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^{1}H NMR SOLVENT SHIFTS INDUCED BY HEXAFLUOROBENZENE IN GERMACRONES, TEN-MEMBERED RING SESQUITERPENES

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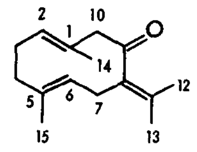
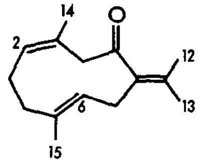
The direction of ^{1}H NMR solvent shifts induced by C_6F_6 observed for some polar solutes is known to be opposed to that of C_6H_6-induced shifts.[1] In a previous communication,[2] we reported that the aromatic-solvent induced-shift (ASIS) method[3] becomes more powerful in problems of organic chemistry when C_6F_6 is also employed as a solvent after C_6D_6 and/or C_5D_5N, having confirmed that carbonyl reference plane rules as shown in FIG. 1, hold good in many monoterpenic carbonyl compounds. In this paper we wish to report the results of some applications of this method to several germacrones, ten-membered sesquiterpenic ketones, and discuss their conformations.

Hikino et al.[4] already described that germacrone (1) adopts conformation A in which the αβ unsaturated carbonyl group assumes an s-trans arrangement and the two double bonds have a crossed orientation (see FIG. 2), on the bases of the ASIS result with C_6D_6 and an X-ray analysis of a crystal of a silver nitrate complex with 1. This revises an earlier report by Šorm et al.,[5] who inferred that 1 adopts conformation B in which the αβ unsaturated carbonyl group assumes an s-cis arrangement and the two double bonds have a parallel orientation. In order to examine conformational arrangements of carbonyl groups in some other germacrones, cis,trans-germacrone (2),[6] cis,cis-germacrone (3),[6] trans,cis-acoragermacrone (4),[7] and pre-isocalamendiol (5),[7] we measured and compared their ^{1}H NMR spectra in CCl_4, C_6F_6, C_6D_6, C_5D_5N, and $CDCl_3$ with those of pyrogermacrone (6) and fukinone (7), which have rigid s-cis configurations for the carbonyl groups.

The TABLE lists the ASIS data observed for the germacrones and related compounds. Variable-temperature ^{1}H NMR spectra of these ten-membered ring ketones in $CDCl_3$ showed that rapid inversion[8] of the ten-membered rings takes place on the NMR time scale at room temperature, because the signals became



(1)



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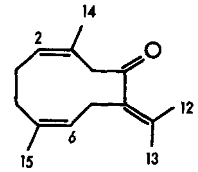

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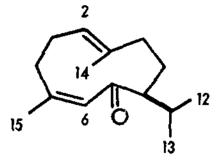

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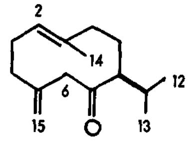

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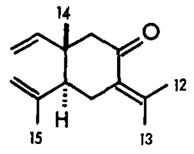

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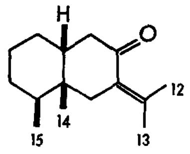

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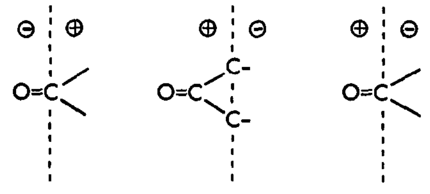
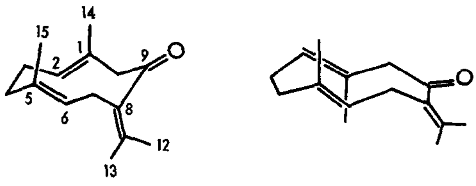


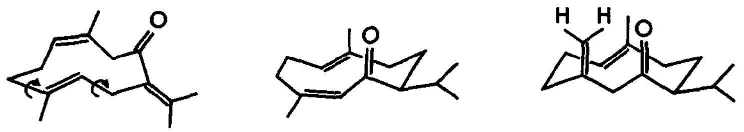
(a) C_6F_6 (b) C_5D_5N (c) C_6D_6

FIG. 1. Carbonyl reference plane rules. Dotted line shows a reference plane.



(A)[4] (B)[5]

FIG. 2. Molecular conformations for 1. Conformation A is preferential.



(C) (D) (E)

FIG. 3. Preferential molecular conformations for 2, 4, and 5 (C, D, and E, respectively).

TABLE. ^{1}H Chemical Shifts (δ) and ASIS Data[a] on Sesquiterpenic Carbonyl Compounds Examined[b]

Proton	δ_{CCl_4}	ASIS (ppm)			δ_{CDCl_3}
		C_6F_6	C_6D_6	C_5D_5N	
(**1**)					
12-H	1.77	+0.10	-0.30	-0.12	1.78
13-H	1.71	+0.08	-0.27	-0.06	1.73
14-H	1.59	-0.03	+0.05	+0.06	1.64
15-H	1.42	-0.01	-0.05	+0.01	1.46
(**2**)					
2-H	5.22	-0.02	-0.01	+0.15	5.31
6-H	5.05	-0.07	+0.02	+0.07	5.08
7-H	2.86	-0.06	+0.03	+0.09	2.92
10-H	2.97	-0.02	+0.01	+0.15	3.06
12-H	1.73	+0.09	-0.26	-0.01	1.73
13-H	1.63	+0.02	-0.16	-0.01	1.67
14-H	1.87	-0.09	+0.14	+0.03	1.88
15-H	1.53	-0.02	0.00	+0.09	1.58
(**3**)					
2-H	5.41	+0.06	-0.05	+0.06	5.50
6-H	5.13	-0.06	+0.06	+0.10	5.17
7-H	3.02	-0.01	-0.03	+0.06	3.09
10-H	3.11	-0.06	+0.08	+0.17	3.21
12-H	1.76	-0.04	+0.04	+0.09	1.76
13-H	1.69	+0.17	-0.21	-0.03	1.71
14-H	1.76	-0.05	-0.03	+0.02	1.82
15-H	1.69	-0.06	-0.12	-0.03	1.71
(**4**)					
2-H	4.97	-0.01	+0.05	+0.12	5.04
6-H	5.94	+0.08	-0.03	+0.18	6.06
12-H 13-H	0.90	+0.07	-0.02	+0.04	0.93
14-H	1.44	-0.01	+0.10	+0.10	1.48
15-H	1.78	+0.15	-0.24	-0.02	1.81
(**5**)					
2-H	5.14	+0.02	-0.09	+0.09	5.22
6-H	2.87	-0.02	-0.04	+0.14	2.98
	3.20	+0.01	-0.18	+0.10	3.29
12-H	0.85	+0.05	-0.06	-0.01	0.87
13-H	0.90	+0.04	-0.08	-0.02	0.92
14-H	1.37	-0.10	+0.11	+0.08	1.42
15-H	4.84	-0.16	+0.18	+0.19	4.88
	4.93	-0.06	+0.09	+0.10	5.02
(**6**)					
12-H	1.97	-0.10	+0.03	+0.14	2.04
13-H	1.78	+0.09	-0.29	-0.09	1.80
14-H	1.03	+0.01	-0.10	-0.01	1.05
15-H	1.78	+0.09	-0.14	-0.03	1.80
(**7**)					
12-H	1.90	-0.12	+0.05	+0.14	1.96
13-H	1.77	+0.11	-0.22	-0.06	1.80
14-H	0.96	+0.11	-0.21	-0.01	0.97
15-H	0.89	+0.07	-0.18	-0.02	0.86

[a] We have chosen CCl_4 and TMS as a reference solvent and an internal standard, respectively. We should like to claim a wide applicability for CCl_4 and $CDCl_3$ in organic chemistry, although cyclohexane might be recommended for the both references;[2] and therefore, we have also described δ values in $CDCl_3$ in the TABLE. ASIS values are indicated by δ(aromatic solvent)-δ(CCl_4); plus sign represents a downfield shift.

[b] ^{1}H NMR spectra were taken with a Varian A-56/60D spectrometer at 40°. Sample concentrations were about 5% (w/v) or less. Accuracies of chemical shifts (δ) are within ±0.01.

much broader as the temperature was lowered down to -50°.

As seen from the TABLE, the downfield and upfield ASIS of the 12-H and 13-H signals of **1** in C_6F_6 and C_6D_6, respectively, show that the enone preferentially forms an s-trans arrangement during rapid inversion of the ten-membered ring in solution. We can further infer from the ASIS values for 14-H and 15-H that conformer A is preferred among the possible four conformers of the s-trans conformation. On the other hand, the 12-H and 13-H signals of **6** and **7** demonstrates typical ASIS features of an s-cis configuration of the enones (see the TABLE).

A similar result was obtained for **2**; the enone is s-*trans* and **2** preferentially adopts conformation C shown in FIG. 3 as indicated by the ASIS of the 14-H signal. However, the 12-H and 13-H signals of **3** behaved in a manner similar to those of **6** and **7** in the aromatic solvents used; this implies that the enone assumes an s-*cis* arrangement as an averaged form in solution.

The ASIS values obtained for **4** showed that 6-H, 12-H, 13-H, and 15-H lie behind the carbonyl reference plane and 2-H and 14-H in front of it; these results suggest that conformation D shown in FIG. 3 is preferential for this molecule. This conformation D was suggested by Yamamura *et al*.[9] in a study of the transannular cyclization reaction of **4**.

In compound **5**, only 14-H and two 15-H's were found to lie in front of the reference plane. Thus, conformation E (FIG. 3) suggested by Yamamura *et al*.[10] is also considered preferential.

Other evidence for the conformations suggested here for compounds **2**-**5** will be reported in the future.

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