592 *J. Org. Chem.* **1988**, *53*, 592–596

^{13}C–^{13}C Coupling Constants in Bridgehead Polycycloalkanecarboxylic Acids

Ernest W. Della,* Hemakanthi Gangodawila, and Paul E. Pigou

School of Physical Sciences, Flinders University of South Australia, Bedford Park, South Australia 5042, Australia

Received August 10, 1987

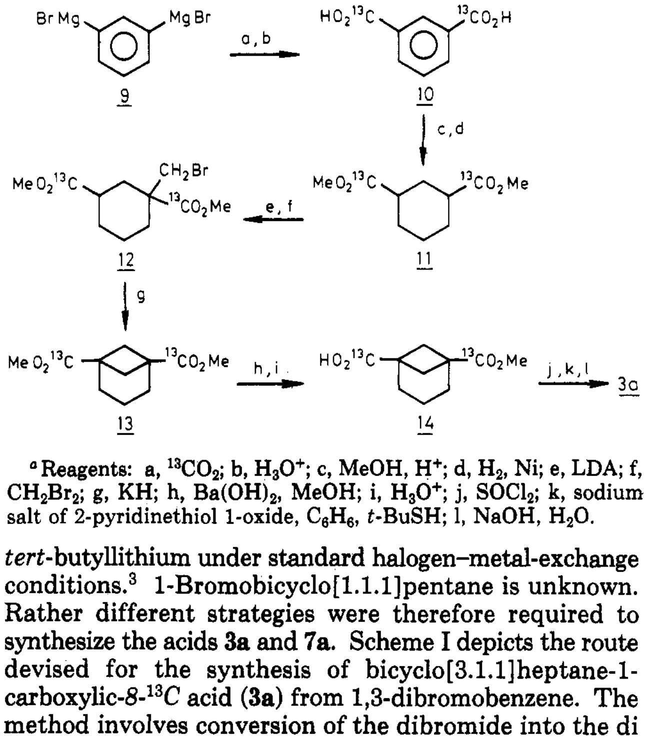
A series of bicyclic and polycyclic systems substituted with the ^{13}C-labeled carboxyl group at the bridgehead have been synthesized for ^{13}C NMR analysis. It is found that one-bond coupling to the bridgehead carbon atoms shows a reasonable correlation with s character. Vicinal coupling to the unsubstituted bridgehead carbon in the bicyclic compounds was observed to be considerably smaller than anticipated. Calculated values of $^3J(^{13}C-^{13}C_{bridgehead})$ obtained by SCF MO calculations performed at the INDO level are in excellent agreement with those determined experimentally and demonstrate that the magnitude of ^3J(C–C) is a reflection of opposing through-bond and through-space contributions. On the basis of the MO calculations, the large four-bond $^{13}C-^1H$ coupling in bicyclo[1.1.1]pentane-1-carboxylic-*6-*^{13}C acid can be attributed almost entirely to the effect of through-space interactions.

Introduction

We recently reported[1] the results of an NMR investigation of the series of polycycloalkanes **1b**–**5b**, **7b**, and **8b** (Figure 1) substituted with ^{13}C-labeled methyl at the bridgehead, with particular emphasis on the magnitude of the one-bond and vicinal $^{13}C-^{13}C$ coupling constants. The latter proved to be especially interesting because in the bicyclic compounds **3b**, **4b**, and **7b**, the values of $^3J(^{13}C_{Me}-^{13}C_{bridgehead})$ were considerably smaller than anticipated on the basis of the number of three-bond pathways available for transmission of coupling information. This was attributed to the presence of through-space interactions involving orbitals centered on the bridgehead carbons in **3b**, **4b**, and **7b** and the fact that contributions to the overall coupling as a result of these interactions oppose those transmitted through the σ bonds. MO calculations at the INDO level supported the operation of the through-space phenomenon and gave values of coupling constants in good agreement with those determined experimentally.

We decided to embark upon a similar investigation of the complementary ^{13}C-labeled carboxylic acids **1a**–**8a** because they allow a direct comparison of the effect of sp^3- vs sp^2-hybridized carbon on the coupling constants. We now report the synthesis and NMR analysis of the acids.

Scheme I[a]



[a] Reagents: a, $^{13}CO_2$; b, H_3O^+; c, MeOH, H^+; d, H_2, Ni; e, LDA; f, CH_2Br_2; g, KH; h, $Ba(OH)_2$, MeOH; i, H_3O^+; j, $SOCl_2$; k, sodium salt of 2-pyridinethiol 1-oxide, C_6H_6, *t*-BuSH; l, NaOH, H_2O.

Results and Discussion

Syntheses. Compounds **1a**, **2a**, **4a**, **5a**, **6a**, and **8a** were synthesized from the corresponding halides by carbonation of the lithio derivatives obtained by metalation of the chlorides **1**, **2**, and **4** (X = Cl) or bromides **5**, **6**, and **8** (X = Br). Lithiation of the bridgehead halides was facilitated by sonication, although reduction of bromocubane (**5**, X = Br) under these conditions was still very slow. Difficulties have been encountered previously in attempts to prepare simple metalated cubanes.[1,2] We have subsequently found that bromocubane undergoes metal–halogen exchange with *tert*-butyllithium quite readily, and this process represents a vastly superior method for the preparation of lithiocubane. Synthesis of the bicyclo[3.1.1]heptyl and bicyclo[1.1.1]pentyl acids **3a** and **7a** presented a problem, however, because neither 1-chlorobicyclo[3.1.1]heptane (**3**, X = Cl) nor 1-chlorobicyclo[1.1.1]pentane (**7**, X = Cl) could be induced to react with lithium even under more forcing conditions.[3] 1-Bromobicyclo[3.1.1]heptane is similarly reluctant to undergo metalation with lithium and, surprisingly, was found to be inert to *tert*-butyllithium under standard halogen–metal-exchange conditions.[3] 1-Bromobicyclo[1.1.1]pentane is unknown. Rather different strategies were therefore required to synthesize the acids **3a** and **7a**. Scheme I depicts the route devised for the synthesis of bicyclo[3.1.1]heptane-1-carboxylic-*8-*^{13}C acid (**3a**) from 1,3-dibromobenzene. The method involves conversion of the dibromide into the di Grignard reagent **9**, which, despite reported difficulties,[4] was accomplished smoothly. Reaction of **9** with 2 equiv of $^{13}CO_2$ gave doubly labeled isophthalic acid (**10**). Alkylation of the diester **11** by way of its enolate anion[5] was effected with dibromomethane; potassium hydride mediated cyclization of the derived product **12** afforded the diester **13**, which was transformed via its half-ester **14** into **3a** by using the reductive decarboxylation method reported recently.[6] The ^{13}C-labeled carbon dioxide released in the final step was recovered as $Ba^{13}CO_3$ by leading the effluent gases into an aqueous barium hydroxide trap. The synthesis of bicyclo[1.1.1]pentane-1-carboxylic-*6-*^{13}C acid (**7a**) was accomplished as depicted in Scheme II. Brominative decarboxylation[7] of 3-phenylbicyclo[1.1.1]pentane-1-carboxylic acid (**15**)[8] gave the bromide **16**, which when

---

[1] Della, E. W.; Pigou, P. E. *J. Am. Chem. Soc.* **1984**, *106*, 1085.

[2] Eaton, P. E.; Castaldi, G. *J. Am. Chem. Soc.* **1985**, *107*, 724.

[3] Della, E. W.; Tsanaktsidis, J., unpublished observations.

[4] See: (a) Millar, I. T.; Heaney, H. *Q. Rev., Chem. Soc.* **1957**, *11*, 109. (b) Ioffe, S. T.; Nesmeyanov, A. N. *Methods of Elemento-Organic Chemistry*; Nesmeyanov, A. N., Kocheshkov, K. A., Eds.; North-Holland: Amsterdam, 1967; Vol. 2, pp 31–32 for leading references.

[5] (a) Gassman, P. G.; Proehl, G. S. *J. Am. Chem. Soc.* **1980**, *102*, 6863. (b) Warner, P. M.; Chen, B.-L.; Wade, E. *J. Org. Chem.* **1981**, *46*, 4795.

[6] Della, E. W.; Tsanaktsidis, J. *Aust. J. Chem.* **1986**, *39*, 2061.

[7] Della, E. W.; Tsanaktsidis, J., manuscript in preparation.

0022-3263/88/1953-0592$01.50/0 © 1988 American Chemical Society

Table I. Carbon-13 Chemical Shifts[a,b] in the ^{13}C-Labeled Carboxylic Acids 1a–8a

no.	C1	C2	C3	C4	C5	C6	C7	C8	C_{COOH}
1a[c]	38.19 (14.19)	27.90 (1.90)	25.24 (−0.76)	23.78 (−0.22)	25.24 (−0.76)	27.90 (1.90)	27.90 (1.90)	25.24 (−0.76)	185.39
2a[c]	52.12 (15.52)	32.94 (2.94)	30.01 (0.00)	37.85 (1.25)	30.01 (0.00)	32.94 (2.94)	42.37 (3.77)		183.78
3a	45.89 (11.76)	30.08 (0.72)	15.69 (−0.26)	27.74 (−1.62)	29.60 (−4.53)	35.32 (2.12)	35.32 (2.12)		182.82
4a[c]	51.76 (12.26)	28.92 (2.62)	27.35 (1.05)	36.56 (−2.94)	42.71 (3.71)	42.71 (3.71)			180.42
5a	55.42 (7.31)	49.46 (1.35)	45.24 (−2.87)	47.89 (−0.22)	45.24 (−2.87)	49.46 (1.35)	45.24 (−2.87)	49.46 (1.35)	178.78
6a	39.06 (2.56)	35.62 (−1.97)	39.06 (2.56)	35.62 (−1.97)	39.06 (2.56)	56.26 (7.80)	35.62 (−1.97)		179.43
7a	42.31 (8.72)	51.36 (0.61)	27.63 (−5.96)	51.36 (0.61)	51.36 (0.61)				175.58
8a	26.33 (16.03)	24.71 (14.41)	33.52 (0.12)	31.07 (1.17)	33.52 (0.12)	24.71 (14.41)	32.68 (−0.72)		181.60

[a] Measured in chloroform-*d*, ±0.04 ppm. [b] Values in parentheses are the substituent-induced chemical shift. [c] Chemical shifts for these compounds dissolved in acetone-d_6 have been reported in ref 2.

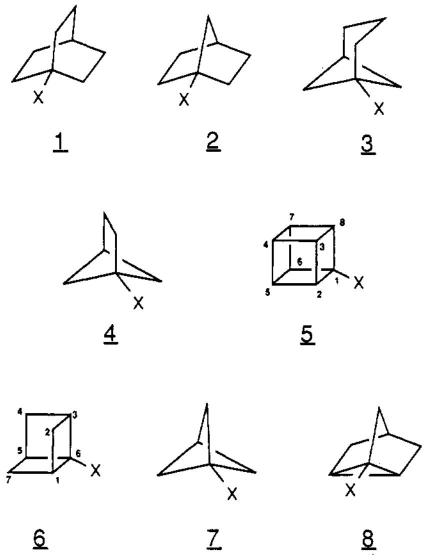
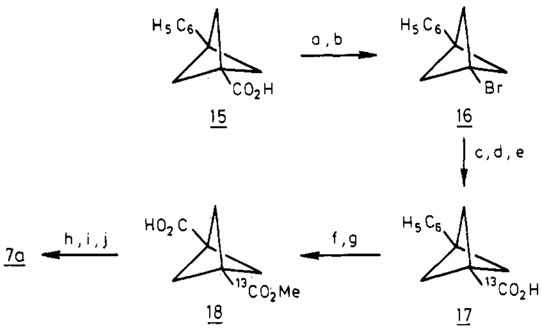


Figure 1. a, X = ^{13}COOH; b, X = $^{13}CH_3$; c, X = ^{1}H.

Scheme II[a]



[a] Reagents: a, $SOCl_2$; b, sodium salt of 2-pyridinethiol 1-oxide, $CF_3CHBrCl$; c, *t*-BuLi; d, $^{13}CO_2$; e, H^+; f, MeOH, H^+; g, $RuCl_3$, KIO_4, CH_3CN; h, $SOCl_2$; i, sodium salt of 2-pyridinethiol 1-oxide, *t*-BuSH; j, NaOH, H_2O.

Table II. ^{13}C–^{13}C Coupling Constants, ^{n}J(C–C),[a] in the ^{13}C-Labeled Carboxylic Acids 1a–8a

no.	^{1}J (C*x*)	^{2}J (C*x*)	^{3}J (C*x*) (ϕ)[b]	^{4}J (C*x*)
1a[c]	58.29 (C1)	0.85 (C2,6,7)	3.54 (C3,5,8) (180)	0.33 (C4)
2a[c]	62.06 (C1)	ncd (C2,6)[d] ncd (C7)	3.82 (C3,5) (161) 5.43 (C4) (180)	
3a	60.39 (C1)	ncd (C2) 1.31 (C6,7)	3.05 (C3) (169) 5.80 (C5) (144)	0.58 (C4)
4a[c]	64.71 (C1)	1.88 (C2) 0.34 (C5,6)	3.42 (C3) (180) 8.54 (C4) (159)	
5a	64.36 (C1)	2.29 (C2,6,8)	2.69 (C3,5,7) (135)	0.78 (C4)
6a	65.48 (C6)	1.54 (C1,3,5)	2.31 (C2,4,7) (121)	
7a	64.55 (C1)	ncd (C2,4,5)	9.68 (C3) (180)	
8a	81.27 (C1)	ncd (C2,6) 2.25 (C7)	0.67 (C3,C5) (147) 3.11 (C4) (180)	

[a] In Hz ± 0.05 Hz. [b] $\phi \equiv C_{COOH}$–C–C–C dihedral angle in degrees. [c] See ref 2 for coupling constants reported previously. [d] Ncd $\equiv$ no coupling detected (≤0.3 Hz).

treated with *tert*-butyllithium in ether/pentane at −60 °C followed by carbonation of the derived lithio derivative with $^{13}CO_2$ yielded the labeled acid **17**. Oxidation of the latter as its methyl ester was effected with potassium metaperiodate/Ru(IV)[9] to give the half-ester **18**. Decarboxylation of **18** under Barton conditions[6] followed by hydrolysis afforded the acid **7a**.

NMR Parameters. The ^{13}C NMR spectra of the acids **1a**–**8a** were measured on chloroform-*d* solutions of the compounds with either 66% or 90% enrichment. The data on the bicycloalkanecarboxylic acids **1a**, **2a**, and **4a** were in reasonable agreement with those described previously by Barfield, Marshall, and their colleagues;[10] there is some discrepancy with several chemical shifts and ^{1}J(C–C) values, and this is ascribed to the effect of the different solvent, acetone-d_6, employed by those workers.

Carbon-13 shifts are assembled in Table I. The substituent-induced chemical shifts of the α carbons that occur upon introduction of the carboxyl group at the bridgehead are also included. These α-effects show a moderate spread ranging from 7.3 ppm in cubanecarboxylic acid (**5a**) to 16.0 ppm in the nortricyclene derivative **8a**, which are to be compared with the average α-effect (ca. 14–16 ppm) of the carboxyl group in unstrained tertiary systems. If the value for the acid **8a** is disregarded, it can be seen that, in the range of substrates under study, the deshielding effect of the carboxyl group decreases with increasing ring strain.

The ^{13}C–^{13}C coupling constants between the substituent and the ring carbons are displayed in Table II. In accordance with the general expectation[11] that one-bond

---

(8) Applequist, D. E.; Renken, T. L.; Wheeler, J. W. *J. Org. Chem.* **1982**, *47*, 4985.

(9) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(10) Barfield, M.; Brown, S. E.; Canada, E. D., Jr.; Ledford, N. D.; Marshall, J. L.; Walter, S. R.; Yakali, E. *J. Am. Chem. Soc.* **1980**, *102*, 3355.

(11) See: (a) Hansen, P. E.; Wray, V. *Org. Magn. Reson.* **1981**, *15*, 102. (b) Egli, H.; von Philipsborn, W. *Tetrahedron Lett.* **1979**, 4265. (c) Khim, T.; Webb, G. A. *Org. Magn. Reson.* **1979**, *12*, 103 for leading references.

Table III. Experimental and Calculated Vicinal Coupling Constants, ^3J(C–C), Involving the Bridgehead Carbons in the Acids 2a–4a and 7a

no.	exptl *J*, Hz	calcd *J*,[a] Hz total	TB[b]	TS[c]	bridgehead C...C dist, Å
2a	5.43 (C4)	5.20	7.92	−2.72	2.32
3a	5.80 (C5)	6.39	12.77	−6.38	2.14
4a	8.54 (C4)	10.47	19.16	−8.69	2.08
7a	9.68 (C3)	11.90	33.11	−21.21	1.85

[a] INDO SCF MO calculations. [b] TB ≡ through-bond contribution to ^3J(C–C). [c] TS ≡ through-space contribution to ^3J(C–C).

carbon–carbon coupling is governed by the product of the s electron densities at the nuclei, the values of ^1J(C–C) in **1a**–**8a** increase regularly along the series, the constituents of which have been arranged in order of increasing s character at the bridgehead. A similar trend was observed by Stöcker[12] for the lower monocyclic carboxylic acid homologues. The predominance of the Fermi contact mechanism in determining the magnitude of the ^1J(C–C) coupling constants in these compounds contrasts strongly with observations[1] in the methyl-substituted hydrocarbons **1b**–**8b** in which the one-bond couplings occur in an unpredictable fashion and within a very narrow range. An alternative view in the case of the acids is that the data should be interpreted with caution inasmuch as the observed correlation between ^1J(C–C) and s character in **1a**–**8a** may simply reflect a fortuitous cancellation of the spin dipolar and spin orbit contributions to the coupling.

The array of carboxylic acids **1a**–**8a** provides a modest range of dihedral angles between the substituent and the ring carbons, and by and large, vicinal coupling in these substrates was found to obey a Karplus-type expression. Thus ^3J(C–C) values vary from 2.31 Hz in **6a** (CCCC dihedral angle 121°) to 3.82 Hz in **2a** (CCCC dihedral angle 161°). The notable exceptions are the couplings to the bridgehead carbons in the bicyclic acids **2a**, **3a**, **4a**, and **7a**. Barfield, Marshall, and their associates have reported previously[10] that the value of $^3J(\mathrm{C_{COOH}}$–C4) in the acid **4a** is considerably smaller than expected if coupling involving C4 in the bicyclo[2.2.1]heptyl acid **2a** is accepted as a reference. In principle, vicinal coupling to the bridgehead carbon in **4a** should be double that in **2a** because in the latter there is one three-bond σ pathway available for transmission of spin information whereas in the lower homologue **4a** there are two such paths. The reduced value of ^3J(C–C) in **4a** was rationalized in terms of a negative contribution to coupling associated with the through-space pathway.

Inclusion of the bicyclic acids **3a** and **7a** in the present study extends the range of compounds having the potential for strong transannular orbital overlap, and in addition, vicinal coupling in **3a** and **7a** can be relayed via two and three equivalent pathways, respectively. Values of $^3J(^{13}\mathrm{C_{COOH}}$–$^{13}\mathrm{C_{bridgehead}})$ in the bicycloalkanecarboxylic acids are reproduced in Table III together with theoretical values obtained by MO calculations performed at the INDO level.[13] For the calculations, experimentally determined molecular geometries of the parent hydrocarbons[14] were used for all compounds except bicyclo[2.1.1]hexane (**4c**). Wiberg and Wendoloski[15] have shown recently by ab initio calculations that the geometry determined by electron diffraction[16] is incorrect; their optimized structure, which has been substantiated by photoelectron spectroscopy measurements,[17] was therefore employed in the calculations.

Inspection of the data in Table III reveals that the experimental coupling constants to the bridgehead carbons in **3a**, **4a**, and **7a** are appreciably smaller than would be predicted on the basis of additivity of coupling constants over multiple paths.[18] Thus, in **2a** vicinal coupling to C4 is 5.43 Hz (calculated 5.20 Hz), and in **3a** and **4a** the values of ^3J(C–C) are 5.80 Hz (calculated 6.39 Hz) and 8.54 Hz (calculated 10.47 Hz), respectively. Despite the fact that three three-bond coupling pathways are available in **7a**, vicinal coupling to C3, 9.68 Hz (calculated 11.90 Hz), is significantly lower than that predicted by simple additivity. The excellent agreement between the experimental and theoretical values of ^3J(C–C) is impressive. A valuable feature of the MO calculations is the facility to dissect the relative importance of the through-bond and through-space contributions to ^3J(C–C). This is achieved by the simple expediency of setting elements of the Fock matrices associated with orbitals centered on the bridgehead carbons equal to 0 in each SCF cycle.[10] Nonbonded interactions are now eliminated in these modified MO calculations, and the values of coupling constants so obtained reflect only mechanisms of coupling transmitted through the σ framework. The data in Table III demonstrate quite convincingly that, in the more constrained bicyclic systems, both bonded and nonbonded contributions to coupling are important, but that the overall effect corresponds to a significant reduction in the magnitude of ^3J(C–C) because the interactions oppose each other.

The extent of the through-space effect is dependent on the efficiency of overlap of the rear lobes of the bridgehead carbon exocyclic bonding orbitals. Such overlap is particularly effective in bicyclo[1.1.1]pentyl derivatives **7** as a consequence of the proximity of the bridgehead carbons and the fact that the relevant orbitals centered on these carbons are collinear. A compelling illustration of the importance of the effect of the through-space interactions in this system is the magnitude of $^4J(^{13}\mathrm{C_{COOH}}$–$^1\mathrm{H_{bridgehead}})$ in **7a**. MO calculations suggest that such coupling is particularly strong (18.72 Hz), being composed almost entirely of transannular contributions (16.96 Hz), with the residue (1.76 Hz) arising from through-bond relay. The theoretical value of ^4J(C–H) is in good agreement with the experimental value (14.22 Hz), and as the calculations demonstrate, the bonded and nonbonded interactions act in concert.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 237 grating spectrometer. ^{1}H and ^{13}C NMR spectra were obtained on a JEOL FX90Q instrument operating at 89.56 and 22.53 MHz, respectively. Samples were dissolved in $\mathrm{CDCl_3}$ which also served as internal lock; chemical shifts are referenced to $\mathrm{Me_4Si}$. For chemical shift measurements, ^{13}C spectra were normally run at 5000-Hz spectral width with 8K data points, corresponding to 0.05-ppm digital resolution. Accurate measurement of coupling constants was performed by recording spectra at 200–400 Hz with 16K/32K data

---

[12] Stöcker, M. *J. Chem. Res., Synop.* **1981**, 52.

[13] QCPE Program FINITE No. 224.

[14] For electron diffraction data on **1c**, see: Yokozeki, A.; Kuchitsu, K.; Morino, Y. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 2017. For electron diffraction data on **2c**, see: Chiang, J. F.; Wilcox, C. F., Jr.; Bauer, S. H. *J. Am. Chem. Soc.* **1968**, *90*, 3149. For electron diffraction data on **3c**, see: Dallinga, G.; Toneman, L. H. *Recl. Trav. Chim. Pays-Bas.* **1969**, *88*, 185. For electron diffraction data on **7c**, see: Chiang, J. F.; Bauer, S. H. *J. Am. Chem. Soc.* **1970**, *92*, 1614.

[15] Wiberg, K. B.; Wendoloski, J. J. *J. Am. Chem. Soc.* **1982**, *104*, 5679.

[16] Chiang, J. F. *J. Am. Chem. Soc.* **1971**, *93*, 5044.

[17] Della, E. W.; Pigou, P. E.; Livett, M. K.; Peel, J. B. *J. Electron Spectrosc. Relat. Phenom.* **1984**, *33*, 163.

[18] Marshall, J. L.; Faehl, L. G.; Kattner, R. *Org. Magn. Reson.* **1979**, *12*, 163.

points, giving 0.02-Hz digital resolution. Mass spectra were determined on an AEI MS30 spectrometer. Analytical GC was performed on a Perkin-Elmer Sigma 3B chromatograph using 6 ft × 0.125 in. stainless steel columns packed with 10% OV-17 on Chromosorb W or 10% Carbowax 20M on Chromosorb G. Barium carbonate-^{13}C (91% enriched) was purchased from Prochem, U.K.

Bicyclo[2.2.2]octane-1-carboxylic-*9*-^{13}C acid (**1a**), bicyclo[2.2.1]heptane-1-carboxylic-*8*-^{13}C acid (**2a**), bicyclo[2.1.1]hexane-1-carboxylic-*7*-^{13}C acid (**4a**), and tricyclo[2.2.1.0^{2,6}]heptane-1-carboxylic-*8*-^{13}C acid (**8a**) were obtained from the corresponding chlorides/bromides as described previously.[1] Tricyclo[3.1.1.0^{3,6}]heptane-6-carboxylic acid (**6**, X = COOH), mp 92.5-95 °C, was synthesized from bicyclo[3.2.1]oct-5-en-3-one as reported.[19] Cubanecarboxylic acid (**5**, X = COOH), mp 124–125.5 °C, was prepared by the published procedures.[20] 3-Phenylbicyclo[1.1.1]pentane-1-carboxylic acid (**16**) was obtained from diethyl phenylmalonate by following the combined literature procedures.[8,21]

1,3-Dicarbomethoxybenzene-*7,8*-^{13}C. A mixture of 1,3-dibromobenzene (4.0 g, 17 mmol) and dried magnesium turnings (0.9 g, 37.5 mmol) in tetrahydrofuran was heated at reflux under an atmosphere of nitrogen for 15 h when GC analysis showed that practically all of the dihalide had been consumed. ^{13}C-Labeled carbon dioxide (75% enrichment) was generated by slow addition of concentrated sulfuric acid onto barium carbonate-^{13}C (7.09 g, 35.8 mmol) and condensed into dry tetrahydrofuran (140 mL) at −78 °C. The suspension of the di Grignard reagent was cooled to 0 °C and then introduced slowly via syringe, with stirring, to the THF solution held at −78 °C. The mixture was allowed to warm to room temperature and then worked up in the usual manner to give the crude diacid **10**. Treatment of the latter with diazomethane furnished 1,3-dicarbomethoxybenzene-*7,8*-^{13}C (2.3 g, 70%).

5-Carbomethoxybicyclo[3.1.1]heptane-1-carboxylic-*8,9*-^{13}C Acid (14). Hydrogenation of 1,3-dicarbomethoxybenzene-*7,8*-^{13}C (2.2 g, 11.2 mmol) was performed as described for the unlabeled isomer[22] and the derived diester **11** alkylated with dibromomethane via its enolate.[5] Cyclization of the latter **12** was effected with potassium hydride,[5] giving 1,5-dicarbomethoxybicyclo[3.1.1]heptane-*8,9*-^{13}C (**13**) (1.2 g, 50%), whose physical properties were in accord with those of the unlabeled isomer. The diester **13** was stirred with a solution of barium hydroxide octahydrate (0.84 g, 2.7 mmol) in methanol (10 mL) and water (3 mL) at room temperature for 18 h.[6] Water was added and the mixture extracted with ether. The aqueous layer was acidified with concentrated hydrochloric acid and extracted with carbon tetrachloride. The organic layer was dried ($MgSO_4$) and evaporated, and the residue sublimed, giving the half-ester **14** (0.62 g, 55%), which had identical physical properties with those of the unlabeled material.[6]

Bicyclo[3.1.1]heptane-1-carboxylic-*8*-^{13}C Acid (3a). Reductive decarboxylation of the half-ester **14** (0.59 g, 3 mmol) was conducted in the manner described for the synthesis of the unlabeled substance.[6] Hydrolysis of the crude product gave the acid **3a**, which was purified by sublimation (0.33 g, 80%) and shown to have physical properties consistent with those of the natural isomer.[6]

Cubanecarboxylic-*9*-^{13}C Acid (5a). Method A. Lithiation of bromocubane[23] (1.0 g, 5.5 mmol) in cyclohexane was performed as outlined previously[1] and the solution added slowly, with stirring, to a cold (−78 °C) ether solution of $^{13}CO_2$ prepared from barium carbonate-^{13}C (1.1 g, 5.4 mmol) as described above. After 30 min, the mixture was allowed to warm to room temperature, and normal workup afforded, after sublimation, pure cubanecarboxylic-*9*-^{13}C acid (**5a**) (0.2 g, 25%), which was found to have the expected physical properties.

Method B. A well-stirred solution of bromocubane (0.53 g, 2.9 mmol) in anhydrous ether (10 mL) cooled to −78 °C was treated dropwise with a solution of 1.7 M *tert*-butyllithium in pentane (3.8 mL, 2.2 equiv). After 3 h, the milky suspension was added via cannula to a stirred solution of $^{13}CO_2$ (70% label, 1.2 equiv) in ether at −78 °C. Workup and sublimation of the product furnished the acid **5a** (0.24 g, 55%), which was identical with the sample obtained above.

Tricyclo[3.1.1.0^{3,6}]heptane-6-carboxylic-*8*-^{13}C Acid (6a). 6-Bromotricyclo[3.1.1.0^{3,6}]heptane[24] (**6**, X = Br) (0.15 g, 0.87 mmol) was treated with a large excess of lithium shot in boiling cyclohexane with ultrasound activation as described for the synthesis of cubyllithium.[1] The solution of the lithiated species **6** (X = Li) was added with stirring to a solution of $^{13}CO_2$ (1.1 equiv) in ether maintained at −78 °C. Normal workup and sublimation of the crude product gave the labeled acid **6a** (33 mg, 25%), which had physical properties identical with those of the natural isomer.

1-Bromo-3-phenylbicyclo[1.1.1]pentane (16). Brominative decarboxylation of the acid **15** to give **16** was performed by a method developed recently in these laboratories.[7] 3-Phenylbicyclo[1.1.1]pentane-1-carboxylic acid (**15**) (3.5 g, 18.6 mmol) was converted by standard treatment with thionyl chloride into the acid chloride (3.9 g), which had bp (Kugelrohr) 95 °C (0.1 mm). A solution of the acid chloride in 1-bromo-1-chloro-2,2,2-trifluoroethane (25 mL) was added dropwise to a vigorously stirred mixture of the sodium salt of 2-pyridinethiol 1-oxide (3.33 g, 22.3 mmol) and 4-(dimethylamino)pyridine (0.2 g) in 1-bromo-1-chloro-2,2,2-trifluoroethane (75 mL) at reflux under irradiation with a 300-W tungsten lamp. After the evolution of carbon dioxide had ceased, the mixture was cooled and filtered through Celite. The filtrate was washed successively with concentrated hydrochloric acid, water, sodium bicarbonate solution, and water. The organic layer was dried ($MgSO_4$) and the solvent evaporated. Distillation (Kugelrohr) (46 °C (0.01 mm)) of the residue gave 1-bromo-3-phenylbicyclo[1.1.1]pentane (**16**) (3.7 g, 88%) as a white solid: mp 32 °C; ^{1}H NMR ($CDCl_3$) δ 2.53 (s, 6 H), 7.32 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 128.34 (C′2), 126.99 (C′4), 126.17 (C′3), 137.66 (C′1), 60.13 (C2), 43.56 (C1 or C3), 36.78 (C3 or C1); mass spectrum, *m/e* 224 (M, 8), 222 (M, 8), 143 (100), 128 (30), 103 (44), 91 (9).[25]

3-Phenylbicyclo[1.1.1]pentane-1-carboxylic-*6*-^{13}C Acid (17). A stirred solution of **16** (2.55 g, 11.4 mmol) in dry ether (15 mL) was cooled to −78 °C under a nitrogen atmosphere and treated dropwise with 1.7 M *tert*-butyllithium in pentane (13.8 mL, 23.4 mmol). The temperature of the mixture was allowed to rise to −50 °C, and stirring was continued for 3 h. Meanwhile a solution of $^{13}CO_2$ (50% label, 22 mmol) in THF (120 mL) was prepared from $Ba^{13}CO_3$ as described above. The solution of the alkyllithium was added slowly to the stirred THF solution held at −78 °C, and after 15 min, the cold bath was removed and the reaction mixture allowed to warm to room temperature. Standard workup followed by sublimation of the residue gave the acid **17** (1.3 g, 60%) as a colorless solid: mp 173–174 °C (lit.[8] mp of the unlabeled isomer 176–176.5 °C).

3-Carbomethoxybicyclo[1.1.1]pentane-1-carboxylic-*6*-^{13}C Acid (18). The acid **17** (1.7 g, 9 mmol) was esterified with diazomethane, and the derived ester was stirred vigorously with a mixture of potassium periodate (30.3 g, 132 mmol), ruthenium trichloride (46 mg), acetonitrile (18 mL), water (28 mL), and carbon tetrachloride (18 mL) as described.[9] The progress of reaction was monitored by ^{1}H NMR. After 5 days, the mixture was worked up[9] and the crude product sublimed to yield the half-ester **18** (1.28 g, 83%) as a colorless solid: mp 138–140 °C (lit.[8] mp of the unlabeled isomer 139.5–140 °C).

Bicyclo[1.1.1]pentane-1-carboxylic-*6*-^{13}C Acid (7a). Conversion of the half-ester **18** (1.28 g, 7.5 mmol) into the corresponding acid chloride was effected with thionyl chloride under standard conditions. A solution of the acid chloride in benzene (15 mL) was added to a suspension of the sodium salt of 2-pyridinethiol 1-oxide (1.37 g, 9.2 mmol), 4-(dimethylamino)pyridine (50 mg), and *tert*-butylthiol (2.15 mL, 19 mmol) in boiling benzene (70 mL) as described.[6] When the evolution of carbon dioxide had ceased, the excess mercaptan was destroyed by stirring

---

[19] Monti, S. A.; Harless, J. M. *J. Am. Chem. Soc.* **1977**, *99*, 2690.

[20] (a) Eaton, P. E.; Cole, F. W. *J. Am. Chem. Soc.* **1964**, *86*, 962, 3157. (b) Chapman, N. B.; Key, J. M.; Toyne, K. J. *J. Org. Chem.* **1970**, *35*, 3860.

[21] Wiberg, K. B.; Dailey, W. P.; Walker, F. H.; Waddell, S. T.; Crocker, L. S.; Newton, M. *J. Am. Chem. Soc.* **1985**, *107*, 7247.

[22] Della, E. W.; Tsanaktsidis, J. *Aust. J. Chem.* **1985**, *38*, 1705.

[23] Della, E. W.; Patney, H. K. *Aust. J. Chem.* **1976**, *29*, 2469.

[24] Della, E. W.; Cotsaris, E.; Hine, P. T.; Pigou, P. E. *Aust. J. Chem.* **1981**, *34*, 913.

[25] Satisfactory microanalytical data on the bromide **16** were not obtained because of its lability.

the mixture for 4 h with calcium hypochlorite. Workup[6] followed by removal of solvent through a column packed with glass helices furnished the crude ester **7** (X = ^{13}COOMe). Hydrolysis of the latter and sublimation of the product gave **7a** (0.62 g, 74%) as a colorless solid. The physical properties of **7a** were consistent with those of the unlabeled substance:[8] ^{1}H NMR (CDCl$_3$) δ 10.24 (s, 1 H), 2.44 (t, 1 H, ^4J = 14.22 Hz), 2.11 (s, 6 H).

Acknowledgment. We thank the Australian Research Grants Committee for financial support.

Registry No. **1a**, 73948-77-3; **2a**, 73948-78-4; **3a**, 112043-87-5; **4a**, 73948-79-5; **5a**, 112043-88-6; **6a**, 112043-89-7; **7a**, 73948-80-8; **8a**, 87969-55-9; **10**, 112043-90-0; **14**, 112043-91-1; **16**, 112043-92-2; **17**, 112043-93-3; **18**, 112043-94-4.

Conformational Effects in the Alkali Metal Reduction of Diaryl Sulfides and Dibenzothiophene

Manuel A. Francisco* and Argo Kurs

Exxon Research and Engineering Company, Clinton Township, Route 22 East, Annandale, New Jersey 08801

Alan R. Katritzky* and Danuta Rasala

Department of Chemistry, University of Florida, Gainesville, Florida 32611

Received April 9, 1987

In alkali metal reductions, the carbon–sulfur bond cleavage that occurs in diaryl sulfides and similar structures such dibenzothiophene is shown to be controlled not by the relative stability of the reactive intermediates but by their degree of conformational freedom. Regardless of the stability of the reactive intermediates, diaryl sulfides suffer carbon–sulfur bond cleavage because the aryl groups are free to assume a configuration that favors cleavage. Dibenzothiophene, although similar in structure to diphenyl sulfide, does not have such freedom and therefore, instead of carbon–sulfur bond cleavage, undergoes ring hydrogenation. The behavior of di-1-naphthyl sulfide and di-4-quinolinyl sulfide support this conclusion and provide further evidence for intramolecular coupling of the aryl moieties at some reactive intermediate stage to form an episulfide type of intermediate. This is then followed by a double carbon–sulfur bond cleavage to extrude sulfur.

Alkali methal reductions in ammonia have been synthetically useful and mechanistically interesting for over 50 years.[1] While these same reactions are now frequently used in synthetic organic chemistry, there are still unresolved questions concerning mechanisms, the nature of reactive intermediates, and the effects of solvent, temperature, and structure.[2]

Our work with the alkali metal reductions of aromatic sulfur compounds has led us to investigate several of these unresolved questions. The literature shows that diaryl sulfides, such as diphenyl sulfide, are cleaved at the carbon–sulfur bond by alkali metals in ammonia to yield a thiophenol and a derivative of benzene.[3] Even with excess metal, the products of carbon–sulfur bond cleavage result, and there is no evidence for ring hydrogenation without carbon–sulfur bond cleavage.

Dibenzothiophene is similar in structure to diphenyl sulfide and can be considered as diphenyl sulfide bonded between the 2- and 2′-positions. Reductions of dibenzothiophene in liquid ammonia with 2–3 equiv of alkali metal reportedly give products of ring hydrogenation with no carbon–sulfur bond cleavage.[4,5]

The reasons for this difference in reactivity between diaryl sulfides and dibenzothiophene with alkali metals in liquid ammonia have not been clear. Differences in metals and conditions could have been sufficient to make the studies on diaryl sulfides not directly comparable to those with dibenzothiophene, and the first step in the present study was to establish the pattern reactivity of dibenzothiophene and diphenyl sulfide under identical reduction conditions with the same alkali metal.

Table I. Summary of Gas Chromatography/Mass Spectral Data for Alkali Metal Reduction Products and Reactants

reactants	*m/e*[a]	products (yield,[b] *m/e*)
dibenzothiophne (**1**)	184	**1a** (major, 186), **1b** (minor, 188)
diphenyl sulfide (**2**)	188	**2a** (98.0, 78), **2b** (66.7, 110), **2c** (5.6, 218)
di-1-naphthyl sulfide (**3**)	286	**3** (57.4, 286), **3a** (10.4, 128), **3b** (13.0, 256), **3c** (1.0, 254), **3d** (13.0, 290), **3e** (5.1, 288)
1-naphthalenethiol (**4**)	160	**4a** (1.3, 130), **4b** (50.0, 162), **4c** (8.3, 322), **4d** (11.1, 318)
di-4-quinolinyl sulfide (**5**)	288	**5** (18.0, 288), **5a** (79.0, 256)

[a] *M/e* is the mass to charge ratio of moleculr ion taken from the mass spectral data. [b] Yields given are on a mole percent and were obtained by integration of the total ion chromatograms from the GC/MS data obtained on each reduction product with tetradecane as an internal standard (Experimental Section).

Results and Discussion

Dibenzothiophene (**1**), diphenyl sulfide (**2**), di-1-naphthyl sulfide (**3**), 1-naphthalenethiol (**4**) and di-4-quinolinyl sulfide (**5**) were reduced with 2 equiv of potassium metal (K^0) in liquid ammonia at -78 °C. The reduction products were characterized by gas chromatography/mass spectroscopy (GC/MS) (Table I). Schemes I–V show the probable cleavage paths of the investigated compounds.

Reduction of Dibenzothiophene (1) and Diphenyl Sulfide (2). Nature of Reactive Intermediates. Compound **1**, on reduction with potassium in liquid ammonia, gives 1,4-dihydrodibenzothiophene (**1a**) as the major product and 1,2,3,4-tetrahydrodibenzothiophene (**1b**) as

---

(1) Birch, A. J.; Slobbe, J. *Heterocycles* **1976**, *5*, 905.

(2) Mullen, K.; Huber, W.; Neumann, G.; Schnieders, C.; Unterberg, H. *J. Am. Chem. Soc.* **1985**, *107*, 801.

(3) Truce, W. E.; Tate, D. P.; Burgde, D. N. *J. Am. Chem. Soc.* **1960**, *82*, 2872.

(4) Huckel, W.; Nabih, I. *Chem. Ber.* **1956**, *89*, 2115.

(5) Gilman, H.; Jacoby, A. L. *J. Org. Chem.* **1938**, *3*, 108.

0022-3263/88/1953-0596$01.50/0 © 1988 American Chemical Society