in the 9-thiabicyclo[3.3.1]non-2-ene skeleton.

Some of the existing theories regarding SIS-values in multiple substituted cyclic compounds are reviewed and reconsidered in view of the new evidence presented here. Mutual repolarization of the C-hetero atom bonds is proposed as an important factor. In the systems under study in this paper an electron donation of the sulfur atom to the *endo* C_6-X group is postulated in order to explain the SIS-values on saturated C atoms. The signals of the unsaturated carbons are assigned assuming that electric field effects play a major role.

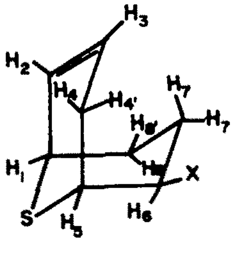
Some years ago it was shown that during solvolysis of *endo*-2, *endo* - 6 - dichloro - 9 - thiabicyclo[3.3.1]nonane in HSO_3F/SO_2 one of the Cl atoms is released whereas no comparable reaction is known for corresponding (bi-) cycloalkanes.[1] It was concluded that the S atom is essential in stabilizing the intermediate cations during the solvolysis process, by electron donation to C_2 and/or C_6.[1] A logical consequence would be to test the presence of interaction between the *endo* C-X bonds and the S atom by spectroscopic means.

In the present case, ^{13}C NMR seems to be the method of choice since it has been shown recently that the presence of interaction between two substituents in a molecule may be detected in some cases from the nonadditivity of substituent-induced shifts (SIS-values).[5,6,11] For the original 2, 6 - dihalo - 9 - thiabicyclo - [3.3.1]nonanes no anomalies could be observed in the ^{13}C NMR spectra so far, mainly because of the complexity of the simultaneous interactions between three centers and the lack of suitable model compounds.

The obvious importance of elucidating some of the backgrounds of non-additivity in ^{13}C SIS-values, a recent article concerning special "sulfur effects" in ^{13}C NMR[16b] as well as the publication of ^{13}C NMR data of some 9 - thiabicyclo[3.3.1]nonanes and unsaturated derivatives[8] prompted us to report our own results on a number of 6 - *endo* - substituted 9 - thiabicyclo[3.3.1] - non - 2 - enes which differ in several aspects from those, published previously.[8]

EXPERIMENTAL AND RESULTS

For further reference the structural formula of the compounds 1–12 will be given in Fig. 1



1: $X = H_{6'}$
2: X = D
3: X = OH
4: X = Cl
5: $X = CH_3$
6: $X = CH_2OH$
7: X = COOH
8: $X = COOCH_3$
9: $X = CONH_2$
10: X = CN
11: $X = CH_2NH_2$
12: $X = OCH_3$
13: $X = (CH_3O)C = N^+H\,Cl^-$
14: $X = CH_2$-tosyl

A. Synthesis and physical properties

Compounds **1**[2], **2**[3], **3**[4], **4**[2] and **12**[2] were prepared according to the literature.

6 -Cyano - 9 - thiabicyclo[3.3.1]*non - 2 - ene* (**10**)

A soln of **4** (2 g; 11.5 mmol) in 8 ml acetone was added dropwise to a stirred soln of NaCN (0.75 g; 15.3 mmol) in 2 ml water. After stirring for 20 h the mixture was poured into water and the product extracted into ether. After the combined ether layers were dried with $MgSO_4$, the solvent was stripped off. Chromatography on silica/$CHCl_3$, yielded 1.32 g of **10** (71%). Recrystallization from petroleum ether 40/60 gave the pure material, m.p. 59–60°. (Found: C, 65.70; H, 6.87; N, 8.41. Calcd. for $C_9H_{11}NS$: C, 65.41; H, 6.71: N, 8.48%).

6 - *Carbiminomethoxy - 9 - thiabicyclo*[3.3.1]*non - 2 - ene hydro - chloride* (**13**). A mixture of dry ether (5ml) and p.a. MeOH (0.4 g: 12.5 mmol) was saturated with dry HCl gas at 0°. Comp **10** (1 g; 6.1 mmol) was dissolved and the mixture was kept

at 0° for 100 hr. The product was collected by filtration, washed with dry ether and dried, yielding 1.2 g of **13** (84.8%). An analytical sample was prepared by dissolving the iminoether in warm MeOH, followed by precipitation with diisopropylether. (Found: C, 51.28; H, 6.74; N, 6.23. Calcd. for $C_{10}H_{16}ClNOS$: C, 51.38; H, 6.90; N, 5.99%).

6 - *Carbomethoxy* - 9 - *thiabicyclo*[3.3.1]*non* - 2 - *ene* (**8**). Comp **13** (10.15 g; 43.5 mmol) was refluxed with 50 ml water for 5 min. The product was extracted into ether. The ether layer was washed with water and dried with $MgSO_4$. Stripping off the solvent yielded 8.1 g of **8** (94.1%), m.p. 36–38°.

9 - *Thiabicyclo*[3.3.1]*non* - 2 - *ene* - 6 - *carboxylic acid* (**7**). A soln of **8** (0.5 g; 2.1 mmol) in 2.5 ml conc. HCl and 2.5 ml glacial AcOH was refluxed for 3 hr. Then the solvent was stripped off. The ppt. was washed with water and EtOH, yielding 0.28 g of **7** (71%), m.p. 155–156°. Recrystallization from aqueous EtOH raised the m.p. to 157–158°. (Found: C, 58.70; H, 6.69. Calcd. for $C_9H_{12}O_2S$: C, 58.57; H, 6.56%).

6 - *Aminomethyl* - 9 - *thiabicyclo*[3.3.1]*non* - 2 - *ene* (**11**). To a stirred mixture of LAH (0.55 g; 14.5 mmol) in 5 ml dry ether was added dropwise a soln. of **10** (1 g; 6.1 mmol) in 5 ml dry ether. After refluxing for 3 hr. the reaction was quenched by adding 0.55 ml water, 0.83 ml 10% NaOH aq and 0.83 ml water. The mixture was filtrated and the ether layer was dried with $MgSO_4$. Stripping off the ether yielded 0.83 g of **11** (83%). (Found: C, 52.32; H, 7.78; N, 6.74. Calcd. for $C_9H_{16}ClNS$ as HCl salt: C, 52.53; H, 7.84; N, 6.8%).

6 - *Hydroxymethyl* -9 -*thiabicyclo*[3.3.1]*non* - 2 - *ene* (**6**). To a stirred mixture of LAH (0.5 g; 14 mmol) in 10 ml dry ether was added dropwise a soln of **8** (4 g; 20 mmol) in 10 ml dry ether. After refluxing for 2 hr the reaction was quenched by adding 0.5 ml water, 0.75 ml 10% NaOH aq and 0.75 ml water. The mixture was filtrated and the ether layer was dried with $MgSO_4$. After stripping off the solvent the residue was chromatographed on silica with $CHCl_3$–5% MeOH, yielding 2.78 g of **6** (81%).

6 - *Tosylmethyl* - 9 - *thiabicyclo*[3.3.1]*non* - 2 - *ene* (**14**). To a soln of **6** (1 g; 5.9 mmol) in 10 ml dry pyridine at −5° was added recrystallised tosylchloride (1.23 g; 1.1 eq). The mixture was kept at 0° for one night. Then 11 ml water was added and the product extracted into ether. The combined ether layers were washed with cold 3 N H_2SO_4, water, $NaHCO_3$ aq and water and dried with $MgSO_4$. Evaporating the solvent yielded 1.8 g of **14** (94%), m.p. 54–55°. Recrystallization from ether raised the m.p. to 55–56° (Found: C, 58.74; H, 6.02. Calcd. for $C_{16}H_{20}O_3S_2$: C, 59.22; H, 6.21%).

6 - *Methyl*- 9 - *thiabicyclo*[3.3.1]*non* - 2 - *ene* (**5**). To a stirred mixture of **14** (1.8 g; 5.6 mmol) in 20 ml dry ether was added LAH (0.11 g, 2.9 mmol). After refluxing for 3 hr the reaction was quenched by adding 0.1 ml water, 0.15 ml 10% NaOH aq and 0.15 ml water. The filtrated ether layer was dried with $MgSO_4$. Evaporating of the solvent followed by chromatography of the residue on silica gel with chloroform yielded 0.59 g of **5** (69%). M.ps were measured with a Mettler FP1 m.p. apparatus. Microanalysis were carried out in our laboratories by Messrs. P. van den Bosch and H. Eding.

B. Spectral assignments

As stated in the introduction, the ^{13}C NMR spectra of **1** and **4** have been published previously,[8] based on analogy with bicyclo[3.2.1]oct-2-enes and on estimated values of substituent induced shifts (SIS-values). Since some of our results differ considerably, the spectral assignment procedure will be outlined in some detail for these compounds.

For compound **1**, the relative positions of ^1H NMR absorptions were determined by a series of homonuclear decoupling experiments at 90 MHz, including INDOR-measurements. (Bruker HX-90R, ambient temperature). $CDCl_3$-solutions with internal TMS were used to measure ^1H NMR chemical shifts. The same samples were used afterwards to measure the ^{13}C NMR spectra at a Varian HA-100 instrument interfaced with a Digilab FTS-NMR-3 Pulsing and Data System. ^{13}C NMR chemical shifts were measured relative to TMS dissolved in 1, 2 - dibromo - 1, 1, 2, 2 - tetrafluoroethane which also served to provide an external ^{19}F lock signal (see below).

Irradiation of the olefinic proton signals of **1** yielded δ_{H_1}, δ_{H_4} and $\delta_{H_{4'}}$ ($\Delta\delta_{H_4H_{4'}} = 0.63$ ppm, see Table 1). The olefinic signal merged into a single line upon irradiation at δ_{H_1}, proving that $\delta_{H_2} \simeq \delta_{H_3}$ and that $|J_{24} + J_{24'} + J_{34} + J_{34'}| = 0$. This is in agreement with an almost planar fragment $C_1-C_2-C_3-C_4$ as seen in a Dreiding model. Further decoupling and INDOR experiments indicated the following order form low to high field: H_1, H_5, H_4, $H_{4'} + H_{6'}$, $H_{8'}$, H_6, H_8, $H_7 + H_{7'}$. The protons at positions 6 and 8 form a complex multiplet at 90 MHz and were only assigned tentatively.

The noise decoupled ^{13}C NMR spectrum of **1** yielded two olefinic signals at 130.88 and 129.82 ppm. The other signals were found at 36.2, 34.2, 33.5(2x), 31.5 and 19.2 ppm. Retain-J spectra yielded doublets for the olefinic signals and at 34.2 and 33.5 ppm and triplets elsewhere. The signals were subsequently observed with CW-decoupling at reduced power and intermittent readjustments of the frequency in steps of *ca* 5 Hz. Irradiation at $\delta_H = 3.17$ ppm and at 2.99 ppm yielded sharpening of one of the ^{13}C NMR signals at 33.5 ppm and at 34.2 ppm, respectively. These signals were therefore assigned to C_1 and C_5, in this order. The second signal at 33.5 ppm remained sharpened over a relatively large range ($\delta_H = 2.8$–2.1) and was hence assigned to C_4. Decoupling at high field ($\delta_H = 1.7$) yielded the assignment of the 19.2 ppm signal to C_7. No absolute certainty was achieved in this way regarding the remaining two signals at 36.2 ppm and 31.5 ppm. This point was solved by comparison of the spectra of **1** and **2**. The proton NMR spectrum showed the same features as that of **1** with the exception of the region between $\delta = 1.5$ and $\delta = 2.0$ which was simplified considerably. The H_5-signal was also narrower. The proton noise-decoupled ^{13}C NMR spectrum showed D-splitting at 36.2 ppm, thus allowing an unambiguous assignment of this signal to C_6 and, consequently the signal at 31.5 ppm to C_8 in **1** and **2**. The chemical shift difference between the olefinic protons was too small to allow the assignments of the olefinic carbon NMR signals to C_2 and C_3 by specific decoupling. Therefore, solvent effects were taken into consideration together with expected values of the SIS-values of the C_6-*endo* substituents (see end of discussion).

The proton NMR spectra of compounds **3** and **4** are relatively simple compared with **1** and **2**: H_6 is shifted downfield, the pattern of the protons at C_7 and C_8 is considerably simplified in **3** and can now be distinguished into two sets: H_8, $H_{8'}$ at $\delta = 2.1$ and H_7, $H_{7'}$ at $\delta = 1.7$. The other changes can be read from Table 1. Assignment of the ^{13}C NMR spectrum of **3** was straightforward, using selective decoupling of the proton signals. Upon irradiation of the signal of H_1, the signal of C_1 showed a clearly resolved triplet fine structure, probably caused by (residual) coupling of C_1 with H_2 and H_3. Since $\delta_{H_2} \simeq \delta_{H_3}$, the carbon spectrum of C_1 will show the reduced value of $|J_{C_1H_2} + J_{C_1H_3}|$ in the triplet. A similar observation was made with the C_4 signal upon irradiation of H_4 and $H_{4'}$. This useful feature enabled the distinction of the signals of C_1 and C_5 in compound **4** where $\delta_{H_1} \simeq \delta_{H_5}$ and served also to substantiate the assignment of the signal at 27.00 ppm to C_4. The other assignments in **4** were based partially upon comparison with the spectra of compounds **1**, **2** and **3**. It seems reasonable, however, to expect similar SIS-values at C_7 and C_8 in compounds **3** and **4**. The alternative assignment would yield considerable incongruence in these values in view of the relatively large differences in shifts of C_7 and C_8 in the

Table 1. ^1H NMR chemical shifts of compounds 1-12

No.	X	H_1	H_2	H_3	H_4	$H_{4'}$	H_5	H_6	H_7	H_8	H_9	H_{10}
1	H	3.17	5.99	5.99	2.67	2.05	2.99	1.51		1.92		
3	OH	3.11	5.97	5.97	2.46		2.93	4.16	1.52-1.82	1.94-2.20	3.02	
4	Cl	3.08-3.21	5.97	5.97	2.59	2.52	3.08-3.21	4.62	1.81	2.19		
5	Me	3.15	5.91	5.91	2.34		2.72	2.20	1.40-1.63	1.80-2.09	0.95	
6	CH_2OH	3.26	5.97	5.97	2.51	2.12-2.34	3.16	2.12-2.34	1.44-1.61	1.83-2.07	3.47	2.91
7	COOH	2.81-3.0	5.95	5.95	2.39-2.77		3.54	3.22	1.66	2.30	10.71	
8	COOMe	3.2	5.92	5.92	2.29	2.21	3.36	2.98	1.8	2.0	3.67	
9	$CONH_2$*	3.10-3.27	5.78	5.78	2.20		2.95-3.10	2.50-2.84	1.36	1.80	6.94	
10	CN	3.34-3.50	6.02	6.02	2.59		3.17	3.24-3.40	2.04	1.87		
11	CH_2NH_2	3.24	5.96	5.96	2.33		3.09	1.95	1.54	2.05	2.59	1.32
12	OMe	3.09	5.91	5.91	2.30		3.0	3.60	1.4	2.1	3.33	

*: 60 MHz

carbon NMR spectra of 1 (and 2). Compared with the assignment by Wisemann *et al.*[8] we interchanged the assignments of C_1 and C_5 in 1 and reassigned the signals of C_4, C_6 and C_8 in the following way: $\overline{C_4 \rightarrow C_6 \rightarrow C_8}$; in compound 4 the reassignments are $\overline{C_4 \rightarrow C_8 \rightarrow C_7}$ while the assignments of C_1 and C_5 were left unchanged.

The assignments in 5, 6 and 11 were all straightforward, based on retain-J experiments and specific proton decoupling in conjunction with homonuclear proton-proton decoupling. In most cases triplet fine structures were observed for the signals of C_1 and C_4. In 8 the signals of C_7 and C_8 could not be distinguished with absolute certainty due to the small $\Delta\delta$ between H_7, $H_{7'}$, H_8 and $H_{8'}$. On the other hand, a clear distinction was possible in the spectrum of 7. The final assignments for C_7 and C_8 in 8 were therefore based on those in 7. The proton NMR spectrum of 9 was of relatively poor quality, probably due to exchange of the amide protons and/or quadrupolar broadening by nitrogen. The ^{13}C NMR spectrum of 9 was assigned by comparison with 7 and 8, resulting in quite consistent sets of chemical shifts. Assignments in 12 are straightforward due to relatively large chemical shift differences in the proton spectrum and easy comparison with 3. The proton spectrum of 10 is complicated by overlap of the signals of H_1, H_5 and H_6. The signals of C_1 and C_4 were assigned based on the triplet fine structure. The other assignments were obtained by comparison with 1 and should be considered partially as tentative.

DISCUSSION

(*a*) *sp_3 - Hybridized carbon atoms in compounds* 1–4

The substituent induced chemical shifts ("SIS-values") presented in this paper for 3 and 4 will first be compared with those, published recently in 2-*endo* substituted bicyclo[3.3.1]nonan-9-ones[5] and 4-*endo* substituted adamantanones.[6] The α-effects in 3 and 4 differ from those in bicyclo[3.3.1]nonanones by only −1.5 ppm and +2.2 ppm, respectively. This is probably not significant. The same is true for β-effects at C_7. The β-effects at C_5 are smaller in 3 and 4 than in the comparable bicyclic ketones: $\Delta(\beta) = -2.5$ ppm for OH in 3 and $\Delta(\beta) = -1.4$ ppm for Cl in 4. Although these discrepancies amount to a reduction of 25–35% of the original β-effect, the origin is not clear at this time.[†] The "steric" γ-*gauche* effects (γ_g), exerted by 6-*endo* OH or Cl on C_4 in 3 and 4 are similar, as in the bi- and tricyclic ketones (with the possible exception of 2-*endo* substituted bicyclo[3.3.1]nonanones[5]) and in monofunctional derivatives, such as cyclohexanes[7a] and adamantanes.[6]

A completely different situation pertains to γ-antiperiplanar effects (γ_a) caused by 2-equatorial (*endo*) OH or Cl on C_8. In the afore-mentioned ketones γ_a at C_8 deviates by *ca* −5 ppm from those in cyclohexanes or adamantanes. Effects on the carbonyl carbon depend on the substituent but have no counterpart in 3 and 4. On the other hand, γ_a-effects at C_8 in 3 and 4 amount to +3.0 ppm and +4.1 ppm, respectively. These numbers deviate from those in mono-functional cyclohexanes and adamantanes by *ca* +4.5 ppm and +4.2 ppm, respectively.

These results are at variance with those of 4, published recently by Wiseman *et al.*[8] Their assignments would have led to the following changes in SIS-values in 4 *with respect to the bicyclo*[3.3.1] *nonan-7-one skeleton*: α +6.3 ppm, $\beta(C_5)$: −1.3 ppm, $\beta(C_7)$: −3.3 ppm, γ_g: +4.3 ppm and γ_a: +0.4 ppm, whereas our results point to relatively small differences in α, β and γ-effects combined with a sizeable change in the γ_a-parameter. The discrepancies between our results and those cited above may serve as a warning against the use of SIS-values derived from mono-functional molecules in systems with two, possibly interacting substituents. Similar warnings have been sounded recently by Stothers[9] and can be

Table 2. ^{13}C NMR chemical shifts of compounds 1–12†

No.	X	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
1	H*	33.66	129.82	130.88	33.44	34.19	36.22	19.10	31.50		
3	OH	32.69	131.15	129.29	26.20	39.57	73.89	27.66	34.50		
4	Cl	32.69	131.01	128.81	27.00	40.19	65.90	30.26	35.64		
5	Me	33.26	130.70	129.51	27.66	39.48	39.88	27.48	33.26	22.98	
6	CH_2OH	34.01	131.01	129.69	27.42	34.94	47.55	22.10	32.60	67.23	
7	COOH**	32.58	130.74	129.59	29.73	39.95	50.05	20.87	32.58	175.50	
8	COOMe	33.07	130.84	129.41	29.83	35.20	50.28	20.84	32.61	174.90	52.74
9	$CONH_2$**	32.74	131.16	129.48	29.31	36.05	50.48	20.96	32.74	176.55	
10	CN	32.51	130.66	129.12	29.60	37.05	35.11	22.94	31.41	122.32	
11	CH_2NH_2	34.04	130.92	129.77	27.91	35.79	48.53	23.84	33.00	48.41	
12	OMe	32.86	131.01	129.07	26.29	35.78	82.71	34.50	25.32	56.51	

† solutions in $CDCl_3$, unless indicated otherwise

* solution in CCl_4

** solution in DMSO-d_6

[†] The steric interaction between the substituents and C_3 in 3 differs considerably from those in the model ketone, as can be judged from molecular models. The γ-effects at C_4 in 3 and 4 are, however, not in accordance with largely differing steric perturbations. See also Ref. 5.

derived from recent work of Robinson *et al.*[10] In these cases, however, geminal disubstitution was always involved in contrast with the present systems, concerned with substituents at least two single bonds apart and not involved in mutual steric interactions. More recently, Duddeck presented non-additivities of two substituents in 1,3-di-equatorial, di-axial or equatorial-axial positions.[11] Although the nonadditivities as such are comparable with those presented here, the explanations are different (*vide infra*).

An approximative and tentative explanation of the large upfield γ_a-effects of OH and halogens at C_2-*endo* in bicyclo[3.3.1]nonan-9-ones has been presented.[5] In fact, three different explanations are presented. In 6-*exo*[†] substituted compounds a through-space charge transfer from the substituent lone pair to the $C_9 = O$ moiety is mentioned, resulting in an upfield shift for C_9 and a relatively large downfield shift of C_6. In 6-*endo*[*] derivatives, an electronic through-σ-bond transmission along X-C_6-C_5-C_9 is proposed whereas, at the same time, a "W-type-interaction" is held responsible for upfield effects at anti-γ-carbons in both exo- and *endo*-substituted compounds. The fact that the same mechanism is inactive in systems lacking the CO group is explained by "changed electronic properties of the bonds and higher steric strain in the system". This "W-type interaction" involves overlap of back-lobe orbitals of the binding orbitals at C_6 and either C_4 or C_8.[12] An analogous mechanism has also been used recently to rationalize ^{13}C-^{13}C vicinal spin-spin couplings in similar systems[13] but has since been amended.[14]

A similar view was offered subsequently by Duddeck *et al.* who referred to an "alternating interaction mechanism" operating within the 6-membered ring.[6b] Afterwards,[11] this mechanism was specified as (through-bond) hyperconjugation as put forward already by Eliel *et al.*:[15] Somewhat curiously, in the original paper of Eliel *et al.*[15] a clear distinction is made between hyperconjugative mechanisms operative for N, O and F but inactive for S and Cl and, on the other hand, backlobe overlap. In Duddeck's paper[11] reference is made to the above-mentioned hyperconjugation but on the other hand, back-lobe overlap is suggested[6b] by referring to Heumann,[5] in order to explain γ_a-effects of halogens.

Wiseman *et al.*[8] observed different γ-effects upon oxidation of the S atom in the bicyclic sulfides to the corresponding sulfones. Unfortunately, the differential shieldings between compound **4** and the corresponding sulfone cannot be used because of the discrepancies in assignments cited earlier. It was clear, however, that carbons β to sulfur (and hence γ to the O atom(s) in the sulfone) with a α- or γ-Cl atom are considerably more sensitive towards the oxidation and show larger upfield shifts. This could very well have a common origin as the effects, evident from the results presented in Refs 6*b*, 11 and 5 and those, found in this work. The relative positions of the $S = O$ and C–Cl bonds are similar to those of $C = O$ and C–X in the bicyclic or tricyclic ketones.

In our opinion the interaction between the $C = O$ group and the *endo* C_6-X moiety, which both have dipolar and strongly polarizable bonds can be discribed as follows. The two dipoles are at an angle of approx. 60° and in opposite directions. Therefore, the inner carbons C_6 and C_9 will carry a larger electron density than the C_6-X carbon in a substituted bicyclo[3.3.1]nonane or the carboxyl carbon (C_9) in unsubstituted bicyclo[3.3.1]nonan-9-one, respectively. A similar situation arises when two equatorial substituents are present in relative γ-positions in disubstituted adamantanes, described recently by Duddeck.[11] In fact, the product of (permanent) dipoles and polarizabilities divided by bond lengths would seem to be the determining factor, for C_6 and C_9. Such an explanation was already mentioned by Eliel *et al.*[15] but was not considered to play an important role.

No definite statements can be made at this stage regarding the upfield γ_a-effects at the unsubstituted CH_2 groups in the bi- and tricyclic ketones until a better understanding is achieved of the relative importance of direct (through space) electric field effects[7] and inductive or hyperconjugative (through bond) influences.[15] It was already pointed out that the non-additivity is remarkably constant in the disubstituted adamantanes.[11][‡]

By the same token, unfortunately, our results for compounds **3**–**12** do not contribute *directly* to a deeper insight into the backgrounds of the γ_a-effects. It can only be concluded that the resulting numerical values of the SIS at C_8 differ from those of the ketones by a substantial amount. If one *presumes* that the sulfur in **3**–**12** will supply lone-pair electrons to C_6-X, the effect will be at least two-fold. First, the sulfur atom will become more positive which will cause a downfield shift of C_8. Secondly, the C_6-X dipole will become weaker giving rise to a smaller downfield shift at C_8. Obviously, the downfield effect of the positive sulfur now overrules the (small) upfield shift caused by the weakened C-X dipole.

After this project was finished, an interesting conclusion pertaining to electron donation by sulfur to an electron-demanding group in γ-position in a 6-membered ring came to our knowledge. Whereas in an earlier publication by Hirsch *et al.* concerned with 1-hetero-4-cyclohexanones no special effects had been reported,[16a] a later investigation of 1-hetero-3-cyclohexanones showed that the S atom caused an abnormally high shielding of the CO carbon atom in β-position.[16b] This was explained by assuming electron donation from sulfur to CO.[16b], Quite interestingly, it can be seen from the data in Ref. 16*b* that the accompanying α-atom in 1-thia-3-cyclohexanone is more deshielded with respect to C_3 in cyclohexanone than C_2 in thiane with respect to cyclohexane. This is in qualitative agreement with our conclusions (*vide supra*). No direct comparison can be made with regard to the carbon γ to sulfur in 1-thia-3-cyclohexanone because this atom is also α with respect to CO.

(*b*) *sp_3-Hybridized carbon atoms in compounds* **5**–**12**

Results for compound **12** are directly comparable to those for **3** except for α- and β-effects, which is logical in view of the extra C atom of the substituent. Direct comparison with the literature is hampered by the lack of 6-*endo*-methoxy-bicyclo[3.3.1]nonan-9-one[§] but

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[*] For convenience the numbering in the bicyclononanone has been changed to that used in **1**–**12**, i.e. the substituent is at C_6.

[‡] In 4-substituted bicyclo[2.2.2]octanones marked deviations from additivity are found at both C_2 and C_4.[6b,11] These deviations are reminiscent of those found in the bi- and tricyclic ketones cited above. The fact that no appreciable deviation from additivity is found at C_6 and C_7[11] could also be explained by the "infavorable" geometry of the (reinforced) dipoles $C_2 = O$ and C_4-X with respect to the C_6 and C_7 methylene main axis of polarizability[17] in the boat form of the 6 membered ring.

[§] Numbering in accordance with molecules **1**–**12**, see above.

the deviations in γ_g and γ_a-values with the appropriately substituted adamantanone[16] are similar to those of 3.

Results for the series 5, 6 and 11 are consistent when the extra shielding or deshielding effects of the OH group in 6 and the NH_2 group in 11 are taken into account. It is of importance to note that the γ_g and γ_a-effects by the Me group in 5 are very similar to those observed in 2-methyladamantane.[18] This can be construed as supporting the mechanism proposed in the previous section for the effects of strongly dipolar *endo* C_6-X groups in the 9 - thiabicyclo[3.3.1]non - 2 - ene skeleton. No electric field interaction is expected from C_6-CH_3, neither will electrons be withdrawn from the S atom, thus "normal" SIS-values should occur, in agreement with our findings.

A similar internal consistency as noted for 5, 6 and 11 is also observed for 7, 8 and 9. The γ_a-effects in all three compounds are 1 ± 0.3 ppm downfield whereas the same parameter in adamantane-carboxylic acid[18] amounts to −1.2 ppm upfield. Apparently, the mechanism described in the previous paragraph is still operative although the strongest dipole (C = O) is now one C atom farther away from the S atom. Also, electric field effects at C_8 are now conformationally avaraged values due to rotation around C_6-C = O.

In cyano-substituted compound 10, finally, the SIS-values are in fair agreement with those in 2 - cyano - adamantane,[18] the γ_g-effect in 10 is only 0.6 ppm less upfield than in 2 - cyano - adamantane. This is probably insignificant.

(*c*) *sp_2 - Hybridized carbon atoms in* 1–12

The sp_2-C signals could not be assigned unambiguously by selective proton decoupling since the NMR signals of H_2 and H_3 have nearly equivalent chemical shifts (Experimental and results). The chemical shifts of compounds 1, 3, 4 and 10 were measured carefully in two or three solvents at low concentrations: CCl_4, $CDCl_3$ and CH_3OH.† These measurements revealed that rather uniform solvent shifts are obtained when the low-field signal of 1 is combined with the highfield signals of 3, 4 and 10 and vice versa. The final assignments were then made on the following assumption. The C_6–X groups in 3, 4 and 10 act as dipoles (or tripoles) with the negative centers on the "inner" atom of the group X (e.g. O for OH). Double bonds are known to be particularly sensitive towards externally applied electric fields as far as the ^{13}C NMR chemical shifts are concerned.[17] The sp_2-C nearest to the positive end of the dipole (or the inner positive center of the tripole) will carry an excess electronic charge and will hence be shifted upfield, the other sp_2-C will be shifted downfield with respect to an unperturbed "standard" molecule, i.e. compound 1 in the present discussion. The downfield effect will probably be of a smaller absolute magnitude due to its larger distance from the perturbing di- or tripole. Consistent results are obtained when the upfield sp_2-signal in 1 is assigned to C_2, the downfield signal to C_3. The reverse situation holds in the substituted derivatives 3–12. Typical "repolarizations" caused by the C-X moieties amount to −2.51 ppm and +1.10 ppm for Cl in 4, −2.20 ppm and +0.66 ppm for C≡N in 10 and −1.98 ppm and +1.10 ppm for OH in 3 (Table 3). More detailed discussions or even model calculations on these systems are not warranted at present due to the uncertain contributions of a partially positive S atom on the shifts of C_2 and C_3 and also because no exact geometries are known for most systems.

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Table 3. SIS-values in ^{13}C NMR spectra of 3–12 (ppm)

No.	$\alpha(C_6)$	$\beta(C_5)$	$\beta(C_7)$	$\gamma_g(C_4)$	$\gamma_a(C_8)$	$\delta(C_1)$	$\delta(C_3)$	$\epsilon(C_2)$
3	+37.67	+5.38	+8.56	−7.24	+3.00	−0.97	−1.59	+1.33
							(−1.98)*	(+1.10)*
4	+29.68	+6.00	+11.16	−6.44	+4.14	−0.97	−2.07	+1.19
							(−2.51)*	(+1.10)*
5	+3.66	+5.29	+8.38	−5.78	+1.76	−0.40	−1.37	+0.88
6	+11.33	+0.80	+3.00	−6.02	+1.10	+0.35	−1.19	+1.19
7	+14.01	+1.06	+1.71	−3.53	+0.80	−0.48	−1.05	+0.92
8	+14.06	+1.01	+1.74	−3.61	+1.11	−0.59	−1.47	+1.02
9	+14.26	+1.85	+1.86	−4.13	+1.24	−0.92	−1.40	+1.34
10	−1.11	+2.86	+3.84	−3.84	−0.09	−1.15	−1.76	+0.84
							(−2.20)*	(+0.66)*
11	+12.31	+0.90	+4.74	−5.53	+1.50	+0.38	−1.11	+1.10
12	+46.49	+1.59	+6.[illegible]	−7.15	+2.99	−0.80	−1.81	+1.19

* From measurement at carefully controlled conditions of compounds 1, 3, 4 and 10 at dilute solutions in $CDCl_3$, see text.

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† Compound 4 could not be measured in MeOH since it is readily converted to 12 under the experimental conditions.

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