Nuclear Magnetic Resonance Investigations of Small Rings. 3. ^{13}C NMR Spectra of Benzo-Annulated and Exo- and Endo-Benzocyclobuta-Annulated Derivatives of *exo*-Cyclopropanorbornane[1]

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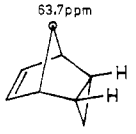
The synthesis and the ^{13}C NMR spectra of annulated bicyclo[2.2.1]heptanes are presented. The benzo and exo- and endo-benzocyclobuta fragments are the substituents on one side, while an exo-cyclopropa fragment is the substituent on the other side of the norbornane skeleton. The configurations of the annulating fragments are well apparent from the ^{13}C NMR data. A good diagnosis in assigning the stereochemistry is the ^{13}C chemical shift of the methano bridge. Considering the norbornane moiety as the basic system, then its methano bridge carbon atom chemical shift should be incremented by +5.9 ppm for an endo-benzocyclobuta substituent, −6.7 ppm for an exo-benzocyclobuta substituent, and by −11.4 ppm for an exo-cyclopropa substituent as result of their annulation. The anti-oriented substituents on the cyclopropyl group increment the chemical shift of the methano bridge carbon atom with +1.6 ppm for the CH_2OH group, +1.8 ppm for the CHO group, and +1.7 ppm for the COOMe group. However, the effect of these substituents on the three-membered ring carbon atoms seems to be identical no matter whether the cyclopropane ring is monocyclic or annulated to substituted norbornanes.

More than a decade ago, Tori et al.[2] discovered the remarkable γ-syn (shielding) and γ-anti (deshielding) effects exerted by a cyclopropane ring annulated to bicyclo[2.2.1]heptane skeleton upon its bridging carbon atom, C_8. In the ^{13}C NMR spectrum of the endo-annulated compound 1, the chemical shift of the bridge carbon atom



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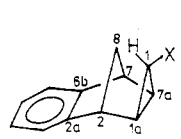
is shifted downfield, while in the exo-isomer **3** it is shifted upfield by comparison with the same carbon atom from norbornene. More recently, new examples were discovered, and thus it was realized that such effects exist whenever a cyclopropane ring is annulated with a cyclopentane moiety.[3] Embedded in a rigid skeleton, a cyclopropane fragment can exert either one[3b-d] or, simultaneously, both effects.[3a,e] The replacement of either cyclopropane[3a,4a,b] or the cyclopentane[5] fragments with larger rings diminishes the γ-anti effect. However, an augmented γ-effect was noted when the cyclopropane ring was replaced by its heterocyclic congeners: oxirane,[6,7] aziridine,[7] and thiirane[7] annulated to bicyclo[2.2.1]heptane[6] or to benzvalene.[7] At present, no unified theoretical approach exists for explaining the γ-syn and γ-anti effects. Steric effects were considered as operative in the case of exo-fused cyclopropanes.[3d] For the deshielding effect of the endo-annulated cyclopropane, Christl[3a,e,4,7] and Kessler[3d] invoked electronic factors resulting from the in-phase interactions occurring among the unoccupied Walsh orbital of the endo-oriented cyclopropane and the highest occupied orbital of the bridge C–C–C bonds. As a result, charge transfer from the bridge C–C–C bonds toward the cyclopropane ring occurs, yielding the downfield shift for the methano carbon atom.

Table I. ^{13}C Chemical Shifts for the *exo*-Cyclopropabenzonorbornanes 4A–D[a]

X	compd	C_1	C_{1a}	C_2	C_8
H	**4A**	15.20	21.04	43.35	37.64
CH_2OH	**4B**	30.34	26.14	42.86	38.80
CHO	**4C**	38.60	30.03	42.94	39.58
COOMe	**4D**	28.64	30.30	42.99	39.38

[a] In ppm, downfield from internal standard Me_4Si, in $CDCl_3$ solutions.

In the present paper we report our results regarding the ^{13}C NMR spectra of bicyclo[2.2.1]heptane derivatives **4–6** and those of the references compounds **7–10**. We add new



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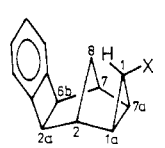

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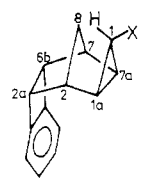

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A : X = H ; B : X = CH_2OH ; C : X = CHO ; D : X = COOMe

examples along with the observations of Tori,[2] Lippmaa,[3b] Stothers,[3c] and Kessler[3d] on the shielding effect of an exo-annulated cyclopropane, and we discuss (i) the hitherto uncommented effects of exo- and endo-annulated benzocyclobuta fragment upon the bridge carbon atom and (ii) the δ-effect of the CH_2OH, CHO, and COOMe on the same atom. We support the earlier findings that the chemical shift of the bridge C_8 carbon atom is a very powerful diagnosis regarding the configuration of rings annulated to

(1) (a) Taken in part from the Ph.D. Thesis of E.O. Hereafter paper 1 from this series should be considered ref 1b and paper 2 is considered ref 1c. (b) Gheorghiu, M. D.; Ciobanu, O. B.; Elian, M. *J. Magn. Reson.* **1981**, *44*, 330. (c) Gheorghiu, M. D.; Pârvulescu, L.; Drăghici, C.; Elian, M. *Tetrahedron Suppl.* **1981**, *37*, 143.

(2) Tori, K.; Ueyama, M.; Tsuji, T.; Matsamura, H.; Tanida, H.; Iwamura, H.; Kushida, K.; Nishida, T.; Satoh, S. *Tetrahedron Lett.* **1974**, 327.

(3) (a) Christl, M. *Chem. Ber.* **1975**, *108*, 2781. (b) Lippmaa, E.; Pekh, T.; Belikova, N. A.; Bobyleva, A. N.; Kalinichenko, A. N.; Ordubadi, M. D.; Plate, A. F. *Org. Magn. Reson.* **1976**, *8*, 74. (c) Cheng, A. K.; Stothers, J. B. *Org. Magn. Reson.* **1977**, *9*, 355. (d) Bicker, R.; Kessler, H.; Zimmermann, G. *Chem. Ber.* **1978**, *111*, 3200, (e) Christl, M.; Herbert, R. *Org. Magn. Reson.* **1979**, *12*, 150.

(4) (a) Christl, M.; Herbert, R. *Chem. Ber.* **1979**, *112*, 2022. (b) Yshii, Y.; Noda, R.; Kawahara, M.; Ogawa, M. *Org. Magn. Reson.* **1984**, *22*, 416.

(5) Günther, H.; Herring, W.; Seel, H.; Tobias, S.; de Meijere, A.; Scrader, B. *J. Org. Chem.* **1980**, *45*, 4329.

(6) Davies, S. G.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 2* **1975**, 861.

(7) Christl, M.; Leinninger, H.; Brunn, E. *J. Org. Chem.* **1982**, *47*, 662.

0022-3263/87/1952-5158$01.50/0

Table II. ^{13}C Chemical Shifts of the *exo*-Cyclopropabenzocyclobutanorbornanes 5 and 6[a]

X		compd	C_1	C_{1a}	C_2	C_{2a}	C_8
H	exo	**5A**	3.90	14.91	36.22	51.83	20.25
	endo	**6A**	0.87	12.81	37.04	50.82	32.31
CH_2OH	exo	**5B**	19.26	20.91	36.34	51.48	22.13
	endo	**6B**	16.24	18.29	37.03	50.48	34.05
CHO	exo	**5C**	28.59	25.60	36.39	50.71	22.06
	endo	**6C**	26.58	22.14	37.21	49.43	33.95
COOMe	exo	**5D**	18.51	25.67	36.37	50.69	21.95
	endo	**6D**	16.04	23.41	37.33	50.00	33.98

[a] All values are in ppm, downfield from internal Me_4Si, in $CDCl_3$ solutions.

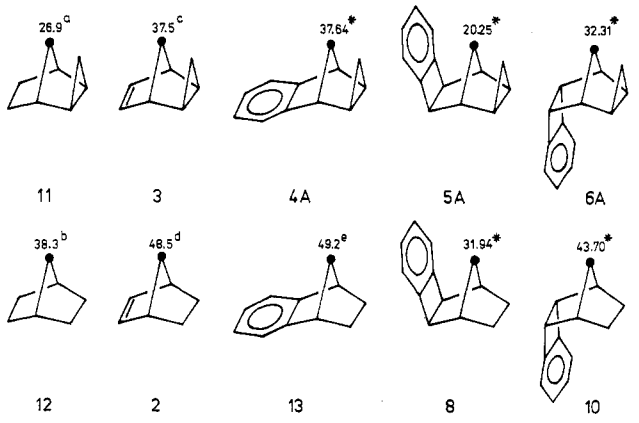


Figure 1. ^{13}C chemical shifts of the methano bridge carbon atom for the cyclopropane annulated compounds (first row) and the corresponding reference compounds (second row): (a) ref 3d; (b) ref 9; (c) ref 3b,c; (d) ref 2,9; (e) ref 2; (*) present work.

the bicyclo[2.2.1]heptane skeleton.[7]

Results and Discussion

The ^{13}C chemical shifts for compounds 4 are collected in Table I, and those of compounds **5** and **6** are presented in Table II. The assignments are straightforward and do not require special techniques. The off-resonance spectra were conclusive for this purpose.

The synthetic routes for the preparation of the norbornane derivatives **4–6** followed the method described by Avram for both the parent hydrocarbons **4A**, **5A**, and **6A**[8a] and the anti-substituted compounds **4B–D**, **5B–D**, and **6B–D**.[8b] In the present paper we shall confine our discussion to the synthetically available exo-annulated cyclopropanes **4**, **5**, and **6**. The corresponding endo-annulated cyclopropanes, except the **4A** isomer,[8c] are still a synthetic challenge.

A. Configuration of the Cyclopropane Ring. According to our experimental results, the γ-syn shielding effect of the exo-cyclopropane ring is also valid in the case of compounds **5A** and **6A** (see the reference compounds **8** and **10**, respectively). Moreover, the shielding effect has virtually the same value, as was noted previously, for the pairs **11**,**12**, **3**,**2**, **4A**,**13**. The γ-syn shielding effect of the annulated cyclopropane to the bicyclo[2.2.1]heptane, from the data mentioned in Figure 1, is estimated at −11.4 ppm. We believe that this increment will be useful in any attempt to define the configuration of an annulated cyclopropane ring to the norbornane skeleton.

B. Configuration of the Benzocyclobuta Fragment. Prior to the present contribution, the configuration of the benzocyclobuta group annulated to the norbornane skeleton was assessed from the chemical shifts of the protons from the methano bridge and from the magnitude of the coupling constant between the bridgehead and benzylic protons. Upfield chemical shifts of the methylene bridge protons are associated with an exo configuration of the benzocyclobuta ring and are related to the shielding anisotropy effect of the aromatic ring.[10] Bridgehead benzylic protons have a ^1H NMR vicinal coupling constant in the range 2–4 Hz, which is typical for an exo-oriented benzylic proton,[10] and thus the benzocyclobuta ring has an endo configuration. If the coupling constant is within the range 0–1 Hz, then the benzylic proton has an endo configuration,[10] and, therefore, the benzocyclobuta ring has an exo configuration.

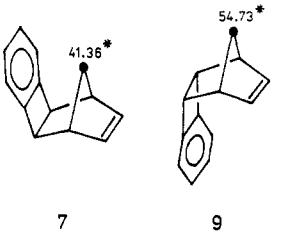


Figure 2. ^{13}C chemical shifts of the bridge carbon atom (marked with ●) for the exo- and endo-benzocyclobuta-annulated bicyclo[2.2.1]heptanes: (*) present work.

The ^{13}C chemical shift of the C_8 atom is, however, more powerful in assigning the stereochemistry of the benzocyclobuta annulated norbornanes. Figure 2 presents our results for the *exo*- and *endo*-benzocyclobutanorbornanes. From the outset one should note the approximate 12 ppm relative upfield shift of the C_8 signal in the case of exo-benzocyclobuta derivatives **5A**, **7**, and **8** with respect to the endo-isomers **6A**, **9**, and **10**. From the results presented in Figure 2, considering the second row (Figure 1) as reference compounds, one can estimate a −6.7 ppm decrement for an exo-annulated benzocyclobuta group and a +5.9 ppm increment for an endo-annulated group. Compared with the cyclopropane ring, the benzylcyclobuta fragment has qualitatively the same shielding effect, upon C_8 atom chemical shift in the exo configuration and a deshielding effect in the endo configuration shift. However, the magnitude of these effects is about half the figures associated with the annulation of cyclopropane (exo, −11.4 ppm, see above; endo, + 15.2 ppm[3c,d]).

C. Effect of the Substituents on the Chemical Shifts of the Cyclopropyl Ring Carbon Atom. The ^{13}C chemical shifts of the cyclopropyl ring presented in Tables

(8) (a) Dinulescu, I.; Enescu, L. N.; Ghenciulescu, A.; Avram, M. *J. Chem. Res. Synop.* **1978**, 456. (b) Ghenciulescu, A.; Enescu, L.; Prasad, H. L.; Chiraleu, F.; Dinulescu, I. G.; Avram, M. *Rev. Roumaine Chim.* **1978**, *23*, 1441. (c) Battiste, M. A.; Coxon, J. M., Posey, R. G.; King, R. W.; Mathew, M.; Palenik, C. J. *J. Am. Chem. Soc.* **1975**, *97*, 945.

(9) Stothers, J. B.; Tan, C. T.; Tes, K. C., *Can. J. Chem.*, **1973**, *51*, 2893.

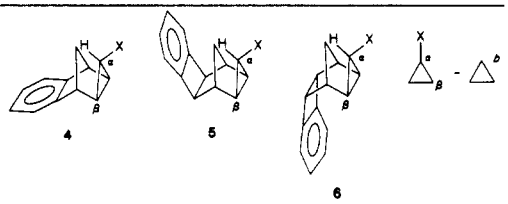
(10) Avram, M.; Chiraleu, F.; Pogany, I.; Dinulescu, I. G. *Rev. Roum. Chim.* **1970**, *15*, 1767 and references cited therein.

(11) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley-Interscience: New York, 1972; p 282.

(12) Olah, G. A.; Westerman, P. W.; Nishimura, J. *J. Am. Chem. Soc.* **1974**, *96*, 3548.

(13) Gordon, M.; Grover, S. H.; Stothers, J. B. *Can. J. Chem.* **1973**, *51*, 2092.

Table III. Differences between Chemical Shifts of the α-Substituted Polycyclic Cyclopropanes 4-6 and the Corresponding Reference Compounds 4A, 5A, and 6A[a]



X		4	5	6	
CH_2OH	C_α	15.1	15.36	15.37	15.8[c]
	C_β	5.10	6.00	5.48	5.3[c]
CHO	C_α	23.40	24.69	25.71	
	C_β	9.00	10.69	9.33	
COOMe	C_α	13.4	14.61	15.17	14.9[d]
	C_β	9.26	10.76	10.60	10.5[d]

[a] In the last column are presented the difference between the chemical shifts of the identically substituted monocyclic cyclopropanes and the parent cyclopropane. Only the shifts for the three-membered ring aroms C_α and C_β are displayed. [b] Reference 11. [c] Reference 12; data converted to $(CH_4)_4Si$ scale by using $\delta_{TMS} = 192.8 - \delta_{CS_2}$. [d] Reference 13.

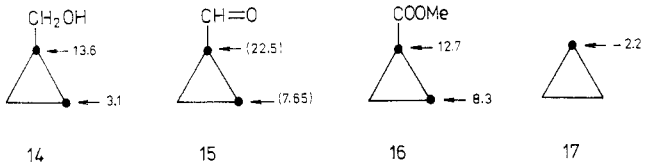


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Figure 3. ^{13}C chemical shifts (relative to $(CH_3)_4Si$) for the parent and substituted cyclopropanes. The figures in parentheses are estimated chemical shifts for C_α and C_β carbon atoms.

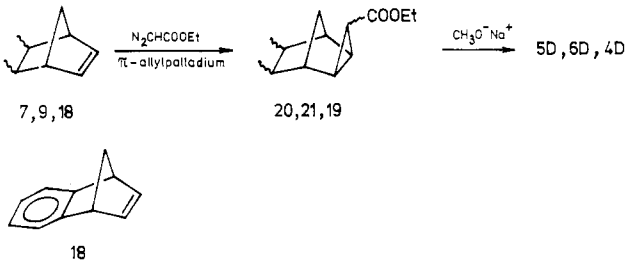
I and II are scattered over 0–40 ppm, as the result of the intrinsic properties of the benzo-, *exo*-benzocyclobuta-, and *endo*-benzocyclobutatricyclo[3.2.1.$0^{2,4}$]octane system. If, however, the relative chemical shifts are calculated with respect to the reference compounds **4A**, **5A**, and **6A**, respectively, then the figures presented in Table III are obtained.

Substituents at C_1 in the cyclopropyl ring exert virtually an identical effect upon the differently annulated norbornane skeletons. A similar trend and magnitude can be traced also in the corresponding monocyclic compounds (last column, Table III). In each case the anti-oriented substituent X[14] exerts a δ-deshielding effect upon the C_8 chemical shift in compounds **4–6**. With the compounds **4A**, **5A**, and **6A** as references, the following group increments are calculated: CH_2OH, +1.6 ppm; CHO, +1.8 ppm; COOMe, +1.7 ppm.

To our best knowledge there are no ^{13}C NMR data for cyclopropanecarboxaldehyde. With the average increments for the C_α (24.7 ppm) and C_β (9.8 ppm), the estimated chemical shift for cyclopropanecarboxaldehyde (**15**) C_α is 22.5 ppm and C_β is 7.65 ppm (Figure 3).

D. Synthesis. Compounds **4B–D**, **5B–D**, and **6B–D** with 1-substituted cyclopropane rings were obtained from the corresponding alkenes **18**, **7**, and **9**, respectively, in several steps. The first stage is a cyclopropanation reaction with ethyl diazoacetate in the presence of π-allylpalladium chloride,[8b] given a mixture of approximately 1:1 of the syn and anti epimers **19–21**. Prolonged treatment with sodium methoxide in refluxing methanol converted the ethyl esters into methyl esters and ensured a complete isomerization of the syn epimer to the thermodynamically more stable isomers **4D**, **5D**, and **6D**, respectively. The cyclopropylcarbinols **4B**, **5B**, and **6B** were obtained in high yields by reduction of the corresponding methyl esters with $LiAlH_4$.

(14) Olteanu, E.; Gheorghiu, M., unpublished results; see also ref 8b.



Oxidation of carbinols **4B**, **5B**, and **6B** with a chromium trioxide–pyridine complex (Sarett procedure[15]) in dichloromethane leads to the cyclopropanecarboxaldehydes **4C**, **5C**, and **6C**, respectively. The unsubstituted cyclopropanes **4A**, **5A**, and **6A** were obtained also from alkenes **18**, **7**, and **9**, respectively, by cyclopropanation with diazomethane in the presence of π-allylpalladium chloride catalyst, as described by Avram.[8a] For the synthesis of norbornanes **13**, **8**, and **10** we have employed a modified procedure, based upon the recently developed method of Olah[16] for carbon–carbon multiple bond reduction. Thus alkenes **18**, **7**, and **9** were reduced with methanol in the presence of 10% Pd/C, with virtually quantitative yield to norbornanes **13**, **8**, and **10**, respectively.

Experimental Section

Carbon-13 NMR spectral were recorded at 80 MHz with a Varian FT-80A instrument with either the switchable $^{13}C/^1H$ or the broadband probe. The following parameters were used: pulse width, 16–20 μs; acquisition time, 1.638–2.047 s; pulse delay, 2–5 s. ^1H NMR spectra were recorded with a Varian EM-360L instrument. Both ^1H and ^{13}C NMR chemical shifts are quoted in ppm relative to Me_4Si. IR spectra were recorded with Carl Zeiss Jena and Specord-instruments. Pyridine was kept on potassium hydroxide, and chromium trioxide was kept before use in a desiccator in the presence of phosphorus pentoxide. Dichloromethane was washed successively with concentrated sulfuric acid, water, saturated sodium chloride solution, dried over calcium chloride, and then distilled at ambient pressure. Melting points are uncorrected.

Norbornenes **7** and **18** were obtained by cycloaddition of benzyne (generated from diazoanthranilic acid) to norbornadiene[17a] and cyclopentadiene,[17b] respectively. Compound **9** was synthesized according to Nenitzescu's procedure from benzocyclobutadiene (generated from 1,2-dibromobenzocyclobutane and Li(Hg)).[17c] Diazomethane addition to **7**, **9**, and **18**, in the presence of catalytic amount of π-allylpalladium chloride[18] gave in high yields cyclopropanes **5A**, **6A**, and **4A** respectively.[8]

The benzo-, *exo*-benzocyclobuta-, and *endo*-benzocyclobutanorbornanes **13**, **8**, and **10**, respectively, were obtained from the corresponding alkenes **18**, **7**, and **9**, respectively, by Olah's procedure.[16] Thus a mixture of alkene (5 mmol), dry methanol (15 mL), Mg turnings (25 mmol), and 25 mg of 10% Pd/C was stirred under nitrogen until the entire quantity of Mg had reacted. Then the reaction mixture was stirred with 15 mL of 3 N HCl and extracted with 3 × 50 mL of dichloromethane. The organic layers were washed with saturated NaCl solution (2 × 50 mL) and then dried over $MgSO_4$. After the removal of solvent under reduced pressure, the yields of hydrocarbons **13**, **8**, and **10** were 98–98%. The physical parameters (bp and IR ^1H NMR spectra) were identical with those reported in the literature for benzonorbornane,[19] *exo*-benzocyclobutanorbornane,[20] and *endo*-

(15) Poos, G. I.; Arth, G. E.; Beyler, R. E.; Sarett, L. H. *J. Am. Chem. Soc.* **1953**, *75*, 422.

(16) Olah, G. A.; Prakash, G. K. S.; Arvanaghi, M.; Bruce, M. R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 92.

(17) (a) Paddon-Row, M. N.; Hartcher, R. *J. Am. Chem. Soc.* **1980**, *102*, 662. (b) Mich, T. F.; Nieuhouse, E. J.; Tufariello, J. J. *J. Chem. Educ.* **1968**, *45*, 272. (c) Nenitzescu, C. D.; Avram, M.; Dinu, D. *Chem. Ber.* **1957**, *90*, 2541.

(18) Sakakibara, M.; Takahashi, Y.; Sakai, S. *Chem. Commun.* **1969**, 396.

benzocyclobutanorbornane,[20] respectively.

General Procedure for Epimerization and Transesterification. To 75 mL of dry methanol was added 0.7 g (30.4 mmol) of sodium. Then to the solution of sodium methoxide in methanol was added 160 mmol of the corresponding mixture of carbethoxycyclopropyl epimers. The mixture was refluxed for 24 h. After the reactioin mixture was allowed to cool to room temperature, 60 mL of water was added, and the ester was extracted with ethyl ether (4 × 50 mL). The combined extract was washed with water until a neutral pH was obtained and dried ($MgSO_4$). The solvent was removed leaving the corresponding carbomethoxycyclopropyl derivative.

1aα,2α,7α,7aα-Tetrahydro-1β-carbomethoxy-2,7-methano-1*H*-cyclopropa[*b*]naphthalene (4D) was obtained in 92% yield: colorless solid; mp 58 °C (CH_3OH) (lit.[8b] mp 88 °C); IR (CS_2, CCl_4) 727 (m), 1153 (s), 1273 (s), 1384 (s), 1430 (s), 1718 (s), 2900 (w), 2940 (w), 2966 (m), 3013 (w), 3040 (w), 3066 (w) cm^{-1}; ^1H NMR ($CDCl_3$) 1.28 (1 H, d, J = 10.5 Hz), 1.45 (1 H, d, J = 10.5 Hz), 1.62 (2 H, d, J = 2.5 Hz), 2.4 (1 H, t, J = 2.5 Hz), 3.32 (2 H, br s), 3.53 (3 H, s), 7.03 (4 H, m); ^{13}C NMR ($CDCl_3$) 28.64 (d), 30.30 (d), 39.38 (t), 42.99 (d), 51.42 (q), 121.14 (d), 125.21 (d), 149.91 (s), 172.93 (s). Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.58. Found: C, 78.42; H, 6.64.

1aα,2α,2aα,6bα,7α,7aα-Hexahydro-1β-carbomethoxy-2,7-methano-1*H*-cyclopropa[*b*]biphenylene (5D) was obtained as a colorless liquid in a 90% yield: mp 94 °C (methanol); IR (CS_2, CCl_4) 707 (m), 727 (m), 1160 (s), 1243 (s), 1217 (m), 1390 (m), 1433 (s), 1719 (s), 2942 (m), 2980 (w), 3026 (w), 3058 (w) cm^{-1}; ^1H NMR ($CDCl_3$) 0.35 (1 H, d, J = 10.5 Hz), 0.45 (1 H, d, J = 10.5 Hz), 1.43 (2 H, d, J = 2.5 Hz), 1.75 (1 H, t, J = 2.5 Hz), 2.43 (2 H, br s), 3.42 (2 H, s), 3.60 (3 H, s), 7.02 (4 H, m); ^{13}C NMR ($CDCl_3$) 18.51 (d), 21.95 (t), 25.67 (d), 36.37 (d), 50.69 (d), 51.46 (q), 121.84 (d), 127.42 (d), 145.42 (s), 173.62 (s). Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.84; H, 6.82.

1aα,2α,2aβ,6bβ,7α,7aα-Hexahydro-1β-carbomethoxy-2,7-methano-1*H*-cyclopropa[*b*]biphenylene (6D) was obtained as a colorless solid: mp 91 °C (methanol); IR (CS_2, CCl_4) 726 (m), 740 (m), 1137 (m), 1160 (s), 1430 (m), 1723 (s), 2893 (m), 2940 (m), 3008 (m), 3053 (m) cm^{-1}; ^1H NMR ($CDCl_3$) 0.92 (2 H, d, J = 2.5 Hz), 1.15 (1 H, d, J = 11.5 Hz), 1.35 (1 H, d, J = 11.5 Hz), 1.54 (1 H, t, J = 2.5 Hz), 2.55 (2 H, m), 3.46 (3 H, s), 3.59 (2 H, m), 7.05 (4 H); ^{13}C NMR ($CDCl_3$) 16.04 (d), 23.41 (d), 33.98 (t), 37.33 (d), 50.00 (q), 51.40 (t), 123.51 (d), 127.00 (d), 146.14 (s), 174.10 (s). Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.87; H, 6.80.

General Procedure for Reduction of Esters 4D, 5D, and 6D to the Cyclopropylcarbinols 4B, 5B, and 6B. A solution of 19 mmol of carbomethoxy derivative **4D**, **5D**, or **6D** in 25 mL of ethyl ether was added dropwise to a magnetically stirred suspension of 26.3 mmol of lithium aluminum hydride in 100 mL of ethyl ether. The reaction mixture was stirred at room temperature for 3 h and for an additional hour at solvent reflux. It was then cooled and quenched with chilled water added dropwise, followed by addition of a 10% solution of sulfuric acid until the precipitate was completely dissolved. The aqueous phase was separated and was extracted with ether (3 × 50 mL). The combined organic phases were washed with a saturated aqueous sodium chloride solution and dried. Removal of the solvent gave the cyclopropyl carbinols **4B**, **5B**, and **6B**.

1aα,2α,7α,7aα-Tetrahydro-1β-(hydroxymethyl)-2,7-methano-1*H*-cyclopropa[*b*]naphthalene (4B) was obtained as a colourless oil: bp 138 °C (2 mm); yield, 96%; IR (CS_2, CCl_4) 733 (s), 1016 (s), 1100 (m), 1392 (m), 1443 (m), 2851 (m), 2907 (m), 2953 (s), 3000 (m), 3324 (m), 3602 (w) cm^{-1}; ^1H NMR ($CDCl_3$) 0.93 (2 H, d, J = 3 Hz), 1.23 (1 H, d, J = 10 Hz), 1.50 (1 H, d, J = 10 Hz), 2.07 (1 H, t × t, J = 7 Hz, J = 3 Hz), 2.77 (1 H, br s), 3.28 (2 H, s), 3.33 (2 H, d, J = 7 Hz), 7.0 (4 H, m); ^{13}C NMR ($CDCl_3$) 26.14 (d), 30.34 (d), 38.80 (t), 42.86 (d), 64.21 (t), 120.67 (d), 124.85 (d), 150.96 (s). Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.57. Found: C, 83.96; H, 7.66.

1aα,2α,2aα,6bα,7α,7aα-Hexahydro-1β-(hydroxymethyl)-2,7-methano-1*H*-cyclopropa[*b*]biphenylene (5B) was obtained in 82% yield as a colorless solid: mp 112 °C (methanol); IR (CS_2, CCl_4) 723 (m), 1006 (m), 1026 (m), 1226 (m), 1736 (m), 2864 (m), 2936 (s), 3010 (m), 3056 (w), 3376 (m), 3613 (w) cm^{-1}; ^1H NMR ($CDCl_3$) 0.48 (1 H, d, J = 12.5 Hz), 0.72 (1 H, d, J = 12.5 Hz), 0.73 (2 H, d, J = 2.5 Hz), 1.27 (1 H, t × t, J = 2.5 Hz, J = 7 Hz), 2.38 (2 H, br s), 3.33 (3 H, s), 3.37 (2 H, d, J = 7 Hz), 7.05 (4 H, m); ^{13}C NMR ($CDCl_3$) 19.26 (d), 20.91 (d), 22.13 (t), 36.34 (d), 51.48 (d), 64.99 (t), 121.79 (d), 127.23 (d), 146.07 (d). Anal. Calcd for $C_{15}H_{16}O$: C, 84.86; H,7.59. Found: C, 84.97; H, 7.50.

1aα,2α,2aβ,6bβ,7α,7aα-Hexahydro-1β-(hydroxymethyl)-2,7-methano-1*H*-cyclopropa[*b*]biphenylene (6B) was obtained in 97% yield as a colorless oil: bp 162 °C (2 mm); IR (CS_2, CCl_4) 713 (m), 735 (m), 1008 (s), 1171 (w), 1450 (m), 2840 (m), 2913 (s), 2933 (s), 3006 (m), 3053 (w), 3333 (w), 3063 (w) cm^{-1}; ^1H NMR ($CDCl_3$) 0.24 (2 H, d, J = 3 Hz), 1.12 (1 H, d, J = 11 Hz), 1.15 (1 H, t × t, J = 7 Hz, J = 3 Hz), 1.43 (1 H, d, J = 11 Hz), 2.46 (2 H, m), 3.06 (2 H, d, J = 7 Hz), 3.53 (2 H, m), 7.03 (4 H, m); ^{13}C NMR ($CDCl_3$) 16.24 (d), 18.29 (d), 34.05 (t), 37.03 (d), 50.48 (d), 64.76 (d), 123.29 (d), 126.44 (d), 146.70 (s). Anal. Calcd for $C_{15}H_{16}O$: C, 84.86; H, 7.59. Found: C, 84.78; H, 7.50.

General Procedure for Conversion of Cyclopropylcarbinols. 4B, 5B, and 6B in Cyclopropanecarboxaldehydes 4C, 5C, and 6C. To 200 mL of dichloromethane was added 14.22 g (180 mmol) of pyridine. The resulting solution was cooled to +5 °C, and 9 g (90 mmol) of chromium trioxide was added. The yellow precipitate and the dark solution were stirred for 5 min at 5 °C and then ca. 1 h at room temperature, until the solution became clear. Then 15 mmol of cyclopropylcarbinol **4B**, **5B**, or **6B** dissolved in 25 mL of dichloromethane was added in one portion. After the mixture was stirred at room temperature, for 15 min, the dark residue formed was separated and washed with 5 × 40 mL of ether. The combined organic phases were washed with a cold aqueous sodium hydroxide solution (5%, 3 × 100 mL), then with 5% HCl aqueous solution (1 × 100 mL), 5% sodium carbonate solution (1 × 100 mL), and then a saturated aqueous sodium chloride solution (2 × 50 mL) and dried over anhydrous $MgSO_4$. After the removal of solvents at reduced pressure, the cyclopropanecarboxaldehyde **4C**, **5C**, or **6C** was obtained.

1aα,2α,7α,7aα-Tetrahydro-1β-formyl-2,7-methano-1*H*-cyclopropa[*b*]naphthalene (4C) was obtained in 90.5% yield as a colorless solid: mp 59–60 °C (methanol); IR (CS_2, CCl_4) 750 (m), 1708 (s), 2820 (m), 2903 (w), 2922 (w), 2980 (s), 3018 (w), 3050 (w) cm^{-1}; ^1H NMR (CDCl3) 1.23 (2 H, m), 1.69 (2 H, d, J = 2.5 Hz), 2.6 (1 H, d × t, J = 2.5, 4.5 Hz), 3.35 (2 H, br s), 7.03 (4 H, m), 9.1 (1 H, d, J = 4.5 Hz); ^{13}C NMR ($CDCl_3$) 30.03 (d), 38.60 (d), 39.58 (t), 42.94 (d), 121.30 (d), 125.40 (d), 149.74 (s), 198.25 (d). Anal. Calcd for $C_{13}H_{12}O$: C, 84.74; H, 6.57. Found: C, 84.72; H, 6.47.

1aα,2α,2aα,6bα,7α,7aα-Hexahydro-1β-formyl-2,7-methano-1*H*-cyclopropa[*b*]biphenylene (5C) was obtained in 82% yield as a colorless solid: mp 62–63 °C (methanol); IR (CS_2, CCl_4) 724 (m), 1710 (s), 2730 (w), 2820 (w), 2850 (w), 2950 (m), 3015 (w), 3060 (w) cm^{-1}; ^1H NMR ($CDCl_3$) 0.56 (1 H, d, J = 11 Hz), 0.68 (1 H, d, J = 11 Hz), 1.53 (2 H, d, J = 1.8 Hz), 2.01 (1 H, m, J = 1.8, 4 Hz), 2.45 (2 H, br s), 3.42 (2 H, s), 7.02 (4 H, m), 9.22 (1 H, d, J = 4 Hz); ^{13}C NMR ($CDCl_3$) 22.06 (t), 25.60 (d), 28.59 (d), 36.39 (d), 50.71 (d), 121.94 (d), 127.55 (d), 145.23 (s), 200.22 (d). Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.75; H, 6.70.

1aα,2α,2aβ,6bβ,7α,7aα-Hexahydro-1β-formyl-2,7-methano-1*H*-cyclopropa[*b*]biphenylene (6C) was obtained in 80% yield as a colorless solid: mp 84 °C (methanol); IR (CS_2, CCl_4) 735 (m), 760 (m), 1710 (s), 2720 (w), 2822 (w), 2900 (w), 2960 (s), 3015 (w), 3030 (w), 3060 (w) cm^{-1}; ^1H NMR ($CDCl_3$) 1.12 (2 H, d, J = 2 Hz), 1.18 (1 H, J = 12.5 Hz), 1.33 (1 H, J = 12.5 Hz), 1.82 (1 H, m, J = 2, 5.5 Hz), 2.61 (2 H, m), 3.65 (2 H, m), 7.13 (4 H, m), 8.7 (1 H, d, J = 5.5 Hz); ^{13}C NMR ($CDCl_3$) 22.14 (d), 26.58 (d), 33.95 (t), 37.21 (d), 49.93 (d), 123.60 (d), 127.06 (d), 146.06 (s), 200.92 (d). Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.61; H, 6.61.

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(19) Wittig, G.; Knauss, E. *Chem. Ber.* **1958**, *91*, 895.
(20) Simmons, H. E. *J. Am. Chem. Soc.* **1961**, *83*, 1657. Miller, R. D.; Kolc, J.; Michl, J. *J. Am. Chem. Soc.* **1976**, *98*, 8570.

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New Molecular Mechanics (MM2) Parameters for Ketones and Aldehydes

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The parameter set in MM2 has been changed to permit more accurate calculations on carbonyl compounds, taking into account ab initio calculations reported recently by Wiberg on 2-butanone and other data which have become available since the original formulation. Several major problems regarding carbonyl compound conformations and energies have been addressed, and the results are uniformly better than they were with MM2(77).

Ketones and aldehydes are important and widespread functional groups found in nature.[1] Numerous synthetic, conformational, and theoretical studies have focused on this broad class of carbonyl-containing compounds.[2] Carbonyl chemistry remains one of the fundamental methods for preparing complex chemical structures. Underlying the successful application of carbonyl chemistry has been an understanding of the geometric and conformational behavior of these compounds, which allows an investigator to make feasible predictions. Certainly, one of the chemist's major goals is to predict accurately the stereochemical course of reactions based on accumulated experimental and theoretical knowledge. Although transition-state geometries may differ significantly from ground-state geometries, a detailed knowledge of the latter is highly desirable.

The use of mechanical models for predicting conformational behavior has had laudable results, most notably with predictions on the stereochemical outcome of additions to the carbonyl moiety.[3] However, such models have relied, perhaps too heavily, on intuition, which may lead to errors.[4] More recently, powerful computational approaches to structure determination have been developed.[5,6] The molecular mechanics technique has been applied to a variety of functionalized molecules with generally excellent results. The molecular mechanics approach originally relied on empirically derived data and still does to a large extent. But it has long been known[7] that ab initio calculations can be used in place of experimental data. When the original MM2 ketone force field was first developed,[8] certain key conformational information was either sketchy or lacking altogether.[6,9] The purpose of this paper is to report a new set of MM2[10] parameters for ketones and aldehydes.[11]

Experimental and theoretical studies are constantly producing new insights into stereoelectronic and conformational behavior of molecules. Much of this new information is in agreement with MM2 predictions. In some cases, MM2 results have pointed out faulty experimental data, which has led experimentalists to reexamine their findings and correct the problems.[12] However, there are situations where new data have indicated errors in the force field,[13] which suggests that the initial data used to

(1) Patai, S. *The Chemistry of the Carbonyl Group*; Interscience: New York, 1966.

(2) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; American Chemical Society: Washington, DC, 1981.

(3) (a) Cram, D. J.; Wilson, D. R. *J. Am. Chem. Soc.* **1963**, *85*,k 1245 and earlier papers. (b) Karabatsos, G. J. *J. Am. Chem. Soc.* **1967**, *89*, 1367. (c) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, 2205. (d) Eliel, E. L.; Senda, Y. *Tetrahedron* **1970**, *26*, 2411. (e) Richer, J.-C. *J. Org. Chem.* **1965**, *30*, 324. (f) Marshall, J. A.; Carroll, R. D. *J. Org. Chem.* **1965**, *30*, 2748.

(4) (a) Wuts, P. G. M.; Walters, M. A. *J. Org. Chem.* **1984**, *49*, 4573. See ref 28. (b) Altona, C.; Farber, D. H. *Top. Curr. Chem.* **1974**, *45*, 1.

(5) The following reviews, books, and original literature citations therein are excellent sources of information: (a) Allinger, N. L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1. (b) Engler, E. M.; Andose, J. D.; Schleyer, P. v. R., *J. Am. Chem. Soc.* **1973**, *95*, 8005. (c) Clark, T. *A Handbook of Computational Chemistry*; Wiley: New York, 1985. (d) Hehre, J. W.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986. Also, see ref 6.

(6) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington DC, 1982.

(7) Allinger, N. L.; Hickey, M. J. *Tetrahedron* **1972**, *28*, 2157.

(8) S. Profeta and N. L. Allinger. This work has never been published in the usual sense, but the results of it form the basis of the MM2 parameter set included in the original program (MM2(77)).

(9) Allinger, N. L.; Tribble, M. T.; Miller, M. A. *Tetrahedron* **1972**, *28*, 1173.

(10) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127 and subsequent papers.

(11) Our philosophy has been and continues to be that we do not want the MM2 calculations to become time dependent. Since new data are constantly becoming available, if we were to incorporate it, the force field would be under constant change. We prefer not to do this. The errors known, which are many, are mostly small. In some cases where they are not very small, they are systematic and well understood and can be allowed for in an ad hoc fashion. However, in a few cases, we have found actual mistakes, typographical errors, and what not, and we have corrected those. In the present case, we feel that the improved data now available for ketones are sufficiently reliable and different that a revision of the ketone calculations is warranted. Versions of MM2 released after this time (which will be MM2(87) and subsequent) will contain these revisions. Earlier versions may be updated by the user by reading in the parameters shown in Table I. The original program is described in ref 10. The latest versions of the program are always available from the Quantum Chemistry Program Exchange, Department of Chemistry, University of Indiana, Bloomington, Indiana 47405, and from Molecular Design Limited, 2132 Farallon Drive, San Leandro, CA 94577. A list of current parameters is always available from N.L.A. (a reprint request card asking for current MM2 parameters is all that is needed).

(12) For example: Clark, T.; Knox, T. McO.; McKervey, M. A.; Mackle, H.; Rooney, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 2404. Also, see ref 6.

0022-3263/87/1952-5162$01.50/0