^{1}H and ^{13}C NMR Spectral Behavior and Isomerism in 7,12-Dimethyl-, 2,7,12-Trimethyl-, and 7,12,15-Trimethyl-8,10-bisdehydro[15]annulenones

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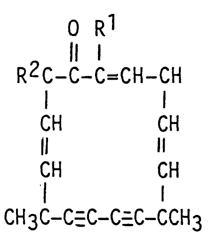
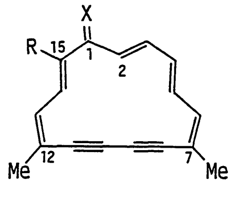
Configurational and conformational isomerism in the bisdehydro[15]annulenones were studied in $CDCl_3$ and CF_3CO_2D–CD_2Cl_2 solutions by ^{1}H NMR spectroscopy. The 7,12-dimethyl compound with the initial "all-*E*" configuration isomerized in both media at ambient temperature to give an equilibrium mixture of isomers but the trimethyl derivatives retained their original configuration under the similar conditions. The charge distribution in the deuterated species was discussed on the basis of the ^{13}C NMR spectra.

A number of large-ring annulenes are known to show configurational and conformational isomerism.[1)] We have recently reported isomerism in dimethyl and trimethyl derivatives of 10,12-bisdehydro[19]annulenone in neutral ($CDCl_3$) and acidic (CF_3CO_2D–CD_2Cl_2) media.[2)] Although these compounds existed as a single configurational isomer when synthesized, they slowly isomerized in these solutions at ambient temperature to give a mixture of several configurational isomers, each of which existed as a mixture of conformational isomers. We reported about ten years ago the syntheses of 7,12-dimethyl- (**1**), 2,7,12-trimethyl- (**2**), and 7,12,15-trimethyl-8,10-bisdehydro[15]annulenone (**3**) and their ^{1}H NMR spectral data in both neutral ($CDCl_3$) and acidic (CF_3CO_2D) solutions,[3,4)] and at that time only one configurational isomer was detected for each compound existing in a single conformation. The behavior observed in the [19]annulenones[2)] put in our mind the possible isomerism in the [15]annulenones and prompted us to reexamine the ^{1}H NMR spectral behavior of compounds **1**—**3** in detail using a high-field FT NMR spectroscopy. The ^{13}C chemical shift data of the bisdehydro[15]annulenones **1**—**3** are also discussed in relevance to their properties.

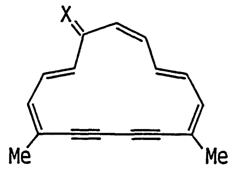


$$\begin{array}{l}
\mathrm{O}\ \ \mathrm{R^1}\\
\|\ \ \ |\\
\mathrm{R^2C{-}C{-}C{=}CH{-}CH}\\
\ \ |\qquad\qquad\quad\ |\\
\mathrm{CH}\qquad\quad\ \ \mathrm{CH}\\
\ \|\qquad\qquad\quad\ \|\\
\mathrm{CH}\qquad\quad\ \ \mathrm{CH}\\
\ \ |\qquad\qquad\quad\ |\\
\mathrm{CH_3C{-}C{\equiv}C{-}C{\equiv}C{-}CCH_3}
\end{array}$$

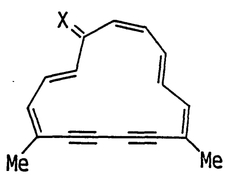
1: $R^1=R^2=H$
2: $R^1=CH_3$, $R^2=H$
3: $R^1=H$, $R^2=CH_3$



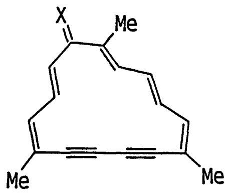
1A: R=H, X=O
4A: R=H, $X=OD^+$
3A: $R=CH_3$, X=O
8: $R=CH_3$, $X=OD^+$



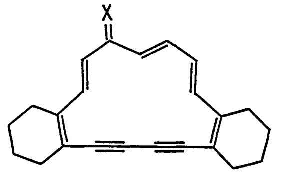
1B: X=O
4B: $X=OD^+$



1C: X=O
4C: $X=OD^+$



2A: X=O
7: $X=OD^+$



5: X=O
6: $X=OD^+$

Results and Discussion

Isomerism in Compound 1. The ^{1}H NMR spectrum of compound **1** synthesized according to the previously reported procedure[3,4)] indicated that **1** existed in almost a single form with a small amount (ca. 10%) of a second isomer (Fig. 1a), which had escaped detection in the previous study made by using a low-field CW NMR spectrometer.[3)] The spectrum of the major isomer was analyzed to give the chemical shifts and the coupling constants given in Table 1 on the basis of the homonuclear double resonance and nuclear Overhauser effect (NOE) experiments. These data clearly indicated the geometry **1A** for the major isomer. Thus, all the CH=CH bonds of **1A** were of *E* configuration (hereafter referred to as "all-*E*" configuration). No essential change was observed in the temperature range of 60 to −60 °C suggesting the conformational homogeneity.[4)]

Compound **1** showed configurational isomerization in $CDCl_3$ at 26 °C with the elapse of time and the minor isomer mentioned above became more and more populated (Fig. 1b). After left standing at ambient temperature for two months **1** consisted of two configurational

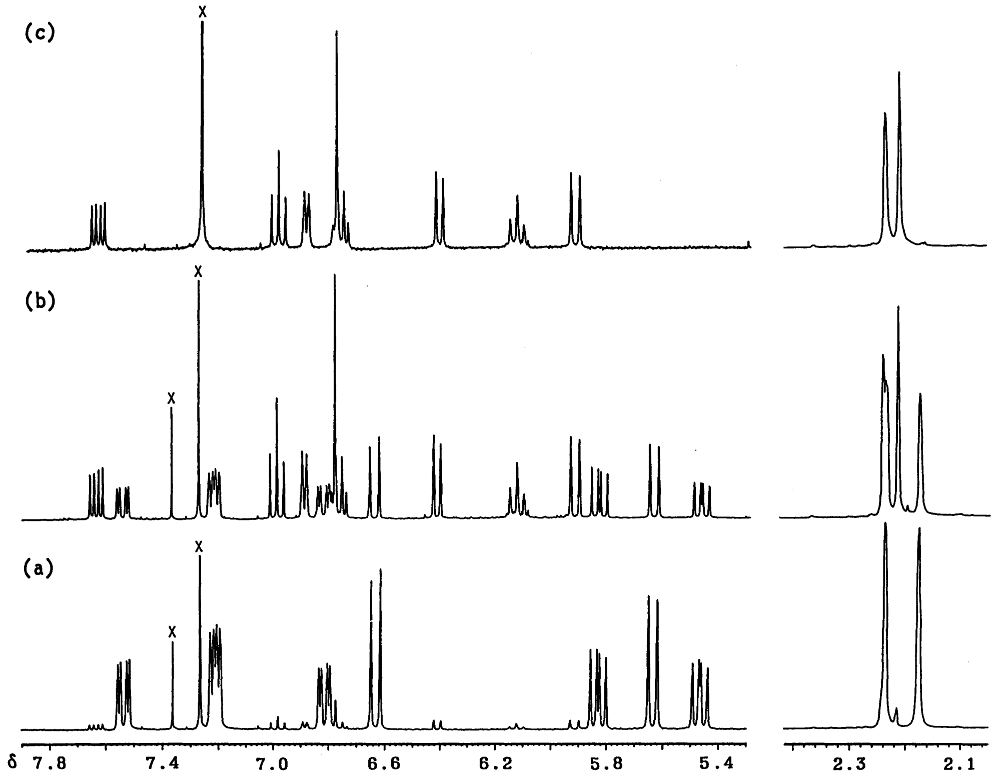


Fig. 1. ^1H NMR spectra in $CDCl_3$ at 26 °C: (a) **1A** contaminated with a small amount of **1B**; (b) A mixture of **1A** and **1B** in a ratio of ca. 1:1; (c) **1B**. Intensities of the methyl proton signals are reduced. Peaks with × are due to impurities.

Table 1. ^1H NMR Data of the Isomers of Compound **1**[a)]

Medium	$CDCl_3$			CF_3CO_2D–CD_2Cl_2 (3:1)		
Proton	Isomer					
	1A	**1B**	**1C**[b)]	**4A**	**4B**	**4C**
2	5.632d	6.408d[c)]		−0.087d	8.151d	8.494d
	(15.6)	(12.7)		(14.8)	(11.6)	(11)
3	7.534dd	6.981m[c)]		9.747dd	9.272dd	8.332t
	(15.6, 4.9)			(14.8, 6.3)	(13.3, 11.6)	(11)
4	6.812dd	6.116m[c)]		8.761dd	0.909dd	8.699dd
	(15.4, 4.9)			(15.1, 6.3)	(14.4, 13.3)	d)
5	5.463dd	6.755m[c)]		−0.158dd	8.935dd	1.473t
	(15.4, 11.7)			(15.1, 12.4)	(14.3, 8.6)	(13.6)
6	7.214d	6.775m[c)]		9.140d	8.483d	8.792d
	(11.7)			(12.3)	(8.6)	d)
13	7.202d	6.880d		9.140d	8.521d	8.666d
	(11.5)	(7.6)		(12.3)	(8.9)	d)
14	5.825dd	7.630dd		0.287dd	9.815dd	9.663dd
	(16.4, 11.5)	(15.6, 7.6)		(15.1, 12.3)	(14.9, 8.9)	(15.3, 8.4)
15	6.629d	5.912d		8.694d	0.496d	0.468d
	(16.4)	(15.6)		(15.1)	(14.9)	(15.3)
7-Me	2.174s	2.213s	2.264s	3.175s	3.114s	3.364s
12-Me	2.234s	2.240s	2.370s	3.259s	3.185s	3.236s

a) Obtained at 26 °C. Chemical shifts are given in δ. In acidic solutions the $CHDCl_2$ signal at δ=5.30 was used as the reference. In parentheses are coupling constants in Hz. b) Only the methyl proton signals were identified. c) First-order analysis could not be made and the spectrum was analyzed by computer simulation using the LAOCN3 program (see text and Table 2). d) Coupling constants could not be determined because of the signal overlap.

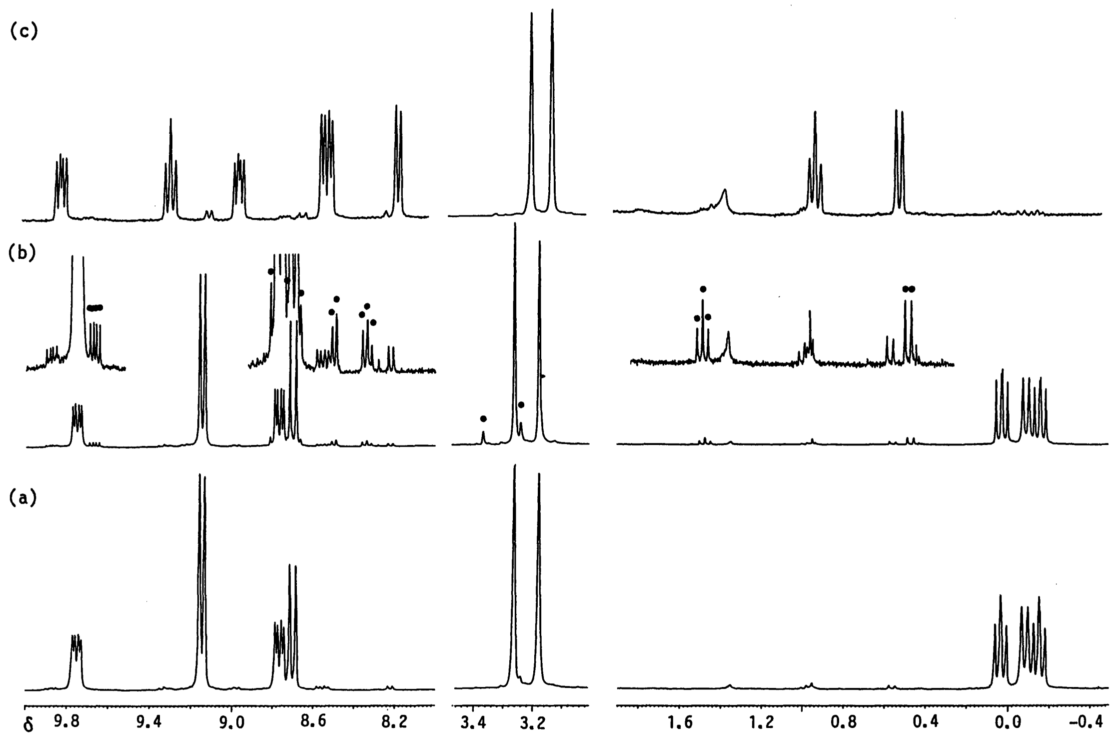


Fig. 2. ^{1}H NMR spectra in CF_3CO_2D–CD_2Cl_2 (3:1) at 26 °C: (a) **4A**; (b) A mixture of **4A** and **4C** in a ratio of ca. 10:1. Peaks with ● are due to **4C** and the other small peaks are due to impurities; (c) **4B**. Intensities of the methyl proton signals are reduced.

isomers **1A** and **1B** in a ratio of 28 : 72. No further change in the ratio was detected by ^{1}H NMR on further standing but broad signals ascribed to decomposition and/or polymerization products gradually developed. Therefore the above ratio is considered to be the one at equilibrium.

Isomer **1B** was isolated by preparative gel permeation chromatography of the mixture. In the ^{1}H NMR spectrum of isomer **1B** in $CDCl_3$ at 26 °C (Fig. 1c), the signals assignable to protons at 2 to 6 positions were considerably distorted from a first-order spectrum because of the proximity of the chemical shifts of 5-H and 6-H, and were thus analyzed as a five-spin system by computer simulation using the LAOCN3 program[5] and the results are given in Table 2. The structure of **1B** could be unambiguously determined as shown: the C^2=C^3 bond is of *Z* configuration and thus six olefinic protons are outside the ring and two are inside.

Both of the isomers **1A** and **1B** show diatropicity under the neutral conditions, since the inner olefinic protons resonate at higher field than the outer protons as expected for a potential 14π-electron system due to polarization of the carbonyl group, as discussed previously.[3,4]

Dissolution of a crystalline sample of **1**, composed of **1A** and **1B** in a ratio of ca. 9 : 1, in CF_3CO_2D–CD_2Cl_2 (3 : 1) gave a dark purple solution containing a deuterated species **4A**, which retained the same geometry as the precursor **1A** as judged by the ^{1}H NMR spectrum (Table 1 and Fig. 2a). Signals due to the minor isomer were hardly detected.

Table 2. Best-Fit Parameters (Hz) of 2-H to 6-H of **1B** Obtained by LAOCN3 Simulation

Chemical shifts[a]		Coupling constants							
2	3204.77	2,3	12.65	3,4	12.63	4,5	14.69	5,6	7.65
3	3491.46	2,4	1.10	3,5	0.21	4,6	−0.90		
4	3058.95	2,5	0.05	3,6	0.15				
5	3378.66	2,6	0.25						
6	3388.45								

a) From internal TMS.

Gradual isomerization of **4A** took place at ambient temperature and after two weeks the solution was composed of two species **4A** and **4C** in a ratio of 10 : 1 (Fig. 2b).

Although the low population of **4C** made it difficult to analyze unambiguously the ^{1}H NMR signals derived from **4C**, the appearance of only two protons at a high field of above δ=2 suggested that **4C** had one *Z*-CH=CH bond. Thus, the structure **4C** with 2-*Z* configuration was assigned as the most reasonable.

Dissolution of isomer **1B** in the TFA medium gave at first the corresponding deuterated species **4B** as revealed by the ^{1}H NMR spectrum (Table 1 and Fig. 2c), but **4B** rapidly isomerized with a half-life of ca. 6 h at 26 °C and finally gave a mixture of **4A** and **4C** in the same ratio as above (10 : 1).

The deuterated species shows large diatropicity because the positive charge is delocalized to the ring and a 14π-electron aromatic system is formed: The inner protons shift upfield and the outer proton downfield.

Neutralization of the TFA solution with aqueous sodium hydrogencarbonate resulted in regeneration of compound **1**. The ^{1}H NMR spectrum of the sample in $CDCl_3$ measured immediately after neutralization showed the presence of **1A** and **1C** in ca. 10 : 1 ratio together with considerable amounts of decomposition and/or polymerization products. Only the methyl proton signals were identified for **1C**, and the geometry of this isomer could not be determined although the same one as **4C** might be assigned. The signals ascribable to **1C** gradually decreased their intensities while the signals due to **1B** appeared and gradually increased their intensities until the ratio of **1A** to **1B** reached ca. 1 : 2.

Thus, it is interesting to note that the 2-*Z* isomer is more stable than the "all-*E*" isomer under the neutral conditions but far less stable under the acidic conditions.

In the case of the bis(cyclohexene)-annelated bisdehydro[15]annulenone **5** synthesized by Howes et al.,[6] two configurational isomers, "all-*E*" and 2-*Z*, were separately isolated in the yields of 15 and 6%, respectively, although the conformation was not determined for either of them. When dissolved in TFA, both isomers gave the same species **6** with "all-*E*" configuration, the conformation being the one shown.[6]

Thus the instability of the 2-*Z* form in an acidic medium seems to be a common feature but the reason for this is still unclear.

Although quantitative analysis was not made, the configurational isomerization was much faster under acidic conditions (e.g. **4B** → **4A**) than under neutral conditions (e.g. **1A** → **1B**). A similar behavior was observed in the bisdehydro[19]annulenone derivatives.[2] This can reasonably be ascribed to the decrease in the bond alternation in deuterated species.

^{1}H NMR Spectral Studies of 2 and 3. Either of the 2,7,12-trimethyl **2** and 7,12,15-trimethyl derivative **3** existed as a single species as shown by the structural formula both in $CDCl_3$ (**2A** and **3A**) and in CF_3CO_2D–CD_2Cl_2 (**7** and **8**) (Table 3, Figs. 3 and 4), and showed no isomerization when left standing at ambient temperature over a month, when signals due to decomposition and/or polymerization products had appeared. The present ^{1}H NMR spectral data confirm the earlier conclusion on the geometries of these species obtained by the low-field CW NMR studies,[4] although some of the chemical shift assignments should be modified.

Isomer **2A** shows somewhat lower tropicity than **1A** and **3A** as judged from the higher-field resonance of the 7- and 12-methyl protons. Similarly the extent of the upfield shifts of the inner protons and downfield shifts of the outer as well as methyl protons upon deuteration is smaller in **7** than in **4A** and **8**. These should be ascribed to the low planarity of the skeleton of **2A** compared with those of **1A** and **3A**. This feature is suggested by molecular model considerations and also by the fact that isomers with the same skeleton as **2A** were not detected in **1** and **3**.

Isomers with the same skeleton as **1B** and **1C** are reasonably expected to be detected for **2**, although an isomer with the same skeleton as **1A** is improbable,

Table 3. ^{1}H NMR Data of Compounds 2 and 3[a)]

Medium	$CDCl_3$		CF_3CO_2D–CD_2Cl_2 (3:1)	
Proton	Isomer			
	2A	**3A**	**7**	**8**
2	—	5.472d (15.5)	—	−0.499d (15.3)
3	5.429d (10.8)	7.609dd (15.5, 5.1)	1.913d (11.8)	9.814dd (15.3, 6.7)
4	7.156dd (15.5, 10.8)	6.822ddq (15.5, 5.1, 0.8)	8.743dd (14.6, 11.8)	8.826dd (15.1, 6.7)
5	5.338dd (15.5, 9.6)	5.253dd (15.5, 11.8)	1.446dd (14.6, 10.8)	−0.640dd (15.1, 12.4)
6	7.230d (9.6)	7.233dquint (11.8, 1.0)	8.649d (10.8)	9.211d (12.4)
13	7.054d (11.0)	7.389dq (11.7, 1.4)	8.625d (11.7)	9.367dq (12.4, 0.8)
14	5.569dd (16.3, 11.0)	5.464d (11.7)	1.019dd (14.9, 11.7)	−0.537d (12.4)
15	6.657d (16.3)	—	8.362d (14.9)	—
2-Me	2.038s	—	2.792s	—
7-Me	2.085s	2.176s	2.848s	3.220s
12-Me	2.191s	2.267s	3.023s	3.344s
15-Me	—	2.181s	—	3.260s

a) Obtained at 26 °C. Chemical shifts are given in δ. In acidic solutions the $CHDCl_2$ signal was used as the reference at δ=5.30. In parentheses are coupling constants in Hz.

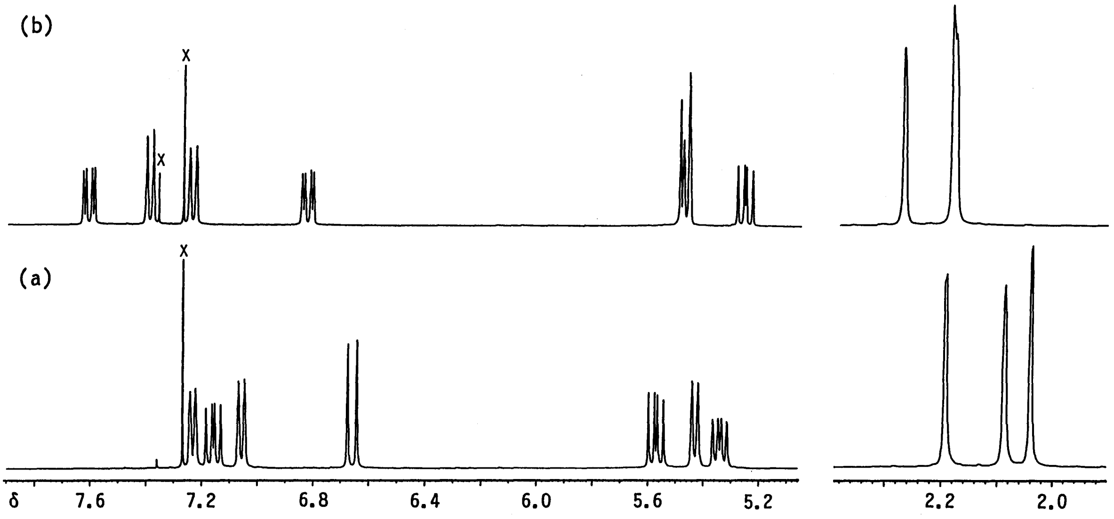


Fig. 3. ^{1}H NMR spectra in $CDCl_3$ at 26 °C of (a) **2** and (b) **3**. Intensities of the methyl proton signals are reduced. Peaks with × are due to impurities.

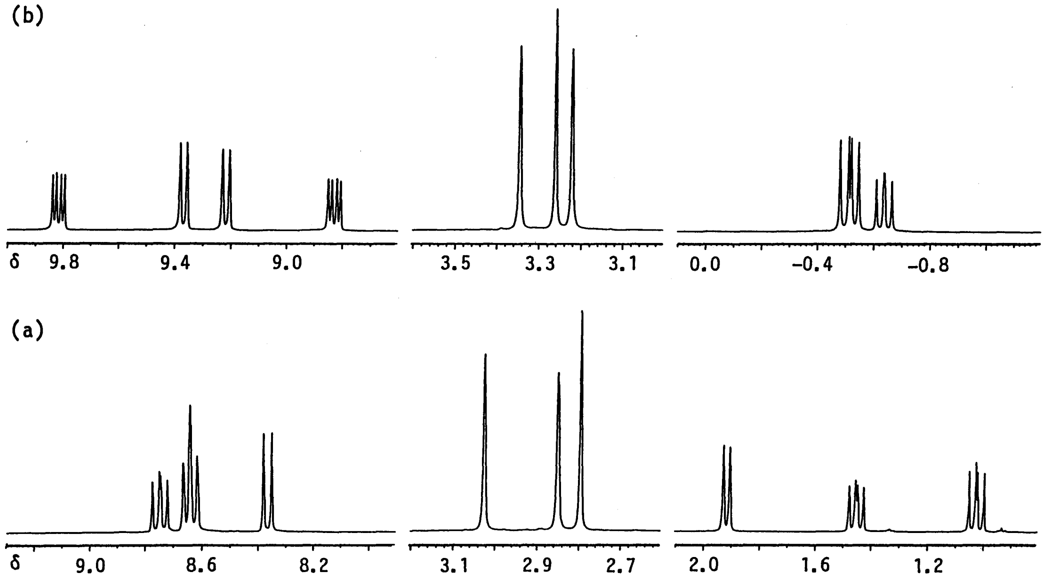


Fig. 4. ^{1}H NMR spectra in CF_3CO_2D–CD_2Cl_2 (3:1) of (a) **7** and (b) **8**. Intensities of the methyl proton signals are reduced.

because the bulky 2-methyl group can not be located inside the macrocycle.

Therefore the presence of only one isomer in **2** (and also in **3**) does not necessarily imply that the observed isomers are the only stable isomers. The reason for the absence of other isomers may be ascribed to a high energy barrier to isomerization (>27 kcal mol^{-1}).

^{13}C NMR Spectra of Compounds 1—3. The ^{13}C NMR spectral data of **1** (**1A** and **1B**), **2**, and **3** in $CDCl_3$ and CF_3CO_2D–CD_2Cl_2 (3 : 1) are listed in Tables 4 and 5, respectively.

Although the ^{13}C chemical shifts do not directly afford information on the tropicity of the species in question, some aspects of the ^{13}C data are worth consideration.

The carbonyl carbon (1-C) signal moves *upfield* by ca. 6—8 ppm upon deuteration in any of the species, and the CH carbons α to the carbonyl group (2-C and 15-C in **1A**, 15-C in **2**, and 2-C in **3**) also shift upfield by 6—10 ppm. The other olefinic carbons show downfield shifts. The extent of the shift is large for the 3-, 5-, 7-, 12-, and 14-carbons (10—18 ppm), while it was rather small for the 4-, 6-, 8-, and 13-carbons (3—5 ppm). These data suggest that the positive charge in the deuterated species is distributed to the ring carbons not uniformly but alternately, and is rather biased to carbons remote from the carbonyl group.[7)]

When a methyl group is attached to a carbon α to the carbonyl group, that carbon moves rather downfield: 2-C

Table 4. ^{13}C Chemical Shifts of Compounds **1**—**3** in $CDCl_3$ at 26 °C[a)]

Carbon	**1A**	**1B**	**2**	**3**
1	191.13	191.10	196.93	191.28
2	126.26	131.23	134.26	125.78
3	138.71	139.93	140.45	138.53
4	128.55	127.09	130.99	128.31
5	133.95	135.39	139.98	133.43
6	140.59	135.87	141.41	140.54
7	123.94	120.52	124.09	123.73
8	84.05	84.06	82.38	84.05
9	84.70	84.93	87.96	84.56
10	88.74	89.55	89.66	88.91
11	91.24	90.52	93.35	91.05
12	129.30	120.90	126.91	126.83
13	138.89	135.01	140.25	137.21
14	141.95	137.25	141.36	136.30
15	132.88	127.97	133.63	140.44
2-Me	—	—	13.57	—
7-Me	20.80	23.34	19.75	20.71
12-Me	21.64	23.65	22.31	21.96
15-Me	—	—	—	12.08

a) Given in δ. Individual assignments of the acetylenic carbons were not made. The assignments of the 7- and 12-carbons are tentative.

Table 5. ^{13}C Chemical Shifts of Compounds **1**—**3** in CF_3CO_2D-CD_2Cl_2 (3:1) at 26 °C[a)]

4A		**4B**		**7**		**8**	
23.44		26.42		15.48	2-Me	14.19	15-Me
24.46		27.50		22.02	7-Me	23.59	7-Me
				25.03	12-Me	24.98	12-Me
94.48	q	96.82	q	93.58	q	95.27	q
97.68	q	98.53	q	98.15	q	97.14	q
97.86	q	100.59	q	98.34	q	98.48	q
101.29	q	102.47	q	103.54	q	101.65	q
116.08	2	119.48		127.33	15	115.53	2
126.70	15	122.77		136.06	4	132.20	4
132.31	4	130.00		138.00	q	139.08	q
139.79	7/12	136.73	q	139.18	q	139.24	q
142.95	13	139.06		142.84	q	141.75	13
143.50	5	140.65		144.56	13	142.24	5
145.57	6	140.86	q	147.13	6	144.49	q
147.87	7/12	148.46		154.40	14	145.69	6
151.68	3	151.82		155.76	5	148.13	14
153.00	14	159.77		156.06	3	149.43	3
183.93	1	183.27	1	191.35	1	183.02	1

a) The CF_3 carbon of the solvent was used as the reference at δ=116.50. Assignments where indicated are based on ^{13}C–^{1}H COSY experiments. "q" denotes a quaternary carbon.

of **2** shifts from δ=134.26 in $CDCl_3$ to somewhere between δ=138 and 143 in TFA, while 15-C of **3** moves from δ=140.44 in $CDCl_3$ to either δ=144.49 or around δ=139 in TFA. This is probably because the carbon atom carrying a methyl group has a higher positive charge density owing to the stabilization by the methyl group.

All the acetylenic carbons move downfield by ca. 10 ppm upon deuteration. The methyl carbons also shift downfield by 2—3 ppm in any species.

Experimental

Compounds **1**—**3** were synthesized according to the reported procedures.[3,4)] ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AM-500 spectrometer operating at 500.1 and 125.8 MHz, respectively. Tetramethylsilane (TMS) was used as the chemical shift reference except for the ^{13}C NMR spectra in CF_3CO_2D-CD_2Cl_2 where the quartet signal due to the CF_3 carbon at δ=116.5 was used as the reference. Preparative gel permeation chromatography was performed on an LC-908 Liquid Chromatograph of Japan Analytical Industry Co., Ltd. with a series of JAIGEL 1H and 2H columns and chloroform as the eluent.

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