

Dependence of the γ Carbon-13 Shielding Effect on Electronegativity

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Three γ effects on ^{13}C shielding in 3,3-dimethylheterocyclohexanes as a function of the hetero-atom X have been examined. The γ -*anti* effect on the equatorial 3-methyl group is small in absolute magnitude but strongly dependent on the polar properties of X. The plot of the ^{13}C shielding of this carbon vs the electronegativity of X is linear, with a slope of -5.8 ppm/electronegativity unit. The γ -*gauche* effects on the axial 3-methyl group and on the 4-carbon are large in absolute magnitude but have quite different dependences on the polar properties of X. Whereas the shielding of the 4-carbon exhibits a linear dependence on electronegativity (slope -3.5), the axial 3-methyl group shows little dependence (slope crudely -0.7), even though the geometric relationship between X and either carbon is almost the same. Neither *gauche* carbon shielding appears to be related to the steric properties of X. The polar component of both the γ -*anti* effect and the γ -*gauche* effect is interpreted as arising from overlap of appropriately positioned parallel orbitals. For the *anti* case, the pathway is the familiar zigzag arrangement of bonds. For the *gauche* case, the pathway may be either through space (the orbitals would be only on X and C- α ; for the 4-carbon, this interaction would be through the center of the ring) or through bonds (there are parallel axial orbitals on all four atoms). The absence of a significant polar effect for the axial 3-methyl group suggests that the *gauche* interaction requires a rigid pathway. The polar component of the general γ -*gauche* effect is superimposed upon a larger contribution that is essentially independent of the nature of X and may be associated with the removal of the hydrogen on the β -carbon and replacement with the γ -X group.

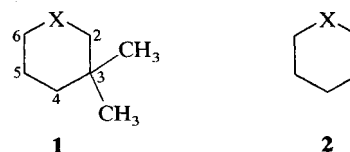
INTRODUCTION

The chemical shift of a ^{13}C nucleus is largely determined by the atoms that are α (directly attached), β and γ to the nucleus. Whereas the α and β effects are reasonably well understood, efforts are continually being made to understand the factors contributing to the γ effect. One complexity not shared by the α and β effects is that the γ effect, being a property of at least four atoms, has a torsional component. The dihedral arrangement between the resonating carbon and the perturbing γ substituent can range from 0 to 180° . Cases in the 60 – 90° region are generally referred to as the γ -*gauche* effect, and those in the 150 – 180° region as the γ -*anti* effect.

The γ -*gauche* effect was originally attributed to steric (van der Waals) interactions between the groups at either end of the four atom fragment.¹ Observation that the effect is independent of the size of the perturbing group, however, led to a variety of alternative explanations, including sensitivity to bond angle changes,² shielding properties of the β -hydrogen that is replaced by the γ substituent,³ or electric field effects.⁴ The γ -*anti* effect has been variously attributed to inductive polarization, electric field effects,⁴ or hyperconjugative interactions of substituent lone pairs.⁵ In addition to the properties of the γ -X group, those of substituents on the intervening α - and β -carbons have also been found to influence the γ effect.⁶ One group has discussed the γ -*anti* effect in

terms of two contributions, an 'angular-dependent downfield γ effect... operating through the σ bond framework' and a mechanistically unspecified effect from compression of the atomic pathway.⁷ The γ -*gauche* effect is always upfield, whereas the γ -*anti* effect is either upfield or downfield.

Almost all previous studies of γ effects have utilized the perturbations of a substituent on a rigid ring system, such as a methyl or chloro group on adamantane. In order to obtain an alternative perspective on the γ effect, we report herein a study in which the perturbing γ substituent is the hetero-atom within a 6-membered ring. We chose the 3,3-dimethylheterocyclohexane system, **1**, as the subject for our study. Observation of the chemical shifts below the coalescence temperature for ring reversal provides three



- a X = CH₂
- b X = NH
- c X = NCH₃
- d X = O
- e X = S
- f X = Te

distinct manifestations of the γ effect within the ring. The 4-carbon is γ -*gauche* to X, the equatorial 3-methyl group is γ -*anti* and the axial 3-methyl is γ -*gauche*. The two γ -*gauche* carbons should respond

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differently, as the 4-carbon has two pathways and the axial 3-methyl has one. Furthermore, this 3-methyl has a hydrogen atom directed toward the hetero-atom, whereas the 4-carbon has no such interaction. Thus, this series provides a parallel set of data on various modes of the γ effect, as a function of the nature of the group or atom X. We previously obtained analogous data on the parent (unmethylated) ring system, **2**.⁸ Comparison of these data with those from **1** provides information on the effect of substitution on the intervening atoms.

RESULTS

1,1-Dimethylcyclohexane (**1a**) was available commercially. All other materials were prepared from 2,2-dimethylglutaric acid. Reaction of this compound with ammonia produced the six-membered imide, which led to 3,3-dimethylpiperidine (**1b**) on reduction with lithium aluminum hydride. Treatment of the secondary amine with formic acid and formaldehyde gave the tertiary amine, 1,3,3-trimethylpiperidine (**1c**). Reduction of 2,2-dimethylglutaric acid with lithium aluminum hydride produced 2,2-dimethylpentane-1,5-diol, which was converted by the action of sulfuric acid to 3,3-dimethyloxane (**1d**) in high yield. Bromination of the diol with triphenylphosphinedibromide led to 1,5-dibromo-2,2-dimethylpentane, which gave 3,3-dimethylthiane (**1e**) on treatment with sodium sulfide or 3,3-dimethyltellurane (**1f**) on treatment with tellurium metal and sodium formaldehydesulfoxylate.

Carbon-13 chemical shifts were measured at room temperature and below the coalescence temperature for ring reversal, in order to obtain distinct values for the axial and the equatorial methyl groups. The resulting shifts are given in Table 1. The variation of these shifts with temperature has been the subject of a separate paper.⁹ Shifts for the thiane¹⁰ and the piperidine¹¹ have been reported previously. Assignments followed readily from analysis of the geminal dimethyl effects on the chemical shifts, as compared with those of the unmethylated heterocyclohexanes. The dimethyl effects were evident from the published cases.^{10,11} The higher field axial-methyl resonance has been confirmed in rigid systems. Questionable assignments were verified by deuteration at the 2 and 6 positions. Results could not be obtained below the

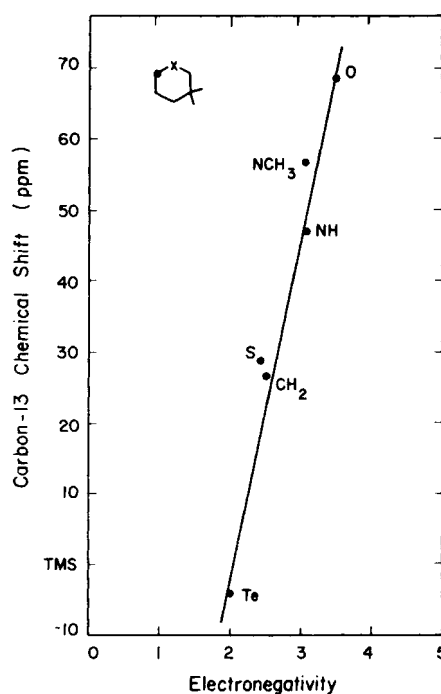


Figure 1. The ^{13}C chemical shift of C-6 in **1** as a function of electronegativity.

coalescence temperature for the tellurium compound, so only the average position for **1f** is given in Table 1. Plots of chemical shifts v. electronegativity are given in Figs 1–7.

DISCUSSION

The α and β effects

It is useful to compare the effects in the dimethyl system **1** with those in the unsubstituted heterocyclohexane system **2**.⁸ The α effect is represented at both the 2 and the 6 positions of **1** (Figs 1 and 2). Both carbons are strongly deshielded by an increase in the electronegativity of X. Such α effects have been related to the electron density at the α -carbon.⁴ There

Table 1. Carbon-13 chemical shifts of the 3,3-dimethylheterocyclohexanes^a

X	Temperature ^b (K)	C-2	C-3	C-4	C-5	C-6	CH ₃ (ave.)	X-CH ₃	ax-CH ₃ ^c	eq-CH ₃ ^c	Temperature ^d (K)
CH ₂ ^e	302	39.86	30.39	39.86	22.82	26.79	28.95	—	24.00	33.68	188
NH	301	59.04	30.08	38.30	23.56	47.26	26.89	—	23.33	30.01	185
NCH ₃	302	68.93	30.96	37.23	22.86	56.87	27.57	47.12	24.67	30.16	200
O	301	78.67	30.54	36.91	23.11	68.66	25.57	—	23.23	27.57	170
S	301	41.26	26.91	39.56	24.15	28.94	28.29	—	23.51	32.69	170
Te	300	11.35	28.96	42.09	25.06	-4.03	29.35	—	—	—	—

^a Measured in 70% CH₂Cl₂, 25% CDCl₃ with added TMS, in ppm from TMS.

^b Temperature for the measurement of the ring carbons and for the average of the geminal CH₃ carbons.

^c Measured at temperatures below coalescence.

^d Temperature for observation of distinct geminal CH₃ carbons.

^e Carbons numbered by analogy to the heterocycles.

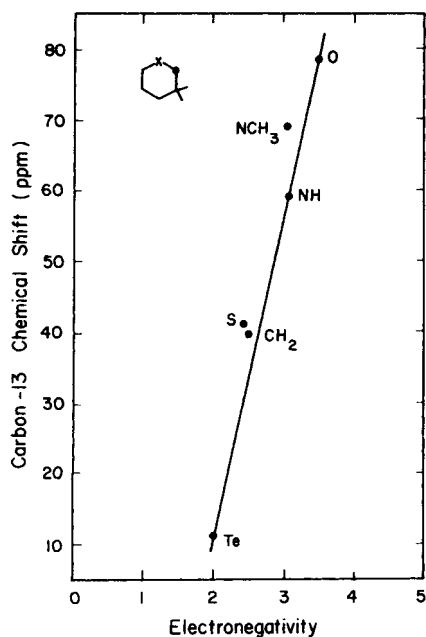


Figure 2. The ^{13}C chemical shift of C-2 in 1 as a function of electronegativity.

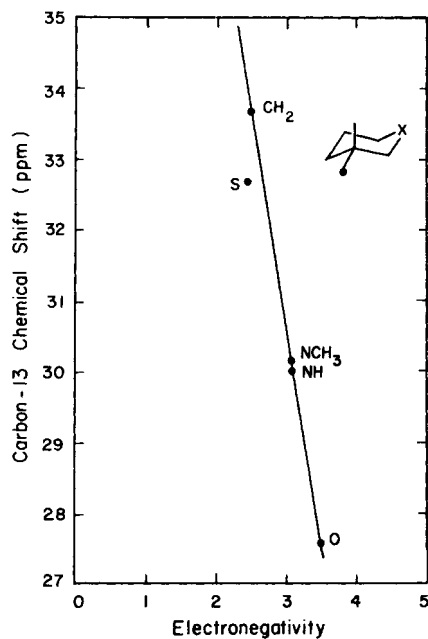


Figure 5. The ^{13}C chemical shift of the equatorial 3-methyl in 1 as a function of electronegativity.

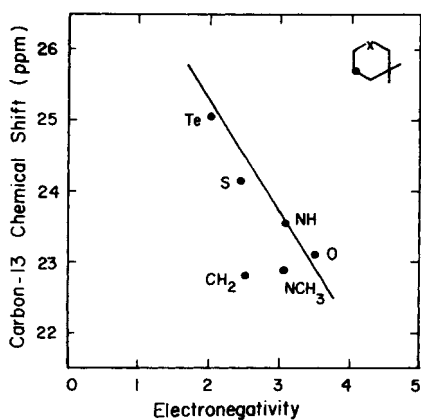


Figure 3. The ^{13}C chemical shift of C-5 in 1 as a function of electronegativity.

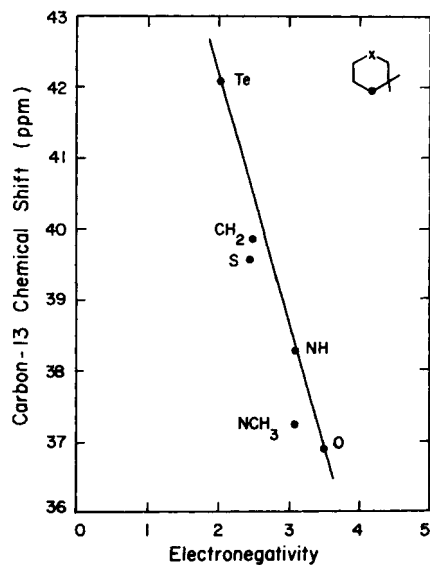


Figure 6. The ^{13}C chemical shift of C-4 in 1 as a function of electronegativity.

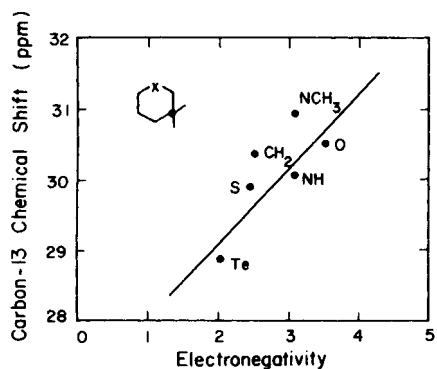


Figure 4. The ^{13}C chemical shift of C-3 in 1 as a function of electronegativity.

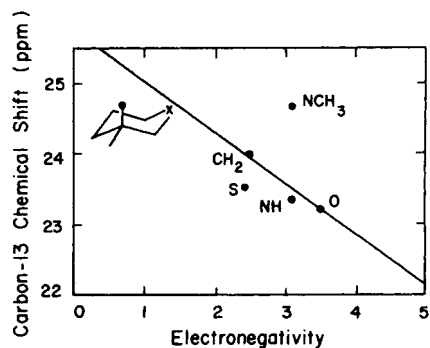


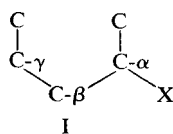
Figure 7. The ^{13}C chemical shift of the axial 3-methyl in 1 as a function of electronegativity.

are only small differences between the effects at the 2- and 6-carbons of **1** and at the 2,6-carbons of **2**. Thus, the slope of the plots of the chemical shift vs electronegativity are 43 ppm/electronegativity unit for the 2-carbon of **1**, 50 for the 6-carbon and 54 for the 2,6-carbons of **2**. The positive sign denotes a downfield shift with increased electronegativity.

Scatter is larger for the β -carbons (Figs 3 and 4); deviations are expected⁸ for S, CH₂ and NCH₃. The situation is rather similar for the 5-carbon of **1** to that for the 3,5-carbons of **2**. Both have negative slopes (-1.5 and -2.5, respectively). These upfield shifts with increased electronegativity have been related to the Pople-Gordon alternation of charge⁸ and to linear electric field effects.⁴ The slope is reversed (+1.1) for the quaternary 3-carbon (Fig. 4). The sensitivity of this carbon to changes in X is very low, some 40 times less than that of the adjacent α -carbon. The reasons are not clear, but an examination of electric field effects may show that the shifts at the 3-carbon of **1** are not in contradiction with those at the 3,5-carbons of **2**.

The γ -anti effect

The equatorial methyl carbon of **1** exhibits a γ -anti effect (no such geometry is present in **2**). The shift is upfield with increased electronegativity of X, and the slope of Fig. 5 is -5.8 ppm/electronegativity unit. The linear nature of Fig. 5 suggests that changes in the γ -anti effect due to X are primarily polar effects. This upfield shift was remarked upon by earlier workers⁵ and attributed to a hyperconjugative interaction. Later, downfield effects were also observed, particularly when either C- α or C- γ carried a carbon substituent at the position normal to the zigzag path (I).⁵ Since our molecules lack such substitution, we do not



address these anomalies. A change of sign is not remarkable, because the absolute magnitude of the γ -anti effect is small.

We feel that the large magnitude of the γ -anti X dependence (-5.8 ppm/electronegativity unit) can be explained on the grounds that electronic communication between nuclei (C- α and X) is facilitated by a planar zigzag pathway.¹² Such upfield shifts over antiperiplanar pathways are well known in NMR spectroscopy. Upfield ¹⁹F shifts (antiperiplanar X-C-C-F) are observed with increased electronegativity of X, for example.¹³ The vicinal hydrogen/deuterium isotope effect on ¹⁹F shielding [H(D)-C-C-F] is also upfield and maximal in the antiperiplanar arrangement.^{14a} These observations can be attributed to the favorable arrangement for σ delocalization when the X-C-C-Y bonds are antiperiplanar.^{14b} Linear electric field effects may also contribute, particularly in substituted cases such as I.

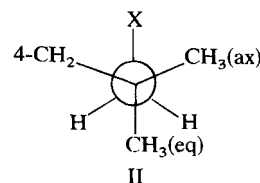
The γ -gauche effect

The polar effect of X on the 4-carbon shift in the unsubstituted system **2** is linear and relatively large (-5.3 ppm/electronegativity unit).⁸ The analogous effect in **1** also is linear (Fig. 6), although the slope is somewhat smaller (-3.5). In considerable contrast, the effect of X on the axial 3-methyl group (Fig. 7) is irregular and small. If a line is drawn through the four points lacking a substituent (CH₂, S, NH, O), the slope is only -0.7 ppm/electronegativity unit.

The typical overall γ -gauche effect (C-C-C-X v. C-C-C-H) is approximately -7 ppm,¹⁵ although the range is large and dependent on the degree of substitution of the carbons. The X dependence of the γ -gauche effect is smaller in magnitude (a range of 1.5 ppm for the axial 3-methyl) than the overall effect of replacement of H by X. The role of H is clearly unique³ (X, of course, cannot be H in **1**, so we examine only the X dependence in this study). It seems unlikely that a classical steric effect or a linear electric field effect can contribute strongly to the shielding of the axial 3-methyl, because its γ -effect is so insensitive to the nature of X.

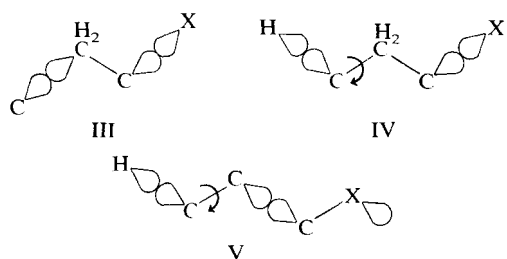
Consequently, we wish to view the γ -gauche effect as the result of at least two important factors. Replacement of H by X, in the general sense, provides a large upfield effect (the Beierbeck-Saunders mechanism³) associated with the presence of additional filled orbitals (covalent bonds and lone pairs) on X. In addition, changing X (CH₂, O, S, etc.) alters these orbitals and has a secondary influence on the γ -gauche effect. In this study, we do not consider substitution on carbons along the pathway, e.g. I, which undoubtedly causes other perturbations.¹²

Any explanation of the γ -gauche effect must consider the large dependence of the 4-carbon on the nature of X, as well as the low sensitivity of the axial 3-methyl to X. At first glance, the geometrical relationships between X and these two carbons appear to be identical (II), i.e. close to 60°. On closer examina-



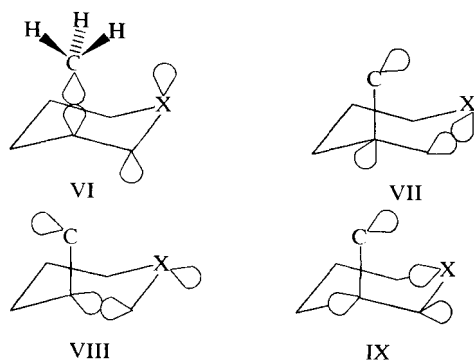
tion, the arrangements of specific polar bonds and lone pairs are seen to be quite different. Furthermore, the relationship between X and the axial 3-methyl group is subject to free rotation about at least one bond (CH₃-C-3). The relationship between X and C-4 is frozen into the ring structure. The specific arrangements of bonds and orbitals for each γ arrangement in this study will now be examined more closely.

If electronic communication down a molecular chain can be associated with the overlap of properly aligned (parallel) orbitals, then the γ -anti arrangement clearly has a distinct pathway from the γ -gauche arrangement. Structure III illustrates a primary contributor to the γ -anti interaction. Because the C- γ -C- β -C- α -X

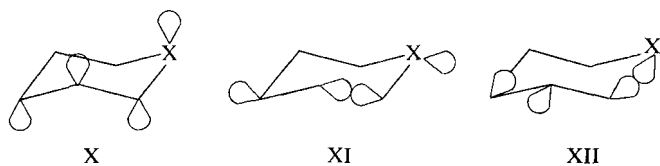


fragment lies in a single plane, this overlap is very effective. Furthermore, it does not depend on orbitals on X or C- γ beyond the C—C—C—X fragment. These are the orbitals whose positions are modulated by internal rotation. Overlap in III is not affected by C- γ —C- β or by C- α —X rotation. Backlobe overlap, as in IV, is clearly modulated by C- γ —C- β rotation (CH₃—C in **1**) and, hence, may contribute less than the type of overlap in III. The hyperconjugative interaction with orbitals on X (V) is modulated by both C- γ —C- β and C- α —X rotation. Furthermore, III depends on only the single overlap integral, whereas V requires a pair of overlap integrals.

The γ -*gauche* arrangements are best seen in the context of the 6-membered ring. Parallel orbital arrangements between X and the axial 3-methyl group are given by VI–IX. Of these, VII–IX are affected by CH₃—C- β rotation. Only VI would convey electronic



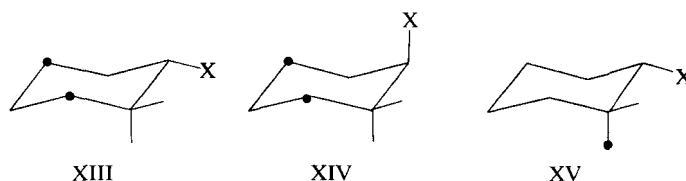
information concerning X to C- γ without modulation by methyl rotation (when X is free to rotate, even this rearrangement is subject to modulation). The analogous arrangements for C-4 are given by X–XII. Each of



these is actually represented twice, because of the pseudo two-fold symmetry of the ring. The ring structure prevents rotation about any of the components of the pathway. Consequently, this γ -*gauche* arrangement is relatively effective in passing electronic information on X to C- γ . This explanation is similar to the one given for the thiane case (**2**, X = S).¹⁰ The cross-ring, through-space interaction, from X directly to

C-4, however, is probably less important than one based on overlap between parallel orbitals on adjacent atoms. The slow time scale of ring reversal compared to that of methyl rotation appears to provide a critical difference between the two γ -*gauche* arrangements. Indeed, the importance of ring rigidity vs methyl-type free rotation has been well documented for the effect of substituents on geminal H—C—H coupling constants.¹⁶

If our explanation of the difference between these two types of γ -*gauche* effects is correct, it should apply to other reported systems. The 1-substituted cyclohexane system¹⁷ provides the best test, because of the relative rigidity of intergroup relationships (XIII–XV). In these cases, the perturbing group X is



attached to the ring and can rotate freely. The resonating carbon atom is either part of the ring and cannot rotate, or is a 2-methyl group that can rotate. Indeed, the γ -*anti* effect depends linearly on the electronegativity of X, with slopes of -3.5 for the effect of equatorial X on C-5 and -2.0 on C-3 (XIII). These plots utilize the data of references 4 and 17 and can be found in Ref. 18. Again, the methyls at C-2 reduce the effect. On the other hand, the γ -*gauche* effect of axial X on the same two carbons (XIV) is almost without dependence on the nature of X. Free rotation, in this case about X, dilutes the electronic effect. The only set in this series that does not fit clearly into the pattern is the γ -*gauche* effect of equatorial X on the axial 2-methyl group (XV). This relationship is relatively linear, with a slope of -3.0 . One possible explanation is that the X group in XV is locked between the two vicinal methyl groups, so that rotation is hindered about all concerned bonds.

SUMMARY AND CONCLUSIONS

We have examined the γ effect of an atom or group (X) on the shielding of three geometrically well-defined carbons in 3,3-dimethylheteracyclohexanes (**1**). Our attention has been directed to the relative shifts of the carbons as X is changed (CH₂, NH, NCH₃, O, S, Te), rather than on the absolute magnitude of the γ effect (C—C—C—H compared to C—C—C—X). As part of the ring, X of course cannot be H. Observation of the dependence of the γ effect on specific properties of X permits definition of its mechanism.

The γ -*anti* effect, as exemplified by the effect of X on the equatorial 3-methyl group, is linearly dependent on electronegativity. The planar zigzag path (I and III) has been associated with facilitated passage of

electronic information in numerous contexts. One possible mechanism is the hyperconjugative action depicted in structure III. The absolute magnitude of the γ -*anti* shift is relatively small. In a general survey of the literature,¹⁵ we have found that typical magnitudes are in the range from +1 to -2 ppm (minus is upfield) for a wide range of perturbing atoms (CH₃, OH, NH₂, Cl and Br, when X is exocyclic and the resonating carbon is within a ring). Thus, small perturbations by substituents along the pathway, for example at C- α and C- γ in I, can easily change the sign of the γ -*anti* effect. Because this effect is so close to zero, the significance of a change in sign should not be emphasized. Our observations also show that the polar influence of X on the γ -*anti* effect is manifested even when the resonating carbon is undergoing free rotation. Thus, the zigzag line-up of orbitals does not require a rigid pathway. Orbitals on the resonating or perturbing atoms that are outside the pathway and, hence, are modulated by rotation must not be involved.

The typical range of the γ -*gauche* effect for the same substituents enumerated in the previous paragraph is -4 to -8 ppm, with little dependence on the steric nature of the perturbing group.¹⁵ Within molecule **1**, the γ -*gauche* effect on the axial 3-methyl carbon is, in fact, almost entirely independent of X. On the other hand, the γ -*gauche* effect on carbon-4 has a dependence on the electronegativity of X that is linear and of comparable magnitude to that in the γ -*anti* case. We attribute this latter dependence to electronic interactions along the network of parallel orbitals in the rigid framework of the ring (X-XII). Although, formally, the axial 3-methyl group has a similar pathway (II), electronic communication is apparently disrupted by the ability of the methyl group to rotate freely (VII-IX). Thus, in contrast to the γ -*anti* effect, the electronic dependence of the γ -*gauche* effect on the polar properties of X requires a rigid pathway.

The γ -*gauche* effect appears to derive primarily from a large contribution that is relatively independent of the nature of the perturbing group X. The explanation in terms of the effects associated with removal of the γ -H appears to be substantiated.³ Superimposed upon this major contribution is a polar effect from X, amounting to 1-4 ppm/electronegativity unit and depending on rotational properties of the pathway.

In a related paper¹⁵ we report that the γ effect appears to have an overall dependence on the dihedral angle within the C-C-C-X pathway. In the present paper, we have examined only two points along this pathway, close to 60° and 180°. Parallel orbitals are also possible at 0°, so that a study of electronegativity effects at that angle would be instructive.

EXPERIMENTAL

Carbon-13 spectra were measured with a Varian CFT-20 NMR spectrometer, operating in the pulsed Fourier transform mode with proton decoupling. From

800 to 2000 scans were routinely accumulated. Proton spectra were measured on a Perkin-Elmer R-20B NMR spectrometer operating at 60 MHz. Chemical shifts are reported in parts per million downfield from tetramethylsilane (TMS). Variable temperature ¹³C spectra were measured for samples dissolved in a 25% CDCl₃/70% CH₂Cl₂ solvent system, with a trace of internal TMS added for reference. Probe temperatures were measured with an Omega model 175 thermocouple inserted into a sample tube containing 30% CDCl₃/70% CH₂Cl₂. The reported temperatures were obtained by averaging the readings before and after the accumulation of data. The field/frequency stabilization of the spectrometer was obtained by locking on the ²H signal of CDCl₃.

2,2-Dimethyl-1,5-pentanediol

A solution of 25 g (0.16 mol) of 2,2-dimethylglutaric acid (Aldrich) in 60 ml of anhydrous diethyl ether was added dropwise to a slurry of 20 g (0.51 mol) of LiAlH₄ in 850 ml of anhydrous diethyl ether. The mixture was refluxed for 24 h, cooled, and quenched with 20 ml of H₂O, 20 ml of 15% NaOH and 60 ml of H₂O. The slurry was filtered and the inorganic salts were extracted with 3 × 150 ml of boiling tetrahydrofuran (THF). The combined ethereal extracts were dried (Na₂SO₄), filtered, evaporated *in vacuo*, and distilled to give a colorless, viscous liquid (19.7 g, 96%), b.p. 137-138°C (12-15 mm Hg) [lit.¹⁹-b.p. 130°C (12 mm Hg)]; ¹H NMR δ 0.85 (6, s, CH₃), 1.2-1.6 (4, m, CH₂), 3.3 (2, s, CH₂), 3.5-3.7 (2, t, CH₂), 3.8 (2, s, OH).

1,5-Dibromo-2,2-dimethylpentane²⁰

Into a nitrogen-purged, 1000 ml, three-necked, round-bottomed flask equipped with a magnetic stirrer and a pressure-equalizing addition funnel, were placed 52 g of triphenylphosphine, 12.74 g (96.5 mmol) of 2,2-dimethyl-1,5-pentanediol and 182 ml of dry dimethylformamide. After the triphenylphosphine had dissolved, approximately 10 ml of Br₂ were added dropwise with stirring, and the temperature was maintained between 20 and 25 °C until the addition of two drops of Br₂ left a persistent yellow tint. The mixture was stirred at room temperature for 8 h. All volatile materials were distilled from the reaction flask, up to 120 °C at aspirator pressure, until triphenylphosphine oxide began to condense in the receiving flask. After 600 ml of H₂O were added to the distillate, the organic layer was separated. The aqueous layer was extracted with 3 × 150 ml of diethyl ether. The combined organic extracts were dried over Na₂SO₄, rotary-evaporated, and distilled to give 10.66 g (43%) of the dibromide, b.p. 83-84 °C (2 mm Hg); ¹H NMR δ 1.01 (6, s, CH₃), 1.3-2.1 (4, m, CH₂), 3.29 (2, s, CH₂Br), 3.29-3.50 (2, t, CH₂Br).

3,3-Dimethylthiane²¹

1,5-Dibromo-2,2-dimethylpentane (15.76 g, 61 mmol) was dissolved in five times its volume of absolute

ethanol. A 1.5 mol equivalent of $\text{Na}_2\text{S}\cdot 9\text{H}_2\text{O}$ (freshly recrystallized from 95% ethanol) was dissolved in enough 70% ethanol to make an approximately 2 M solution. One-half of the Na_2S solution was transferred to a 250 ml, round-bottomed flask equipped with two addition funnels, a magnetic stirrer, and a reflux condenser. The mixture was stirred and heated to reflux. The ethanol solution of the dibromide and the remainder of the ethanol solution of Na_2S were then added at such rates that both additions were complete in 1 h. The addition funnels were removed, and the mixture was refluxed for 24 h and then steam-distilled until the distillate no longer formed a precipitate when tested with ethanolic HgCl_2 . The distillate was diluted with 50 ml of H_2O and extracted repeatedly with pentane until the aqueous layer no longer reacted with ethanolic HgCl_2 . The combined pentane extracts were dried over Na_2SO_4 , concentrated, and distilled at atmospheric pressure to give 5.9 g (75%) of 3,3-dimethylthiane b.p. 169–170 °C [lit.²¹—b.p. 168 °C (760 mm Hg)]; $^1\text{H NMR}$ δ 1.05 (6, s, CH_3), 1.2–1.5 (2, m, CH_2), 1.6–2.0 (2, m, CH_2), 2.37 (2, s, CH_2), 2.4–2.7 (2, m, CH_2).

3,3-Dimethyloxane²²

2,2-Dimethyl-1,5-pentanediol (16.6 g, 0.13 mol) was placed in a 1000 ml, round-bottomed flask equipped with a magnetic stirrer, a heating mantle and an addition funnel. After slow addition of 120 ml of 50% H_2SO_4 , the product was distilled directly from the reaction mixture. The organic layer was separated, dried over Na_2SO_4 , and stored under N_2 . Further purification was not required. The yield was 12.3 g (85%); $^1\text{H NMR}$ δ 0.85 (6, s, CH_3), 1.3–2.0 (4, m, CH_2), 3.1 (2, s, CH_2), 3.3–3.7 (2, t, CH_2).

2,2-Dimethylglutarimide²³

2,2-Dimethylglutaric acid (3.9 g, 24 mmol) was placed in a 50 ml, round-bottomed flask equipped with a condenser and a gas inlet. Gaseous NH_3 was allowed to pass over the diacid while the flask was slowly heated to 190 °C. The condensed crystals of the imide were collected after 4 h. Excess condensed H_2O was removed from the reaction flask and heating was continued. This process was repeated until all the diacid had been consumed. The crude imide (7.6 g, 81%) was used without further purification in the subsequent reduction [m.p. 142–145 °C (lit.²⁴ m.p. 150 °C)]; $^1\text{H NMR}$ (CDCl_3) δ 1.25 (6, s, CH_3), 1.6–2.0 (2, t, CH_2), 2.6–2.8 (2, t, CH_2), 7.2 (1, s, NH).

3,3-Dimethylpiperidine²⁵

Into a N_2 -purged, 1000 ml, three-necked, round-bottomed flask equipped with a condenser, a drying tube, a magnetic stirrer and a N_2 inlet were placed 8.0 g of LiAlH_4 and 150 ml of dry THF. 2,2-Dimethylglutarimide (7.6 g, 54 mmol) in 200 ml of dry THF was added dropwise with stirring and ice bath

cooling. After addition was complete, the mixture was refluxed for 15 min, then stirred at room temperature for 24 h. The reaction was carefully quenched with 8 ml of H_2O , 8 ml of 15% NaOH solution, and 24 ml of H_2O , and stirred overnight to homogenize the inorganic salts. The mixture was suction-filtered, and the inorganic salts were extracted thoroughly with boiling THF. The combined organic extracts were dried twice over KOH pellets. The product was separated and distilled under vacuum with the aid of a fraction cutter/Vigreux assembly. After most of the THF had distilled, CaH_2 was added to the residue. Distillation was continued to give 4.9 g (80%) of 3,3-dimethylpiperidine: b.p. 133–135 °C; $^1\text{H NMR}$ δ 0.87 (6, s, CH_3), 1.2–1.6 (4, m, CH_2), 2.4 (2, s, CH_2), 2.5–2.8 (2, t, CH_2).

1,3,3-Trimethylpiperidine²⁶

3,3-Dimethylpiperidine (4.86 g, 43 mmol), formic acid (4.7 ml, 0.11 mol) and 37% formaldehyde solution (3.54 ml, 0.047 mol) were placed in a 500 ml Erlenmeyer flask. The mixture was warmed on a steam bath until gas ceased to evolve, and then for an additional 2 h. To this mixture 5 ml of HCl was added, and the excess formic acid and formaldehyde were evaporated off on the steam bath. The clear, brown residue was dissolved in 3 ml of H_2O and made alkaline with excess 25% NaOH solution. The amine was separated and the aqueous residue was saturated with NaOH pellets to precipitate additional product. The combined organics were dried twice over KOH pellets. Bulb-to-bulb distillation produced 4.0 g (73%) of 1,3,3-trimethylpiperidine.

3,3-Dimethyltellurane²⁷

Because of the extreme sensitivity of the product to air oxidation, this reaction sequence and work-up were carried out under an inert atmosphere. Into a N_2 -purged, three-necked, round-bottomed flask equipped with a condenser, a magnetic stirrer and a gas inlet, were placed 24.8 g (0.21 mol) of sodium formaldehydesulfoxylate, 5.5 g (43 mmol) of Te powder and 15.8 g (0.40 mol) of 1,5-dibromo-2,2-dimethylpentane in 20 ml of 95% ethanol. After addition was complete, the mixture was stirred at room temperature for 12 h until the color had changed to a creamy beige. Subsequent steam distillation afforded approximately 0.5 ml of product. Because of the inefficiency of the steam distillation, the reaction mixture was extracted with CH_2Cl_2 . The combined organic extracts were dried over Na_2SO_4 and stored under N_2 at 5 °C. Further purification was found to be inadvisable, as it promoted oxidation of the product. Approximately 5.5 g (c. 60%) of the product was obtained.

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