

**THE ^{13}C NMR SPECTRA OF SOME
TRICYCLO[2.2.0.0^{2,6}]HEXANE DERIVATIVES.
UNEXPECTED HIGH FIELD ABSORPTIONS DUE TO
ADDITIVE γ -ANTI SUBSTITUENT EFFECTS**

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ABSTRACT

By means of the ^{13}C NMR spectra of tricyclo[2.2.0.0^{2,6}]hexane and thirteen of its derivatives the effects of substituents in endo-3- and endo-5-positions on the ^{13}C chemical shifts have been determined. The γ -anti effects are at least as large as in monosubstituted cyclobutanes, where the shielding values of second-row hetero substituents exceed those in unstrained systems by far, and higher-row and carbon substituents still cause substantial upfield shifts. In the title system the γ -anti effect of a substituent in the endo-3- and endo-5-position are operative additively, and thus shift the absorption of C-1 upfield by a maximum of 27 ppm with respect to the unsubstituted hydrocarbon.

INTRODUCTION

Although the origins and the transmission mechanisms of substituents effects on the ^{13}C chemical shifts are only little understood, these effects have great importance for the determination of configurations and conformations of organic compounds (1). The diagnostic value of the γ -gauche effects were recognized first. Thereafter γ effects in antiperiplanar configurations were discovered, which may cause downfield (2,3) as well as upfield shifts (4). They are still under vigorous investigation, and the interpretations proposed earlier (3,4) have been modified or revised (5).

Generally, γ -anti effects show a magnitude of up to several ppm but may be enhanced to a multiple thereof in strained systems. Thus, we found that the substituents Br, Cl, OH, and OCH₃ in the 5-position of tricyclo[4.1.0.0^{2,7}]hept-3-ene derivatives give rise to downfield shifts of the C-7 resonance by ca. 15, 14, 12 and 11 ppm, respectively, and even a methyl group causes a deshielding of 3.7 ppm. Interestingly, the former substituents also exert γ -gauche effects, deshielding the C-1 signal by 3.2-3.9 ppm (6). Tetracyclo[4.1.0.0^{2,4}.0^{3,5}]heptane derivatives exhibit considerable γ effects in addition to unprecedentedly large δ effects (6,7).

In this work we report the ^{13}C NMR data of 3-substituted and 3,5-disubstituted tricyclo[2.2.0.0^{2,6}]hexanes. The huge shielding observed at the C-1 absorption relative to that of the unsubstituted hydrocarbon **1** at first appeared

to us to be associated with γ -*gauche* effects. Consequently, the *exo,exo* stereochemistry was ascribed to compound **5** (8). Mechanistic evidence (9) and the fact that in spite of the *endo* bridge between C-3 and C-5 in the tetra- and pentacyclic derivatives **8-14** their signals of C-1 indicate shielding, enforce revision of this assignment.

RESULTS AND DISCUSSION

Table 1 summarizes the ^{13}C chemical shifts and the one-bond $^{13}\text{C-H}$ coupling constants. The latter characterize the different types of carbon atoms. Being simultaneously the member of a cyclopropane ring and two cyclobutane rings C-1 in **1** shows a value of 189.0 Hz, from which an *s* character of the corresponding carbon orbital of 38% is derived (10). The coupling constant of C-2,6 (177.2 Hz, 36% *s* character) is similar in magnitude to that of C-1,4 in bicyclo[2.1.0]pentane (178.1 (11), 176 Hz (12)). As a bridgehead carbon of two anellated four-membered rings, C-4 exhibits a C-H coupling of 158.8 Hz (33.5% *s* character). The remaining carbons C-3,5 show coupling constants of 134.0 and 137.5 Hz closely similar to that of cyclobutane (136 Hz (1a)).

Compared to **1** in the derivatives **2-14** all the coupling constants except those of C-4 in **11** (13) and probably also **9** (13) are increased, most substantially. This is true also for C-1, which is remote from the site of substitution and which reaches a maximum value of 207.4 Hz in **6**. The origin of these enhancements is related to the increased electronegativity of the substituents with respect to hydrogen in **1**. This effect should not be of major importance in **9** and **11**, in which C-3,5 carry carbon substituents. In these examples the additional five-membered ring should increase the strain of the system with the consequence of a larger *s* character of the orbitals forming the CH bonds at C-1, C-2,6, and C-3,5.

In the unsymmetric compounds the α substituent effects provide a reliable assignment of the C-3 and C-5 resonances. As expected, the β effects are smaller and less variable. Accordingly, the absorptions of C-2 and C-6 appear at δ 16 - 27.4. With respect to **1** the tetracyclic compounds **9-14** reveal an inherent high field effect of the C-2 and C-6 signals, since the β effects of the bridges between C-3 and C-5 are extremely small in **9** and **10** (14) even directed to higher field. The C-4 absorptions are concentrated between the narrow region of δ 40.5 - 50.2, with the exception of δ 55.7 in **11**. The difference between this chemical shift and the corresponding one in **9** (δ 47.3) is due to the special effect of the double bond in cyclopentenes fixed in the envelope conformation (cf. $\Delta\delta$ 9.8 ppm for C-7 in norbornane and norbornene) (15).

The γ -*gauche* effects, which 3-substituents exert on C-5 and vice versa are not surprising, but the γ -*anti* effects deserve a detailed discussion. They are contained in the C-1 absorptions, which show the surprising span of δ 9.7 - 36.7. Indeed, the notation γ -*anti* effects meets the point only approximately, since the dihedral angles $\text{R}^1 - \text{C-3} - \text{C-4} - \text{C-1}$ and $\text{R}^1 - \text{C-3} - \text{C-2} - \text{C-1}$ deviate considerably from the antiperiplanar arrangement. Inspection of molecular models gives values of about 140 and 230°, respectively.

¹³C NMR of Tricyclo[2.2.0.0] Hexanes

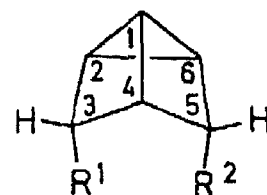
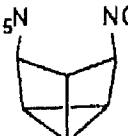
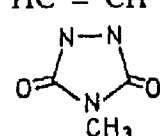


TABLE 1

¹³C Chemical Shifts (in ppm Downfield from Internal Tetramethylsilane) and One-Bond ¹³C-H Coupling Constants (Hz, in Parentheses^a) of Tricyclo 2.2.0.0^{2,6} - hexane and Some of its 3-*endo*-Substituted and 3,5-*endo,endo*-Disubstituted Derivatives in CDCl₃

No.	R ¹	R ²	C-1	C-2	C-3	C-4	C-5	C-6
1 ^b	H	H	36.7 (189.0)	18.1 (177.2)	35.5 (134.0) (137.5)	40.5 (158.8)	35.5 (134.0) (137.5)	18.1 (177.2)
2	OH	H	24.1 (197)	26.4 (184)	66.6 (155)	45.9 (160)	30.5 (137.2)	19.4 (179)
3	OCH ₃ ^c	H	24.0 (200)	24.2 (180)	74.4 (152)	43.3 (162)	30.7 (140)	19.8 (180)
4	OH	OH	9.7 (203.7)	27.0 (181.6)	69.6 (160.3)	49.0 (161.8)	69.6 (160.3)	27.0 (181.6)
5 ^{b,d}	OH	NHCO ₂ ^t Bu ^e	13.6 (203.0)	26.1 ^f (182)	68.5 (158.1)	49.0 (163.2)	50.6 (155.4)	26.2 ^f (182)
6	OCOCH ₃ ^g	NHTs ^h	15.7 (207.4)	24.9 ^f (189)	68.1 (168.3)	48.7 (166.7)	52.6 (155.2)	25.9 ^f (182)
7	SC ₆ H ₅ ⁱ	NHTs ^h	24.8 (205.2)	25.1 ^f (185)	49.3 (160.3)	49.2 (167)	52.6 (155.2)	27.3 ^f (184)
8			20.8 (199)	27.4 (181)	55.7 (152.2)	45.7 (159)	55.7 (152.2)	27.4 (181)
9 ^k	H ₂ C-CH ₂ ^l		22.4 (191.0)	17.7 (180.9)	46.8 (145)	47.3 (m)	46.8 (145)	17.7 (180.9)
10 ^{n,o}	(NC) ₂ C - C(CN) ₂ ^p		22.0 (206)	16.0 (192)	54.8 (164)	47.8 (167)	54.8 (164)	16.0 (192)
11 ^k	HC = CH ^q		30.3 (192.7)	21.0 (182.4)	50.5 (150.0)	55.7 (156.4)	50.5 (150.0)	21.0 (182.4)
12			15.1 (203.5)	20.0 (186.6)	62.1 (167.6)	50.1 (164.9)	62.1 (167.6)	20.0 (186.6)
13	N - NH ^s CONHCH ₃		13.4 (200.8)	19.3 ^f (187)	63.1 ^t (161.8)	48.8 (163.8)	62.2 ^t (158.8)	18.5 ^f (188)
14 ⁿ	N = N		16.4 (201.5)	20.7 (188.3)	81.7 (168.4)	47.3 (165.2)	81.7 (168.4)	20.7 (188.3)

^aOriginating from methine carbons most of the signals of the tricyclic skeleton appear as doublets in the proton coupled spectra. Only C-3,5 in 1 as well as C-5 in 2 and 3 produce triplets. ^bFrom ref. 8. ^cCH₃ 53.9 (q 140). ^dThe *exo,exo* configuration proposed in ref. 8 has to be revised. ^eC=O 155.3(s); C (quart.) 79.0(s); CH₃ 28.5 (q 126.5). ^fAssignment may be exchanged. ^gC=O 169.4(s); CH₃ 21.4 (q 129.4). ^hC₆H₅-4-CH₃: C-1' 143.4(s); C-2', C-3' 126.8 (d 165), 129.7 (d 161); C-4' 138.3(s); CH₃ 21.5 (q 127). ⁱC₆H₅: C-1'' 134.6(s); C-2'', C-3'' 129.1 (d 162), 130.2 (d 162); C-4'' 126.8 (d 165.5). ^jC₆H₅: C-1''' 144.6(s); C-2''' 110.2 (d 156.6); C-3''' 128.6 (d 158.1); C-4''' 115.6 (d 161.8). ^kFrom ref. 13. ^lCH₂ 29.4. ^mCoupling constant not determined due to overlap of peaks. ⁿFrom ref. 14. ^oSolvent [D₆]acetone. ^pC(quart.) 48.9(s); CN 112.1(s). ^qCH(olefin) 136.6 (d 164.7). ^rC=O 157.3(s); CH₃ 25.4 (q 141.9). ^sC=O 161.9(s); CH₃ 26.5 (q 137.5). ^tAssignment may be exchanged. ^uSolvent C₆D₆/CH₂Cl₂.

By comparison of the chemical shifts of C-1 in **3** and **1** in the γ -anti effect of the OCH₃ group is calculated to be -12.7 ppm. As obtained from **2** and **1** that of the first OH group is -12.6 ppm. Compounds **4** and **2** show that the second OH group with a value of -14.4 ppm has an even larger effect. Obviously, the *endo* substituents in positions 3 and 5 exert an additive γ -anti effect. This is also seen in the spectra of compounds **5**, **6**, and **12-14**, which carry an oxygen and a nitrogen function or two nitrogen functions at C-3 and C-5. These substituents cause an upfield shift of the C-1 signal by 20.3 - 23.1 ppm relative to that of **1**. Most probably the reason for these large effects is associated with the structural feature of the cyclobutane ring connecting the substituent and the γ carbon by two antiperiplanar bond pathways.

Shielding γ -anti effects have been observed only when the substituent under consideration both possesses a lone pair and is a second-row element. The hyperconjugative interaction between the lone pair and a parallel δ bond orbital of the γ carbon, which is transmitted by the C _{α} -C _{β} δ bond, is believed to be responsible for this shielding (4). Furthermore, the presence of axial hydrogens at C _{α} and C _{γ} has been shown to be necessary (5). Compound **2-6** and **12-14** fulfill these conditions. In view of the strongly different nature of the oxygen (OH, OCOCH₃) and nitrogen substituents (NHCO₂^tBu, NHTs, urazol, hydrazine, and azo functionalities) their γ -anti effects exhibit remarkably little variation. The two nitrogen substituents of **8** cause a distinctly smaller upfield shift of 15.9 ppm, presumably as a result of the diminished ability of the lone pairs to enter into hyperconjugation due to interaction with two tricyclo [2.2.0.0^{2,6}]hexane systems. Sulfur, as a third-row element, in the phenylthio substituent of **7** exerts only a very small shielding of at most 1-2 ppm. The total upfield shift including the effect of the NHTs group amounts to 11.9 ppm.

Considering the previous understanding of the γ -anti effect the value of -14.9 ppm caused by the two methylene substituents in **9** is surprising. If in fact hyperconjugation is responsible, this example demonstrates the ability of CH bonds to act in this manner. In **10** the electron withdrawing nitrile functionalities give rise to a substantial increase of all the CH coupling constants. However, the γ -anti effect of the dicyanomethylene groups, exhibiting a value of -14.7 ppm, does not suffer from this electron deficiency. Within the current hypothesis the C-CN bonds would have to be involved in hyperconjugation. The minimum upfield shift (-6.4 ppm) is observed in the olefin **11**. Why the π electrons of the unsaturated bridge would hardly qualify for hyperconjugation is puzzling. The much larger effect (-20.3 ppm) of the azo functionality in **14**, which also possesses a π bond, probably finds its origin in the interaction of the lone pairs. Although the lone pairs on the nitrogens of the urazole derivative **12** have a completely different orientation in space relative to those of **14**, the γ -anti effect observed does not deviate substantially (-21.6 ppm). Especially, the big difference between the γ -anti effects in **11** and **14** on one side and the similarity of them in **12** and **14** reveal the deficiency of insight into the interrelation between molecular constitution and substituent influence.

^{13}C NMR of Tricyclo[2.2.0.0] Hexanes

The literature offers only scattered reports of ^{13}C chemical shifts of cyclobutane derivatives. That the γ -*anti* effects being operative in these compounds mimic those in the tricyclo[2.2.0.0^{2,6}]hexane system reasonably well is shown in Scheme 1. Compared to cyclobutane (16) the OH group of cyclobutanol (17) exerts a γ -*anti* effect of -9.8 ppm, which amounts to about three quarters of the OH effects in 2 and 4. The methyl group of methylcyclobutane (18) causes a γ -*anti* effect of -3.8 ppm thus supporting the finding in the spectrum of 9. Surprisingly, the carboxyl groups of cyclobutane carboxylic acid (18) is nearly as active (-3.6 ppm) as a methyl group. Although in halocyclobutanes (19) the shielding of C-3 relative to the chemical shift of cyclobutane decreases ongoing from fluorine (-11.9 ppm) to chlorine (-6.1 ppm) and bromine (-3.6 ppm), deshielding does not occur above iodine (0.5 ppm). The γ -*anti* effect of a phenylthiogroup (-3.2 ppm, Scheme 1) is obtained from a bicyclo[2.1.1]hexane derivative (20) with the substituent in the pseudoequatorial position. Four closely related compounds reveal upfield shifts of 1.7 - 2.5 ppm (20). These values are in excellent agreement with the observed phenylthio effect in 7.

Scheme 1



R	$\delta^{\text{C-3}}$	R	$\delta^{\text{C-3}}$	R	$\delta^{\text{C-6}}$
H	22.4 ¹⁶	F	10.5 ¹⁹	H	39.3 ¹⁵
OH	12.6 ¹⁷	Cl	16.3 ¹⁹	C ₆ H ₅ S	36.1 ²⁰
CH ₃	18.6 ¹⁸	Br	18.8 ¹⁹		
CO ₂ H	18.8 ¹⁸	I	22.9 ¹⁹		

Obviously, in cyclobutane derivatives and other highly strained systems (6,7) the rules derived largely from the numerous data of cyclohexane (4) and adamantane (5) derivatives require modification. The shielding γ -*anti* effects of second-row hetero substituents (NR₂, OR, F) are strongly increased and higher-row (Cl, Br, SC₆H₅) as well as carbon substituents (CH₃, CH₂) still cause remarkable upfield shifts.

EXPERIMENTAL

The syntheses of the compounds 1 (21), 2 (9), 4-8 (9), and 14 (22) have been described, those of 3, 10 (14), 12, and 13 will be published elsewhere.

The ^{13}C NMR data of 9 and 11 have been taken from ref. 13. We have recorded the spectra in the PFT mode at ambient temperature with internal deuterium lock using a Bruker WH-90 spectrometer operating at 22.64 MHz. Proton-coupled spectra were obtained by using the gated decoupling mode. The concentrations of the samples were

not standardized. The error limit for the chemical shifts is approximately 0.1 ppm and in the coupling constants the last digit of each value given in table 1 is uncertain.

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