Anal. Calcd for $C_{24}H_{36}N_4O_9$: C, 54.95; H, 6.92; N, 10.68. Found: C, 54.79; H, 7.22; N, 10.59).

The nine peptide fragments were then condensed by the azide procedure to minimize racemization. Two residues of Asn (position 24 and 40), two residues of Trp (position 25 and 37), and three residues of Asp(OBzl) (position 9, 15, and 21) were introduced by the stepwise *p*-nitrophenyl ester procedure.[16] Poor solubility in DMF prompted the use of DMSO-DMF mixtures for acylations beyond the octapeptide stage.

Purification of intermediates including the protected pentatriacontapeptide, Z(OMe)-(GIP 9-43)-OH (mp 230–233°; $[\alpha]^{25}D$ −8.4° in DMF; R_f 0.66 in $CHCl_3$–methanol–water 8:3:1; amino acid ratios in a hydrolysate with 3 *N* Tos-OH: $Asp_{6.14}Thr_{0.90}Ser_{1.78}Glu_{5.39}Gly_{1.38}Ala_{2.35}Val_{1.00}Met_{0.68}Ile_{2.72}Leu_{2.51}Tyr_{0.75}Phe_{1.05}Trp_{1.33}Lys_{5.05}His_{0.77}$ recovery 86%; Anal. Calcd for $C_{273}H_{362}N_{54}O_{70}S_2 \cdot 9H_2O$: C, 57.06; H, 6.67; N, 13.16. Found: C, 57.33; H, 6.48; N, 12.86), was carried out by batchwise washing with 5% acetic acid and water followed by repeated precipitation from DMF or mixtures of DMF and DMSO with methanol or ethyl acetate. The compounds were characterized by thin layer chromatography, elemental analysis, and amino acid analyses of 3 *N* Tos-OH hydrolysates.

Z(OMe)-(GIP 9-43)-OH was deblocked with TFA in the presence of anisole containing 2% ethanedithiol and condensed with the azide corresponding to I. The resulting product, without further purification, was exposed to hydrogen fluoride for 60 min at 0°. Anisole containing 2% ethanedithiol and skatol served as scavengers to avoid alkylation. The resulting deblocked peptide was immediately converted to the corresponding acetate with Amberlite CG-400 (type 1, acetate form) and purified by column chromatography on Sephadex G-25 and CM-cellulose. To elute the desired compound, 0.2 *M* acetic acid was used in the former step and 0.01 *M* ammonium bicarbonate (pH 7.8)[17] in the latter. Absorbency at 280 mμ due to Trp served to monitor the chromatographic purification.

The tritetracontapeptide thus purified exhibited a sharp single spot on thin layer chromatography in two different solvent systems: R_f 0.54 and 0.77 in 1-butanol–pyridine–acetic acid–water 30:6:20:24 and 30:20:6:24 respectively. Its purity was further assessed by amino acid analyses of 3 *N* Tos-OH hydrolysates and aminopeptidase AP-M digests:[18] (ratios are given in parentheses): $Tyr_{1.65(1.70)}Ala_{3.16(2.97)}Glu_{6.53(0.99)}Gly_{2.14(2.24)}Thr_{1.97}Phe_{2.13(1.66)}Ile_{3.71(4.02)}Ser_{2.48}Asp_{6.46(3.60)}Met_{0.63(0.64)}Lys_{5.60(5.43)}Arg_{0.85(0.93)}Val_{1.00(1.00)}Trp_{1.20(1.63)}Leu_{2.37(2.15)}His_{0.79(0.90)}$ Gln + $Thr_{(6.58\ calcd.\ as\ Thr)}$Asn + $Ser_{(4.45\ calcd\ as\ Ser)}$, average recovery 93 and 82%, respectively.

When administered by continuous drop infusion to Heidenhein pouch dogs, synthetic GIP (1 μg kg^{-1} hr^{-1}) suppressed gastric acid secretion stimulated by tetragastrin (4 μg/kg). The intravenous administration of synthetic GIP (1 μg/kg) to rats elicited insulin release.

References and Notes

(1) Amino acid, peptides, and their derivatives mentioned in this communication are of the L configuration. The following abbreviations are used: Z = benzyloxycarbonyl, Z(OMe) = *p*-methoxybenzyloxycarbonyl, Tos = *p*-toluenesulfonyl, OBzl = benzyl ester, O-*t*-Bu = *tert*-butyl ester, ONP = *p*-nitrophenyl ester, DMF = dimethylformamide, DMSO = dimethyl sulfoxide, TFA = trifluoroacetic acid, DCC = dicyclohexylcarbodiimide, HOBT = *N*-hydroxybenzotriazole.
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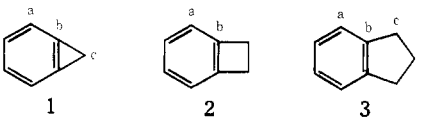
One-Bond ^{13}C–^{13}C Coupling Constants in Benzocycloalkenes[1]

Sir:

Considerable interest has been focused recently on ^{13}C–^{13}C spin–spin coupling constants, since these parameters yield, together with ^{13}C–^{1}H coupling constants, valuable information about structure and bonding in organic molecules.[2] Whereas long range ^{13}C–^{13}C coupling constants are best accessible from ^{13}C labeled material,[2] those over one bond can be obtained in suitable cases from the ^{13}C-satellites in proton decoupled ^{13}C Fourier transform NMR spectra of compounds containing ^{13}C in natural abundance.[3,4]

We now report the results of those measurements for the benzocycloalkenes **1–4** and for 1,2-diethylbenzene (**5**). The data, including those for toluene,[5] are collected in Table I.



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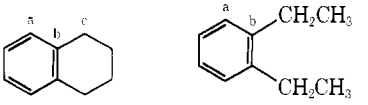

4 5

Not unexpected, the carbon–carbon coupling constants of benzocyclopropene (**1**) are exceptional, owing to the special bonding situation in the three-membered ring. Using eq 1[6]

$$^{1}J(^{13}C\text{–}^{13}C) = Ks(i)s(j) \qquad (1)$$

that relates $^{1}J(^{13}C$–$^{13}C)$ data to the product of the fractional s character of the two orbitals ϕ_i and ϕ_j forming the CC bond and that is well established for hydrocarbons,[4,7,8] the

Table I. One-Bond $^{13}C-^{13}C$ Spin–Spin Coupling Constants (Hz)[a] for Compounds 1–5[b] and for Toluene[c,d]

	1	2	3	4	5	Toluene
J(a,b)	87.1	59.8	59.8	58.6	57.3	57.3
J(b,c)	20.8	35.4	41.5	41.5	43.9	44.2

[a] Maximum error ±1.22 Hz as determined by the experimental conditions; neat samples were measured with a Bruker HX-90 spectrometer operating at 22.63 MHz with simultaneous broad band ^1H decoupling at 90 MHz. [b] This work. [c] Reference 5. [d] For the chemical shift data of 1–5 see reference 9.

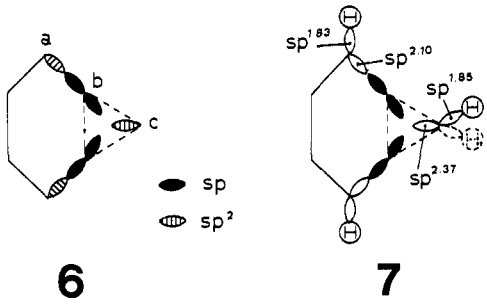

Figure 1. Hybridization models for the σ-bonds of benzocyclopropene.

Walsh model **6** for **1** can be tested with $K = 550$, a value that has been found reliable to ±50 Hz[4,7] for similar compounds. J(a,b) = 91.7 and J(b,c) = 22.9 Hz is obtained, in good agreement with the experimental results (Table I). An even better agreement with experiment is possible for J(b,c) if one considers the $^{13}C-^1H$ coupling constant of 170 Hz found at the methylene position of **1**.[9] Using eq 2[10]

$$^1J(^{13}C-^1H) = 500s(i) \qquad (2)$$

one finds 3.6% more s character in the CH_2 bonds of **1** than in those of cyclopropane ($^1J(^{13}C-^1H)$ = 161 Hz[10]). Consequently, each CC single bond in the three-membered ring of **1** has 1.8% less s character and a corrected coupling constant J(b,c) of 20.4 Hz results. A similar argument applies to J(a,b), since the $^{13}C-^1H$ coupling constant at C(a) of **1** again is larger than the corresponding value for the model compound, this time benzene (168.5 vs. 158.3 Hz[9,11]). The difference in s character amounts to 2.0% for the CH bonds at C(a) in both compounds and this in turn leads to a calculated J(a,b) of 88.9 Hz. Thus, the simple hybridization model **7** is in excellent agreement with the experimental $^{13}C-^1H$ and $^{13}C-^{13}C$ coupling constants. sp-Hybridization at C(1) and C(2) of **1** also explains the deformation of the benzene ring found for this compound[12] and the cyclopropene character at these carbons and the C(1)–C(2) bond established by X-ray analysis for 3,6-diphenyl-7,7-dicarbomethoxy-**1**.[13,14]

For **2** J(b,c) has increased but is still smaller than for indane (**3**) and tetraline (**4**). The value of 35.4 Hz agrees well with that found for the corresponding coupling constant in methylenecyclobutane (34.2 Hz[4]), indicating that the bonds of the four-membered ring of **2** still have enhanced p character. The $^{13}C-^1H$ coupling constant of 138 Hz for the CH_2 bonds[9,15] supports this interpretation. J(a,b) signals "normal" behavior for the benzene ring of **2**. The $^{13}C-^1H$ coupling constant at C(a), however, is again larger than in benzene (162 Hz[9]). A hybridization trend similar to that derived for **1** but less pronounced seems, therefore, indicated. Thus, the picture obtained for **1** and **2** lends experimental support to the Finnegan–Streitwieser model[16,17] for the enhanced acidity of protons α to strained ring systems.[18]

The data for toluene show that the methyl group in **5** does not exert any substituent effect on J(b,c). This is also true for J(a,b) in toluene, since the same value is found for $^1J(^{13}C-^{13}C)$ in benzene,[7] and other observations point in the same direction.[3]

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Synthesis, Characterization, and X-Ray Structure of a Tetrahydrofuran Adduct of μ-Iodo-bis[tris(2-diphenylarsinoethyl)amine]nickel(I) Tetraphenylborate

Sir:

The tripod ligand tris(2-diphenylarsinoethyl)amine, $N[CH_2CH_2As(C_6H_5)_2]_3$, nas$_3$, reacts with nickel(II) halides to give five-coordinate complexes of nickel(II) having the general formula $[NiX(nas_3)]B(C_6H_5)_4$ (I), X = Br, I.[1] In the presence of sodium tetrahydroborate, nickel(I) complexes with the formula $[NiX(nas_3)]$ (X = Cl, Br, I)[2] are obtained. If the complexes (I) are treated with $NaBH_4$ in ethyl alcohol in less than stoichiometric amounts, however, dimeric compounds of nickel(I) having the general formula $[Ni_2X(nas_3)_2]B(C_6H_5)_4$ (X = Br, I) are obtained. This reduction can be ascribed only partly to $NaBH_4$, as the $NaBH_4$:Ni(I) ratio is 1:2; the tetraphenylborate ion, which has previously been found to reduce nickel(II),[3] is thought to be responsible for completing the reduction.

The molecular structure of the compound $[Ni_2I(nas_3)_2]B(C_6H_5)_4 \cdot 3THF$ has been determined by a three-dimensional X-ray analysis. The crystals are monoclinic, space group $C2/c$, with lattice constants a = 15.476 (2) Å, b = 25.820 (3) Å, c = 27.209 (3) Å, β = 96.42 (2)°, V = 10804.0 Å^3, d_{measd} = 1.45 g cm^{-3}, d_{calcd} = 1.444 g cm^{-3},