Experimental Section[24]

Procedure. The reactions were conducted in the flow system previously described,[2] but only with alumina catalyst F[3] (Houdry HA-100, containing 0.4% sodium ion). Experiments 1–7 involved the use of 2-propanol as solvent and propylating agent. In expt 8 a solution of 2 g of phenol in 56 mL of benzene was added dropwise to the preconditioned catalyst while a mixture of nitrogen (33 mL/min)[25] and propene (117 mL/min)[25] was passed through the catalyst bed. Processing of the effluent as before gave 0.32 g of neutral, dark brown liquid. In expt 9–12 a solution of 6.9 g of substrate in 44 mL of benzene was added dropwise to the catalyst, but the gas stream consisted of nitrogen only. Product mixtures were collected as before[2] and analyzed quantitatively by VPC at 150 °C (isothermally) on a 1 cm × 2.4 m column of Chromosorb W (60–80 mesh) impregnated with 10% DC-550 silicone oil. Accuracy and reproducibility were noted previously.[2] All starting materials were available from commercial sources. Data for the various experiments are presented in Tables I and II.

Isolation and Identification of Reaction Products. All of the products listed in Tables I and II were isolated from one or more crude reaction mixtures by preparative VPC as colorless liquids. They were variously identified by direct comparison with authentic reference samples (retention time, infrared and ^{1}H NMR spectra), by comparison with literature data on infrared spectra,[26] and by elemental analysis. Previously unreported NMR spectral data (CCl_4) are as follows. For 2,4-diisopropylphenol (**39**): δ 1.20 [d, J = 7 Hz, 2 $CH(CH_3)_2$], 2.78 and 3.17 (2 overlapping pentets, J = 7 Hz, 2 $CHMe_2$), 5.24 (s, OH), 6.47 (d, J = 8 Hz, H-6), 6.78 (dd, J = 8, 2 Hz, H-5), 6.93 (d, J = 2 Hz, H-3). For 2,5-diisopropylphenol (**40**): δ 1.12 and 1.17 [2 overlapping d, J = 7 Hz, 2 $CH(CH_3)_2$], 2.68 and 3.18 (2 overlapping pentets, J = 7 Hz, 2 $CHMe_2$), 5.68 (s, OH), 6.46 (d, J = 1.8 Hz, H-6), 6.70 (dd, J = 8, 1.8 Hz, H-4), 7.05 (d, J = 8 Hz, H-3). For 2,6-diisopropylphenol (**41**): δ 1.20 [d, J = 6.5 Hz, 2 $CH(CH_3)_2$], 3.08 (6 peaks of septet, 2 $CHMe_2$), 4.69 (s, OH), 6.5–7.1 (m, 3 aromatic H). For 2,4,6-triisopropylphenol (**42**): δ 1.19 [d, J = 7 Hz, $CH(CH_3)_2$ at C-4] which overlaps 1.23 [d, J = 7 Hz, $CH(CH_3)_2$ at C-2 and C-6], 2.5–3.4 (m, 3 $CHMe_2$), 4.44 (s, OH), 6.81 (s, 2 aromatic H).

Registry No. 1, 108-95-2; **2**, 622-85-5; **3**, 645-56-7; **8**, 644-35-9; **9**, 88-69-7; **10**, 23167-99-9; **11**, 6626-32-0; **13**, 74663-48-2; **19**, 99-89-8; **36**, 618-45-1; **37**, 67-63-0; **38**, 115-07-1; **39**, 2934-05-6; **40**, 35946-91-9; **41**, 2078-54-8; **42**, 2934-07-8.

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[24] See note 17, ref 2.

[25] Measured at room temperature and pressure.

[26] D. D. Shrewsbury, *Spectrochim. Acta*, **16**, 1294 (1960).

Applications of Carbon-13 Nuclear Magnetic Resonance Spectroscopy. 24.[†] The Spectra of Cyclopropane-Annelated Bicyclo[2.2.2]octanes, Three-Membered-Ring Effects and Chemical Shift Nonequivalence

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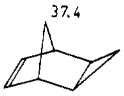
The ^{13}C NMR spectra of cyclopropane-annelated bicyclo[2.2.2]octanes have been measured and the three-membered-ring effect on carbon chemical shifts was determined. The unusual deshielding mechanism operative for the methano bridge in cyclopropane-annelated norbornanes is absent for an ethano bridge. The sensitivity of ^{1}H and ^{13}C for the intrinsic anisochronism of the "propeller-shaped" trishomobarrelene system was studied, using various prochiral groups.

Introduction

The peculiar bonding situation in cyclopropane has been revealed by various spectroscopic techniques and a recent addition to the long list of remarkable observations[1] is the unusual substituent effect exerted by an annelated cyclopropane ring on the carbon-13 chemical shifts in a number of polycyclic compounds. Tori et al.,[2] for example, reported strong shielding and deshielding, respectively, for the C-7 resonance in the isomeric tricyclooctenes **1** and **2** if compared to the unsubstituted reference compound norbornene (**3**), and Christl[3] observed both effects intramolecularly in tetracyclo[4.1.0.0^{2,4}.0^{3,5}]heptane (**4**) as he compared the ^{13}C chemical shifts of this compound with those of tricyclo[3.1.0.0^{2,6}]hexane (**5**).



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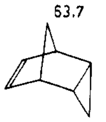

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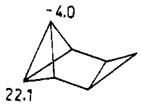

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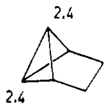

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Whereas the shielding can be classified empirically as a typical γ-effect, the deshielding seems to operate through charge transfer from the σ framework to the antibonding Walsh orbital (A_2')[4] of the three-membered ring. A qualitative MO model (Figure 1) nicely explains these findings.[3] It also accounts for the results found for C-7 in *endo*-epoxynorbornane and -norbornene.[5] In addition,

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[†] For Part 23 see H. Günther and A. Gronenborn, *Heterocycles*, 11, 337 (1978).

[1] For reviews see: (a) D. Wendisch, *Methoden Org. Chem.* (Houben-Weyl), 4/3, 1971; (b) A. de Meijere, *Angew. Chem.*, **91**, 867 (1979); *Angew. Chem., Int. Ed. Engl.*, **18**, 809 (1979).

[2] K. Tori, M. Ueyama, K. Tsuji, H. Matsumura, and H. Tanida, *Tetrahedron Lett.*, 327 (1974).

[3] M. Christl, *Chem. Ber.*, **108**, 2781 (1975).

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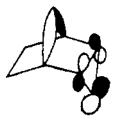


Figure 1. Orbital interaction in tricyclo[3.2.1.0^{2,4}]octane (cf. text).

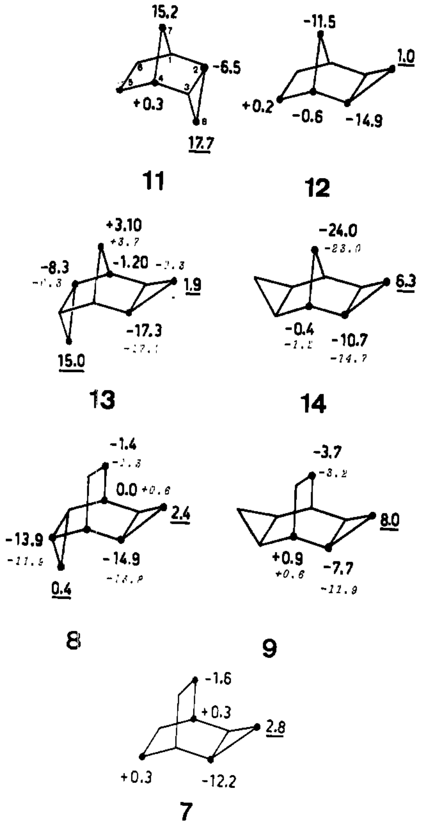
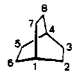


Figure 2. Effect of cyclopropane annelation for the norbornane and bicyclo[2.2.2]octane skeleton; substituent-induced chemical shifts $\Delta\delta$ are given in parts per million relative to the parent systems. Underlined numbers are δ values, italic values are predicted relative shifts ($\Delta\delta$), assuming additivity of the cyclopropane annelation effect.

related observations made for the ^{13}C chemical shifts of norbornadiene can be rationalized on the basis of MO arguments.[6]

Since orbital interactions are fairly sensitive to the stereochemistry involved, it was intriguing to investigate the effect of annelated cyclopropane rings for other bicyclic systems. With the recently synthesized series of polycycles **7**–**10**[7] and bicyclo[2.2.2]octane (**6**)[8] as a reference system, a promising set of compounds was at hand for this purpose, especially since the data for the complete series of structurally related norbornane derivatives **11**–**14** (see Figure 2) were available from the literature.[9] The latter results have already shown that a cyclopropyl group affects the ^{13}C chemical shifts of a methano bridge quite differently from those of an ethano bridge in a syn arrangement as well as in an anti arrangement (compare, for example, C-7 in **12** with C-5,6 in **11** and C-7 in **11** with C-5,6 in **12**). Results for a symmetrical system were therefore desirable. At the same time, 1-substituted trishomobarrelenes were of interest in connection with the C_{3h} symmetry of **10** and its consequences for the chemical shifts of various prochiral groups.[10] The ^{1}H and ^{13}C NMR spectra of the substituted systems **10a**–**d** were therefore studied.



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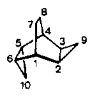

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10, *X* = *H*

10a, X = $-CH(CH_3)_2$

10b, X = $-CH(C_2H_5)_2$

10c, X = -cyclopropyl

10d, X = $-CH_2-C_6H_5$

Table I. ^{13}C NMR Chemical Shift Data (δ, ppm from Me_4Si) for **6**–**10** and for **18**[a]

	C-1,4	C-2,3	C-5,6	C-7,8	C-9	C-10
6	23.9	26.0	26.0	26.0		
7	24.2	13.8	26.3	24.4	2.8	
8	23.9	(11.1)	(12.1)	24.6	(2.4)	(0.4)
9	24.8	18.3	18.3	22.3	8.0	8.0
10	22.2	9.5	9.5	9.5	0.7	0.7
18	30.6	30.0	30.0	20.2	25.1	25.1

[a] Tentative assignments are given in parentheses.

Results and Discussion

1. The Effect of Cyclopropane Annelation. Established shielding effects of the three-membered ring, approximate ^1J (C, H) data from ^{1}H-coupled spectra, and the multiplet structure observed in these as well as off-resonance-decoupled spectra were used as assignment aids for the δ (^{13}C) values of **6**–**10**; a detailed discussion of this aspect is given in the experimental section. The results are collected in Table I, where tentative assignments are given in parentheses.

From the chemical shifts caused by successive annelation of cyclopropane rings to the bicyclo[2.2.2]octane skeleton the syn effect is the one most clearly recognized in the series **7**–**10**. It served to differentiate between δ(5,6) and δ(7,8) in **7** ($\Delta\delta$ = −1.9 ppm) and is clearly present for δ(2,3) in **8** ($\Delta\delta$ = −2.7 ppm, with **7** as reference) as well as for δ(7,8) in **9** ($\Delta\delta$ = −3.7 ppm, with **6** as reference). Finally, for δ(2,3) in **10** it amounts to −4.3 ppm if **7** is used as a reference. These findings are thus completely analogous to the screening effect found in 7-methylnorbornane, where the *syn*-CH_2 resonances are shielded by 3.7 ppm.[11]

A more interesting comparison is possible with compounds **11**–**14**,[9] and Figure 2 summarizes the shielding effects of the cyclopropyl ring in the norbornane and the bicyclo[2.2.2]octane skeleton. Parallel behavior is found in four cases: (1) the bridgehead carbons C-1,4 are rather insensitive to the introduction of cyclopropyl rings; (2) the methine carbons of the cyclopropyl rings are shielded with respect to the methylene carbons in the parent structure; (3) six-membered-ring carbons in a syn position to the cyclopropyl group are shielded; (4) six-membered-ring carbons in an anti position to the cyclopropyl group are slightly deshielded. Observation 2 is clearly a consequence of the incorporation of these carbons into a three-membered ring and 3 may be classified as a γ-effect. Together with 4 it shows that, in fact, the bicyclo[4.1.0]heptane segments in **11**, **12**, and **7** behave rather similarly, especially

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[4] W. L. Jorgensen and L. Salem, "The Organic Chemists Book of Orbitals", Academic Press, New York, 1973.

[5] S. G. Davis and G. H. Whitham, *J. Chem. Soc., Perkin Trans.* 2, 861 (1975).

[6] M. Christl and R. Herbert, *Org. Magn. Reson.*, **12**, 150 (1979).

[7] A. de Meijere, C. Weitemeyer, and O. Schallner, *Chem. Ber.*, **110**, 1504 (1977); A. de Meijere, O. Schallner, C. Weitemeyer, W. Spielmann, *Chem. Ber.*, **112**, 908 (1979).

[8] G. E. Maciel and H. C. Dorn, *J. Am. Chem. Soc.*, **93**, 1268 (1971).

[9] A. K. Cheng and J. B. Stothers, *Org. Magn. Reson.*, **9**, 355 (1977).

[10] W. B. Jennings, *Chem. Rev.*, **75**, 307 (1975).

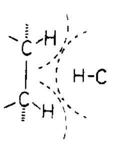
[11] E. Lipmaa, T. Pekh, J. Paasivirta, N. Belikova, and A. Platê, *Org. Magn. Reson.*, **2**, 581 (1970).

Table II. ^{13}C NMR Chemical Shift Data (δ, ppm from Me_4Si) for Substituted Trishomobarrelenes 10a–d

compd	C-1	C-4	C-2	C-3	C-9	C_α	C_β	$C_{\beta'}$	C_γ	$C_{\gamma'}$	C_δ	C_ϵ
10a	22.29	34.68	9.32	11.65	0.72	35.80	17.40	17.68	–	–	–	–
b	22.62	35.43	9.78	12.70	1.05	50.67	22.55	22.86	13.40	13.91	–	–
c	22.88	31.18	9.13	13.06	0.38	20.06	0.19	−0.30	–	–	–	–
d	22.78	32.84	9.47	13.99	0.53	47.80	139.38		130.54	–	127.72	125.68

if one notes that the cyclopropyl methine carbon shift in **7** is close to the arithmetic mean of the respective shifts in **11** and **12**. An exception is the cyclopropyl methylene group in **11** that is strongly deshielded.

In contrast, the abnormal shielding and deshielding effect exerted on the methano bridge (C-7) in norbornane by an *exo*- or *endo*-cyclopropyl group, respectively, is not found for the ethano bridge either in norbornane (C-5,6 in **11** and **12**, respectively) or in the bicyclo[2.2.2]octane skeleton (C-7,8 and C-5,6 in **7**, respectively). As far as the shielding is concerned, the strong interaction between C-7 and the cyclopropyl methylene groups in **12** that results from a direct C–H···H–C repulsion is replaced in the case of an ethano bridge by the less stringent interaction of type **15**. The upfield shift originating from steric constraints is thus greatly diminished. In line with these arguments is the finding that the *syn*-$CH_2 \cdots H_3C$ interaction in 2-methylbicyclo[2.2.2]octane (**16**) leads again to a larger γ-effect of −5.7 ppm.[12]



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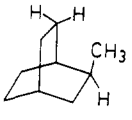

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On the other hand, the deshielding effect due to HOMO–LUMO charge transfer as discussed in the introduction is practically absent for the ethano bridge in both series, the downfield shifts only amounting to 0.2–0.3 ppm. As one possible explanation we suggest that the geometry does not allow sufficient orbital overlap and the charge transfer to the three-membered ring that operates in **2** and **4**, as well as in **11** and **13**, is strongly attenuated. The only structure where such an effect should perhaps be more pronounced is compound **17** which so far has escaped its attempted synthesis. As a model, however, the bridged system **18** is available, but here we find a shielding effect for C-7,8 ($\Delta\delta$ = −5.8 ppm if **6** is used as reference) instead of the expected deshielding. All other carbons in this compound are substantially deshielded as a result of the C-9,C-10 bond that gives rise to α- and β-effects. We also note a considerable downfield shift for C-1,4, formally in a γ position to the C-9,C-10 bond.

17

18

The apparent absence of any orbital interaction of the type described by Figure 3a for an ethano bridge and even more the opposite behavior found for C-7,8 in **12** suggest a second explanation that also takes the antibonding σ orbital of the 7,8- or 5,6-bond into account. As shown in Figure 3b, the symmetry properties would allow a back donation of charge from the bonding Walsh orbital E′ of the three-membered ring[4] to the $H_2C–CH_2$ bridge that could exactly cancel the charge transfer in the opposite direction indicated by Figure 3a. No net result would then be expected.

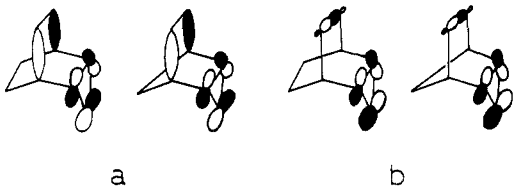
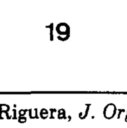


Figure 3. Orbital interaction in tricyclo[3.2.2.0^{2,4}]nonane and tricyclo[3.2.1.0^{2,4}]octane (cf. text).

In general then, as for other substituent effects on ^{13}C chemical shifts in norbornane and bicyclo[2.2.2]octane,[12,13] the effects of three-membered rings are largely similar. The existence of a special shielding mechanism operative for the C-7 methylene carbon in **11–14** and related systems (see introduction) is, however, supported.

As far as the introduction of a second cyclopropyl ring in the pairs **13**/**8** and **14**/**9** is concerned, we observe additivity of substituent effects in both series, as indicated by the predicted shielding effects given in italics in Figure 2, with the exception of the cyclopropyl methine carbons in **14** and **9**, where strong deviations to higher field are noted ($\Delta\delta$ ~4 ppm in both systems). On the other hand, an extra 2-ppm downfield contribution is present in the shift of the methine carbons of the endo ring in **13** and **8**. Finally, with regard to the cyclopropyl methylene group, the resonances for endo and exo arrangements are drastically different in **11**, **12**, and **13**. Because of symmetry there is no endo–exo distinction of substituents in the bicyclo[2.2.2]octane system. We note, however, that $\delta(9)$ is sensitive to the geometry of cyclopropane annelation. For **7** a typical value of 2.8 ppm is found that is not much affected if another cyclopropane ring is introduced in an endo arrangement as in **8**. The latter compound then shows the new CH_2 resonance at high field (0.4 ppm), a value that prevails for the symmetrical system **10**. The introduction of another exo ring as in **9**, on the other hand, leads to substantial deshielding for C-9, an effect equally observed in the norbornane series (**12**/**14**). Remarkable is also the large difference for the endo cyclopropyl methylene resonance in **13** and **8** that results from the strong downfield contribution present already in **11**.

2. Chemical Shift Nonequivalence in Substituted Trishomobarrelenes. For prochiral groups in the 1-position that contain a plane of symmetry, the trishomobarrelene skeleton **10** introduces the necessary requirement to observe diastereotopic nuclei. In fact, it is a "propeller-shaped" molecule like the bicyclic trisulfoxide **19** introduced by Binsch and Franzen[14] as a model for the



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[12] J. B. Stothers and C. T. Tan, *Can. J. Chem.*, **54**, 917 (1976).

[13] P. J. Garratt and R. Riguera, *J. Org. Chem.*, **41**, 465 (1976).

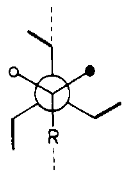
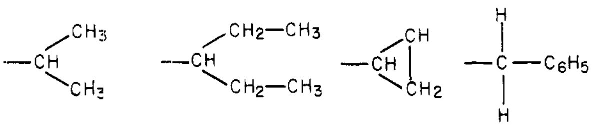


Figure 4. Diastereotopic groups in 1-substituted trishomobarrelene.

investigation of intrinsic anisochronism in attached prochiral moities (Figure 4). With the substituents available in the series **10a–d** the sensitivity of such groups as well as that of their different nuclei (^{1}H, ^{13}C) to the asymmetric environment can be tested if the magnitude of their geminal nonequivalence is determined. The complete results of our ^{13}C NMR measurements are given in Table II, where the assignment of the trishomobarrelene part was based on the data for **10**.

As in the case of **19**, the C_{3h} symmetry of the trishomobarrelene unit eliminates possible contributions to the observed nonequivalence that result from differently populated conformations with respect to the C–C bond between C-1 and X, and the $\Delta\delta$ values measured for the prochiral groups represent the intrinsic anisochronism of this particular structure. For compounds **10a–d**[18] the following chemical shifts (ppm) between nonequivalent groups have been found.



$\Delta\delta(^1H)$ 0.0 0.211
$\Delta\delta(^{13}C)$ 0.28 0.31 0.51 0.49

In addition, for **10a** and **10b** ^{13}C NMR measurements at different temperatures and in different solvents were made. These results are collected in Table III.

It is clear that the complexity of the proton spectra makes the ^{13}C measurements much more practical in all cases except for **10d** where the AB system of the diastereotopic methylene protons is readily analyzed. In addition, the magnitude of the geminal nonequivalence is larger for ^{13}C than for ^{1}H if nuclei occupying approximately the same position in space are compared (see, e.g., $\Delta\delta(^{13}C)$ in **10a** vs. $\Delta\delta(^1H)$ in **10d**). The absence of any detectable ^{1}H nonequivalence between the CH$_3$ groups in **10a**, even at 400 MHz, is most striking in this context. On the other hand, due to the lower gyromagnetic ratio of ^{13}C, the $\Delta\nu$ values (Hz) are approximately three times larger for ^{1}H than for ^{13}C in the pair **10a**/**10d** and are thus formally better resolved. General conclusions about the sensitivity and qualification of either ^{1}H or ^{13}C NMR for the detection of geminal nonequivalence are, therefore, difficult to make.

In comparing our results with those in the literature, we find that the ^{13}C chemical shift nonequivalence found for C_α in **10a–c** is an order of magnitude smaller than the one observed for C-1 of diphenylmethyl groups attached to an asymmetric carbon in compounds of type **20**.[15] This is not surprising since these data—that are in the order of 1–3 ppm—also contain a conformational contribution to $\Delta\delta$. On the other hand, the intrinsic anisochronism found for methyl carbons in halogenated alkanes[16] is approximately three times as large as the $\Delta\delta$ values found in our case. Of interest is also the observation that $\Delta\delta$ for the methyl carbons in **10b** is larger than that for the methylene carbons in the same compound or the methyl carbons in **10a** by 40% and 45%, resp. Due to conformational effects the methyl groups in **10b** are apparently closer to the trishomobarrelene skeleton than their methylene neighbors. Such effects have also been noted in open-chain compounds[10,17] and were explained in the same way.

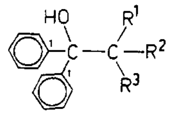


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Table III. Temperature and Solvent Dependence of the ^{13}C NMR Chemical Shift Nonequivalence (Intrinsic Anisochronism) for Compounds 10a and 10b (ppm)[a]

solvent/temp, °C	10a		10b		
	$\Delta\delta(CH_3)$	concn	$\Delta\delta(CH_2)$	$\Delta\delta(CH_3)$	concn
CDCl$_3$/room temp	0.28	0.44	0.33	0.52	0.46
CDCl$_3$/−60	0.30		0.45	0.35	
CS$_2$/room temp	0.29	0.35	0.29	0.49	0.29
CS$_2$/−60	0.33		0.44	0.29	
pyridine/room temp	0.28	0.44	0.30	0.55	0.46

[a] Experimental error ±0.01 ppm.

For the isopropyl compound **10a** there is practically no temperature and no solvent effect for the chemical shift nonequivalence of the methyl carbon resonances. For the isopentyl compound, however, a strong temperature dependence in CDCl$_3$ as well as in CS$_2$ is observed with the interesting finding that the $\Delta\delta$ value for the CH$_3$ groups decreases with decreasing temperature, whereas the $\Delta\delta$ value for the CH$_2$ groups increases. Since in this compound, as mentioned above, conformational changes due to rotation around the CH–CH$_2$ bonds are possible, the experimental findings are not unexpected. By comparison of the room temperature results in the three solvents CDCl$_3$, CS$_2$, and pyridine, there is no pronounced solvent effect on the chemical nonequivalence. A small decrease for $\Delta\delta(CH_3)$ as well as $\Delta\delta(CH_2)$ exists, however, for CS$_2$.

Due to the high field available it became possible also to determine the geminal and vicinal H,H coupling constants from the ^{1}H spectrum of **10a** by first-order analysis. These data may serve as reference values for related structures and they are given in Table IV.

Experimental Section

The syntheses of the compounds studied have been described elsewhere.[7,18] ^{13}C NMR spectra have been obtained with a Bruker HX-90 spectrometer operating at 22.63 MHz or a Bruker WH-400 FT NMR spectrometer operating at 100.63 MHz. Both instruments were equipped with ^{2}H stabilization. A 12K Nicolet 1083 computer and a Bruker Aspect 2000 computer, respectively, were used for data collection. The concentration was 1 M in CCl$_4$/CDCl$_3$ (3:1) and the experimental error for the δ values is smaller

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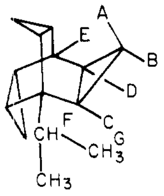
Table IV. ^1H NMR Chemical Shifts (δ, ppm relative to Me_4Si) and Coupling Constants (Hz) of 1-Isopropyltrishomobarrelene



chemical shifts (±0.001 ppm)

δ_A	δ_B	δ_C	δ_D	δ_E	δ_F	δ_G
0.767	0.041	0.364	0.497	2.366	1.697	0.992

coupling constants (±0.3 Hz)

J_{AB}	J_{AD}	J_{AC}	J_{BD}	J_{BC}	J_{CD}	J_{DE}	J_{FG}
(–) 5.3	3.8	3.8	7.8	7.8	8.1	4.7	6.8

than 0.1 ppm. The concentrations for the measurements of the substituted trishomobarrelenes **10a–d** are given in Table III.

For the assignment of the carbon resonances the following criteria were employed: **6**, off-resonance decoupling[19] and $^1J(^{13}C, {}^1H)$ values of 134.5 and 127.0 Hz for the CH and CH_2 groups, respectively; **7**, C-9 triplet at highest field (^1J = 163 Hz), C-2,3 doublet (^1J = 165 Hz), C-1,4 doublet (^1J = 134 Hz), C-5,6 and C-7,8 triplets; **8**, C-9 and C-9a triplets (^1J = 159 Hz) at highest field, C-2,3 and C-5,6 doublets (^1J = 161, 166 Hz), C-1,4 doublet (^1J = 136.2 Hz), C-7,8 triplet (^1J = 128.7 Hz); **9**, C-9 triplet (^1J = 158 Hz), C-2,3,5,6 doublet (^1J = 164 Hz), C-7,8 triplet (^1J = 128 Hz), C-1,4 doublet (^1J = 133 Hz); **10**, off-resonance decoupling and relative intensity; **18**, C-7,8 triplet (^1J = 126 Hz), C-2,3,5,6 doublet of highest relative intensity (^1J = 166 Hz), C-1,4 doublet (^1J = 137 Hz), C-9,9a doublet (^1J = 171 Hz).

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Registry No. 6, 280-33-1; **7**, 278-80-8; **8**, 63180-69-8; **9**, 63180-71-2; **10**, 70469-89-5; **10a**, 74925-50-1; **10b**, 74925-51-2; **10c**, 74925-52-3; **10d**, 74925-53-4; **18**, 28339-41-5.

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Hydrolysis Kinetics of an Amphiphilic Fatty Acid Ester. Real and Artifactual Effects of Reactant–Product Aggregation

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The hydrolysis of (4-(palmitolyloxy)phenyl)trimethylammonium iodide in 30% aqueous ethanol is accompanied by a sudden increase in solution turbidity if the initial ester concentration is $>10^{-4}$ M. The turbidity is attributed to aggregates of the palmitic acid product containing a small proportion of the ester. A methodology for extracting the reaction rate from the absorbance change requires the combination of a dual-wavelength photometer and a direct fit of the data to a single exponential. It is found that the reaction rate is left largely unaffected by the aggregation process. Turbidity measurements and microscopic examination reveal particle sizes in the 1–2-μm range where the wavelength dependence of light scattering is weaker than that for smaller particles. This improves the effectiveness of the dual-wavelength technique which uses the absorbance at a reference wavelength to cancel out drift due to variations in either source intensity or sample turbidity. Thus, artifacts due to turbidity changes, even in these strongly scattering preparations, are eliminated.

Introduction

The study of reactions in micellar systems is an extremely active and maturing area of physical organic chemical research.[1] It owes its rapid development, in part, to the fascination and importance of chemistry at an interface and, in part, to the applicability of the well-established techniques and analyses of solution kinetics.

As more complex systems are studied, including better models for biological membranes, these traditional techniques may have to be modified. Biochemists and biophysicists have long had to contend with turbid preparations where the change in absorbance due to an intracellular reaction of interest is small compared to a relatively constant scattering and absorbing background. Chance developed the dual-wavelength photometer to deal with these situations.[2] The particle size would have to be quite large (>300 Å) for scattering to interfere with the large absorbance changes which can be conveniently chosen in a homogeneous or micellar reaction. We report here a simple saponification of a surfactant ester which is complicated by formation of large aggregates of reactant and product and an accompanying sudden drastic increase in turbidity unlike anything normally encountered with either biological or chemical reactions. The dual-wavelength technique of Chance is simplified to allow the separation of the real from the artifactual effects of the aggregation on the reaction kinetics.

Experimental Section

Materials. By the procedure of Bruice et al.[3] for the dodecanoic acid ester, (4-(palmitoyloxy)phenyl)trimethylammonium iodide was prepared by trifluoroacetic anhydride induced condensation of palmitic acid and (4-hydroxyphenyl)trimethylammonium iodide. Recrystallization first from ethanol–water and then from methanol–diethyl ether gave analytically pure ester in 54% yield: mp 156–158 °C; IR (Nujol mull) 1760 cm^{-1}; NMR (Me_2SO-d_6) δ 0.82 (t, J = 7 Hz, 3 H), 1.1–2.0 (br s, 28 H), 3.63

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