^{1}H and ^{13}C NMR Spectral Studies of C-2 Substituted Isomeric *exo*- and *endo*-5-Methylbicyclo[3.2.1]octane-6,8-diones†

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A detailed analysis of the ^{1}H and ^{13}C NMR spectra of C-2 aryl and alkyl/desalkyl substituted isomeric *exo*- and *endo*-5-methylbicyclo[3.2.1]octane-6,8-diones is presented. The chemical shift of the C-5 angular methyl, the C-2 alkyl/olefinic (C-10)/C-2 methine protons, the aromatic proton shieldings and the characteristic AMX and ABX spectral pattern of the ketomethylene and bridgehead protons were found to be sensitive to the phenyl ring orientation (anisotropy). These distinctive features could be used for configurational distinction for this class of compounds. With increasing *ortho*-methoxy substitution on the phenyl ring, considerable deshielding of the bridgehead proton was observed (*ca.* 0.6 ppm). Absence of the C-2 alkyl group in the desalkyl isomers resulted in substantial changes in the chemical shifts of different protons. A study of the NMR spectra of the corresponding bicyclic compounds with C-2 methoxy/hydroxy substitution instead of the aryl group revealed that the anisotropy of the phenyl ring and the electronegative oxygen substituents have opposite effects.

The ^{13}C NMR spectral assignment of each carbon resonance of C-2 aryl and alkyl/desalkyl substituted isomeric *exo*- and *endo*-5-methylbicyclo[3.2.1]octane-6,8-diones and the corresponding C-2 methoxy/hydroxy/chloro and methyl bicyclic compounds are reported. Additional *ortho*-methoxy substitution on the phenyl ring was found to produce considerable high field shifts of the C-10 and C-1 carbon resonances. A high-field shift was observed for the C-6 and C-8 carbonyl carbons, presumably due to 1,3-dicarbonyl interactions. The chemical shifts of C-1′ aromatic, C-10 alkyl and C-2 carbons, which are sensitive to *exo*/*endo* isomerism, could be utilized in differentiating a pair of isomers.

INTRODUCTION

One of the most significant aspects of NMR spectroscopy is its utility in differentiating and identifying stereoisomers of a particular compound, and a study of NMR parameters often leads to unequivocal assignment of stereochemical configurations. In addition, the sensitivity of ^{13}C shieldings to the stereochemical environment provides direct access to the study of substituent effects on the nuclei. Various reports[1–8] of the NMR spectra of substituted bicyclo[3.2.1]octane systems have clearly demonstrated the variations of shielding parameters with substituents and their stereochemistry. In the course of our studies on the total synthesis of B-seco-steroids, we had isolated and unambiguously characterized[3,9] a number of C-2 aryl and alkyl substituted isomeric *exo*- and *endo*-5-methylbicyclo[3.2.1]octane-6,8-diones, **2** and **3** respectively, in the MeOH–HCl reaction of the seco-dione of type **1** [2-methyl-2-(3-aryl-3-alkyl-prop-2-ene)cyclopentane-1,3-dione]. The well defined[1,9b,10] molecular structure of the bicyclic diketones **2–5** prompted us to analyse their ^{1}H and ^{13}C NMR spectra in detail. The results of this investigation are discussed in this paper.

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^{1}H NMR SPECTRA

The ^{1}H NMR spectra of the well characterized[3,9,10] compounds **2** and **3** were systematically examined for parameters that could differentiate and characterize the configurational isomers, so that the spectra–structure correlations could have general significance. The most significant differences observed between these *exo* and *endo* isomers **2** and **3** respectively, have been tabulated (Tables 1–5) and are individually discussed.

RESULTS

Chemical shifts of the C-5 angular methyl group

The C-5 angular methyl group is shielded (see Table 1) in all the *exo* isomers **2** (δ 0.94–0.97) relative to the *endo* isomers **3** (δ 1.06–1.09), except in the case of the C-2 desalkyl compounds **2a** and **3a**.

Chemical shifts of the C-2 methyl, olefinic (C-10) and C-2 methine protons

A clear pattern which can be attributed to *exo*/*endo* isomerism has been recognized in the chemical shifts

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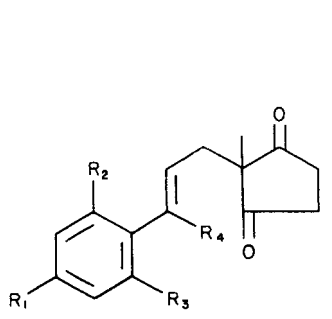

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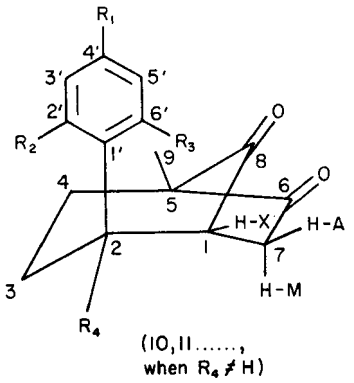

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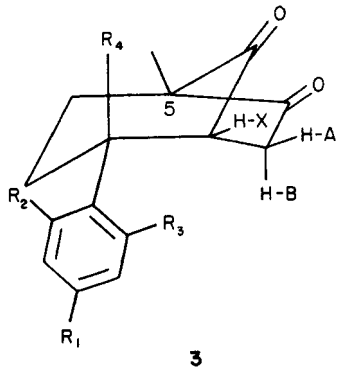
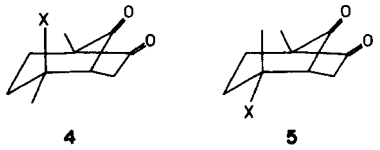


3

a : $R_1 = OCH_3$, $R_2 = R_3 = R_4 = H$
b : $R_1 = OCH_3$, $R_2 = R_3 = H$, $R_4 = CH_3$
c : $R_1 = OCH_3$, $R_2 = R_3 = H$, $R_4 = CH_2CH_3$
d : $R_1 = OCH_3$, $R_2 = R_3 = H$, $R_4 = CH_2CH_2OCH_3$
e : $R_1 = OCH_3$, $R_2 = R_3 = H$, $R_4 = CH_2CH(CH_3)_2$
f : $R_1 = H$, $R_2 = OCH_3$, $R_3 = H$, $R_4 = CH_3$
g : $R_1 = R_2 = OCH_3$, $R_3 = H$, $R_4 = CH_3$

h : $R_1 = R_2 = OCH_3$, $R_3 = H$, $R_4 = CH_2CH_3$
i : $R_1 = R_2 = OCH_3$, $R_3 = H$, $R_4 = CH=CH_2$
j : $R_1 = R_2 = OCH_3$, $R_3 = H$, $R_4 = CH_2CH_2OCH_3$
k : $R_1 = R_2 = OCH_3$, $R_3 = H$, $R_4 = CH_2CH(CH_3)_2$
l : $R_1 = R_2 = OCH_3$, $R_3 = H$, $R_4 = CH=C(CH_3)_2$
m : $R_1 = H$, $R_2 = R_3 = OCH_3$, $R_4 = CH_3$



4 5

a: X = OCH_3
b: X = OH
c: X = Cl

of the C-2 methyl, olefinic (C-10) and C-2 methine protons (see Table 1). The equatorial methyl/olefinic (C-10)/C-2 methine protons in *exo*-**2** are always more shielded than the corresponding protons in the *endo*-**3** isomers. These shieldings are much more significant for the olefinic (*exo*-**2i**, **2l** and *endo*-**3i**, **3l**) and the methine (*exo*-**2a** and *endo*-**3a**) proton signals. The observed shieldings are contrary to the expected trend, since equatorial alkyl groups/protons generally occur at lower field than their axial counterparts.[11]

Ketomethylene and bridgehead protons in *exo*-bicyclic compounds 2: AMX pattern

A characteristic AMX pattern exhibited by *exo*-aryl-*endo*-alkyl/desalkyl bicyclic compounds **2** is observed in the region of δ 2.44–4.05 (see Table 2) which could be analysed by first-order analysis. The *exo*- and *endo*-ketomethylene protons H-A and H-M, respectively, were differentiated from their vicinal coupling constants with the bridgehead proton H-X. H-A,

Table 1. Chemical shifts of the C-5 angular methyl and C-2 substituents (R_4) in *exo*/*endo* isomers 2 and 3

Bicyclic	C-5 angular methyl group			C-2 substituent (R_4)		
compound	*exo*-2	*endo*-3	Δδ(3−2)	*exo*-2	*endo*-3	Δδ(3−2)
a	1.12	1.05	−0.07	3.51[a]	3.66[a]	0.15
b	0.95	1.09	0.14	1.30[b]	1.35[b]	0.05
c	0.95	1.09	0.14	—	—	—
d	—	1.09	—	—	—	—
e	0.94	1.09	0.15	—	—	—
f	0.95	1.09	0.14	1.43[b]	1.47[b]	0.04
g	0.95	1.08	0.13	1.39[b]	1.44[b]	0.05
h	0.95	1.07	0.12	—	—	—
i	0.97	1.07	0.10	6.19[c]	6.42[c]	0.23
j	0.95	1.07	0.12	—	—	—
k	0.94	1.07	0.13	—	—	—
l	0.95	1.06	0.11	4.67[c]	5.75[c]	1.08
m	—	1.07	—	—	1.49[b]	—

Chemical shift values for [a]C-2 methine proton, [b]C-2—CH_3 group, [c]C-10 Olefinic proton.

Table 2. Chemical shifts and coupling constants of the ketomethylene and bridgehead protons in *exo*-bicyclic compounds 2

	Chemical shifts				Coupling constants[b]	
2	H-A	H-M	Δδ(H-M−H-A)	H-X	*J*(AX)	*J*(AM)
a[a]	2.44	2.70	0.26	3.02	7.72	19.48
b	2.68	2.95	0.27	3.31	7.72	19.49
c	2.65	2.97	0.32	3.34	7.72	19.12
e	2.65	2.99	0.34	3.32	7.80	19.40
f	2.61	2.93	0.32	4.05	8.40	19.11
g	2.59	2.91	0.32	3.97	8.09	20.12
h	2.57	2.95	0.38	3.97	8.09	19.49
i	2.58	2.86	0.28	4.05	8.30	19.50
j	2.59	2.95	0.36	4.00	8.09	19.12
k	2.56	2.96	0.40	3.94	8.40	19.50
l	2.60	2.98	0.38	4.03	8.09	19.40

[a] H-A, H-M and H-X refer to H-A, H-B and H-M in structure **2a**.
[b] $J(MX) \approx 0$ Hz.

being in the *exo* configuration, appeared as a doublet of doublets at δ 2.44–2.68 with two coupling constants, $J(AX) \approx 8$ Hz and $J(AM) \approx 19$ Hz. The *endo*-ketomethylene proton H-M, absorbing at δ 2.70–2.99 (doublet), had only the $J(AM)$ geminal coupling (19 Hz) and no vicinal coupling [$J(MX) \approx 0$ Hz]. Dreiding models show that the dihedral angle H-X—C-1—C-7—*endo*-H-M is close to 90° and, therefore, the coupling constant could be close to zero. The absence of such a coupling with the bridgehead proton is well documented.[1,2,12] In all the *exo*-aryl bicyclic compounds **2**, a significant difference of $\Delta\delta$ (H-M − H-A) of 0.26–0.40 ppm results (see Table 2) in the observed AMX pattern. The chemical shift of the bridgehead proton H-X, which appears as a sharp doublet, varied with substitution on the phenyl ring (see Table 2). In all the *p*-methoxyphenyl substituted isomers **2a–c**, **e**, H-X absorbed between δ 3.02 and 3.34, whereas with an additional methoxyl group (**2g–2l**), or with only an *ortho*-methoxy group (**2f**), H-X was relatively deshielded and appeared at δ 3.94–4.05. In the C-2 desalkyl isomer **2a** H-A, H-M and H-X absorbed upfield relative to the C-2 alkyl bicyclic compounds **2** (see Table 2).

Table 3. Chemical shifts and coupling constants of the ketomethylene and bridgehead protons in *endo*-bicyclic compounds 3

	Chemical shifts				Coupling constants		
3	H-A	H-B	$\Delta\delta$(H-B − H-A)	H-X	J(AX)	J(BX)	J(AB)
a	2.80[a]	2.80[a]	~0	3.20[b]	~8	~0	~−20
b	2.43	2.45	0.02	3.12	8.14	0.32	−19.19
c	2.44	2.48	0.04	3.24	8.13	0.26	−19.25
d	2.40	2.42	0.02	3.19	7.80	0.30	−19.13
e	2.40	2.42	0.02	3.17	9.18	−0.72	−19.50
f	2.38	2.41	0.03	3.81	8.71	−0.48	−18.73
g	2.39[c]	2.39[c]	~0	3.75	8.45	~0	~−20
h	2.40[c]	2.40[c]	~0	3.80	8.08	~0	~−20
i	2.43[c]	2.43[c]	~0	3.85	8.80	~0	~−20
j	2.35[c]	2.35[c]	~0	3.77	8.80	~0	~−20
k	2.28[c]	2.28[c]	~0	3.80[d]	8.00	~0	~−20
l	2.40[c]	2.40[c]	~0	3.70[d]	8.00	~0	~−20
m	2.55	2.57	0.02	4.06	8.02	−0.02	−19.20

[a] Approximate values are given since these protons form part of a complex spin system.
[b] Refers to H-M in structure **3a**.
[c] Deceptively simple ABX type spectrum,[14] $\Delta\delta(AB) < 4.0$ Hz.
[d] Overlaid with the aromatic methoxyl signal.

Ketomethylene and bridgehead protons in *endo*-bicyclic compounds 3: ABX spin systems

The *endo*-bicyclic compounds **3** exhibited an ABX spectrum for the ketomethylene and bridgehead protons in the region δ 2.28–4.06. Compounds **3g–l** exhibit an A_2X-like spectrum, with a doublet for the ketomethylene protons and a triplet for the bridgehead proton with a splitting of 4 Hz. This could be considered as a deceptively[13,14] simple ABX system, the total separation of the lines in the H-X triplet indicating $J(AX) + J(BX)$. Thus, in **3i**, the line width of 8.80 Hz represents $J(AX) + J(BX)$ and $J(AX) \neq J(BX) \neq 4.40$ Hz. Isomers **2** and **3** have the same rigid bicyclo[3.2.1]octane-6,8-dione skeleton and, hence, changes at C-2 (i.e. phenyl *exo* or *endo*) are not expected to alter the H-X—C-1—C-7—*endo*-H-B angle. $J(AX)$ and $J(BX)/J(MX)$ can thus be assumed to be the same for both the *exo*-**2** and *endo*-**3** isomers; therefore $J(AX) \approx 8.80$ Hz, $J(BX) \approx 0$ Hz and $J(AX) + J(BX) = 8.80$ Hz. The chemical shifts and coupling constants for H-A, H-B and H-X of all the bicyclic compounds (**3b–f, m**) which exhibited more than five lines for their ABX patterns were calculated using the LAOCN3 computer program.[15] The values $J(AX) \approx 8$ Hz, $J(BX) \approx 0$ Hz, $J(AB) \approx 20$ Hz and $\Delta\delta(AB) \approx 4$–6 Hz were used as the input for LAOCN. It was found that for **3b–f** and **m**, $\Delta\delta(AB) \approx 10$–12 Hz, and in **3g–j** $\Delta\delta(AB) < 4$ Hz. The *exo*-ketomethylene proton H-A had a vicinal coupling constant of $J(AX) \approx 8$ Hz and a geminal coupling of $J(AB) \approx -19$ Hz, while the *endo*-ketomethylene proton H-B experienced a very small vicinal coupling constant [$J(BX) \approx -0.72$ to 0.32 Hz]. The large geminal coupling (~19 Hz) of the two ketomethylene protons in **2** and **3** is largely due to the effect of the C-6 carbonyl group in the rigid five-membered ring.[2,16] The ketomethylene protons in **3** experience very similar shieldings [$\Delta\delta(AB) \approx 0$–0.04 ppm, Table 3], in contrast to the large difference of 0.26–0.40 ppm in **2** (Table 2). In the C-2 desalkyl compound **3a**, H-A and H-B are significantly deshielded compared with those in **3b–m** (Table 3), and $\Delta\delta$(**3a–3b**) = 0.36 ppm. The H-X bridgehead proton is deshielded (Table 3) with increasing *ortho*-methoxy substitution on the phenyl ring, similar to that observed in the *exo*-bicyclic compounds **2**. H-A, H-M and H-X in the *exo*-isomers **2** were always deshielded compared with those in the corresponding *endo*-isomers **3** [$\Delta\delta$(**2–3**) 0.1–0.4 ppm], except for *exo*-**2a** where they were shielded relative to those in **3a** (see Tables 2 and 3).

Chemical shifts of the aromatic protons of the methoxy-substituted phenyl ring in *exo*/*endo* isomers 2 and 3

The pairs of *exo*/*endo* isomers in which the substituent is a *p*-methoxyphenyl group show an interesting correlation. The *ortho* protons in the *endo* isomers **3b–e** are shielded relative to the corresponding protons in the *exo* isomer **2b**, **c** and **e** (0.14–0.16 ppm, Table 4), but the *meta* protons remain almost unchanged. The C-2 desalkyl isomers **2a** and **3a** again show the opposite trend (see Table 4).

The *exo*/*endo* isomers **2g–l** and **3g–l**, having a 2,4-dimethoxy-substituted phenyl group, exhibit a different correlation compared with **2b**, **c**, **e** and **3b–e** (see Tables 4 and 5). The proton *ortho* to both the methoxy groups (H-3′) was deshielded [$\Delta\delta$ (**2–3**) ≈ −0.03 ppm] and the proton *ortho* and *para* to the methoxy groups (H-5′) was shielded [$\Delta\delta$(**2–3**) ≈ 0.06 ppm] in the *endo* isomers **3g–l** compared with the *exo* isomers **2g–l**. However, the proton *meta* to both the methoxy groups (i.e. *ortho* to the bicyclic system) (H-6′) remained unaltered in both isomers.

The aromatic protons in the *exo*- and *endo*-*ortho*-methoxyphenyl-substituted bicyclic compounds **2f** and

Table 4. Aromatic protons of the *p*-methoxy-substituted phenyl groups in *exo*- and *endo*-bicyclo[3.2.1]octane-6,8-diones 2 and 3

Bicyclic compound	*meta*-protons[a]	Δδ(2–3)	*Ortho*-protons[b]	Δδ(2–3)
	Chemical shifts, δ, of			
2a	6.89	0.03	7.19	−0.03
3a	6.86		7.22	
2b	6.89	0.01	7.33	0.14
3b	6.88		7.19	
2c	6.89	0.01	7.28	0.16
3c	6.88		7.12	
3d	6.89		7.15	
2e	6.88	0.01	7.30	0.15
3e	6.87		7.15	

[a] *meta* to the bicyclic system and *ortho* to the methoxy group.
[b] *ortho* to the bicyclic system and *meta* to the methoxy group.

Table 5. Aromatic protons of the 2,4-dimethoxy substituted phenyl groups in *exo* and *endo* isomeric pairs 2 and 3

Bicyclic compound	H-3′[a]	Δδ(2–3)	H-5′[b]	Δδ(2–3)	H-6′[c]	Δδ(2–3)
	Chemical shift, δ, of					
2g	6.41	−0.03	6.54	0.05	7.05	−0.01
3g	6.44		6.49		7.06	
2h	6.41	−0.03	6.52	0.06	6.99	0
3h	6.44		6.46		6.99	
2i	6.42	−0.03	6.52	0.06	7.12	0.01
3i	6.45		6.46		7.11	
2j	6.42	−0.03	6.52	0.06	7.00	—
3j	6.45		6.46		~7.04[d]	
2k	6.43	−0.02	6.54	0.08	7.01	—
3k	6.45		6.46		~7.04[d]	
2l	6.39	−0.05	6.52	0.06	6.99	—
3l	6.44		6.46		~7.02[d]	

[a] H-3′ = *meta* to the bicyclic system and *ortho* to both methoxy groups.
[b] H-5′ = *meta* to the bicyclic system and *ortho* and *para* to the 2,4-dimethoxy groups.
[c] H-6′ = *ortho* to the bicyclic system and *meta*- to both methoxy groups.
[d] Approximate values are given since these protons appear as broad signals.

3f give the following trends. The proton *ortho* to the methoxyl group is shielded and the proton *para* to the methoxyl group is deshielded in the *endo* isomer **3f** compared with the *exo* isomer **2f**, while the other protons (*meta* to the methoxyl group) remain unaltered (see Experimental).

Variation of the chemical shift of the bridgehead proton with temperature

NMR temperature studies (+55 to −50 °C) carried out in order to assess the effect of the phenyl ring orientation on the chemical shifts of **2f**, **3f** and **3m** demonstrated that the bridgehead proton is considerably deshielded on lowering the temperature (cf. *exo*-**2f**, from δ 4.03 to 4.11; *endo*-**3f**, from 3.75 to 4.05; and *endo*-**3m**, from 4.03 to 4.11).

DISCUSSION

Systematic differences were found in the shieldings of various protons of the *exo* and *endo* isomers **2** and **3**, respectively, which could be used to identify such isomeric compounds. To rationalize these observations, it was necessary to find the origin of the differences in the chemical shift values and the substituent effect (at C-2) from the structural information found for the investigated compounds (*endo*-**3f** and **3m**) from x-ray analysis.[9b,10] In the *endo*-bicyclic compounds **3f** and **3m**, the phenyl ring is inclined at 80.7° and 106.5°, respectively, to the cyclohexane ring (i.e. the C-2—C-5—C-9—C-10 plane). It is also seen from the x-ray analysis that the bridgehead proton in the bicyclo[3.2.1]octane skeleton lies almost in the plane of the aromatic ring in both *endo* isomers **3f** and **3m** at distances of 3.79 and 4.02 Å, respectively, from the benzene centre. Thus, the bridgehead proton in *endo*-bicyclic compounds **3** lies in the deshielding region of the ring anisotropic effect.[17] The introduction of additional methoxy substituents results in a conformational distortion, so that the bridgehead proton approaches ideal coplanarity with the aromatic ring (as is evident from the x-ray results of *endo* isomers **3f** and **3m**) and, hence, is maximally deshielded. On the introduction of an *ortho*-methoxy group the bridgehead proton becomes more deshielded (Table 3). In general, the bridgehead proton in the *exo*-bicyclic compounds **2** is more deshielded than that in the *endo* isomers **3** (cf. Tables 2 and 3), which may be a reflection of the extent of coplanarity of H-X with respect to the aromatic ring.[17] A parallel trend of a downfield shift of the bridgehead proton with increasing *ortho* substitution, as noted above, is also observed. The downfield shift of the bridgehead proton at lower temperatures also points to the restricted rotation of the phenyl ring with respect to the skeletal structure (cf. Ref. 18).

The ketomethylene protons in the *endo*-bicyclic compounds **3**, by virtue of the phenyl ring disposition, are shielded by the ring anisotropy.[17] The *exo*-bicyclic compounds **2**, on the other hand, have the phenyl ring well removed from the ketomethylene protons, so that the chemical shift values lie well within the expected range.[2] As can also be seen from Tables 2 and 3, the chemical shifts of these protons, unlike the bridgehead proton, are virtually independent of the substitution on the phenyl ring.

A comparison of the spectra of the isomeric pairs **2f** and **3f** with **2g** and **3g** reveals that the pattern, as well as the chemical shifts, does not change for *ortho*-methoxyphenyl and 2,4-dimethoxyphenyl substitution (Tables 1–3). It is thus evident that only orientation (steric) factors modify the magnetic environment of the bridgehead and ketomethylene protons, and electronic factors (for example, resonance) are not involved.

A change in alkyl substitution (see Tables 1–5) does not affect the spectral characteristics or the chemical shifts of the protons of the bicyclic compounds, and the generalizations made above also hold good. This is probably due to the less significant change in steric bulk or the anisotropy of the alkyl groups compared with the aromatic ring. On the other hand, the C-2 desalkyl compounds **2a** and **3a** do show a striking contrast in their chemical shift trends (especially for the bridgehead and ketomethylene protons) (see Tables 1–4), even though they exhibit characteristic spectral patterns (AMX, ABX) similar to the other **2** and **3** isomers. This is presumably due to the conformational changes consequent on the removal of the alkyl substituent.

In spite of the definite systematic trends observed in the ^{1}H NMR spectra of C-2 isomeric aryl- and alkyl-5-methylbicyclo[3.2.1]octane-6,8-diones **2** and **3**, the corresponding compounds with C-2 methoxy or hydroxy substituents showed marked differences in their NMR spectral pattern. The ^{1}H NMR spectra of the C-2 *exo*- and *endo*-methoxy-substituted isomeric 2,5-dimethylbicyclo[3.2.1]octane-6,8-diones **4a** and **5a** (obtained from MeOH–HCl reaction of the triketone **6**, along with other products[19]) showed an ABX [δ 2.45–2.80 (AB multiplet, 2H), 2.90–3.02 (m, 1H)] and an ABC [δ 2.40–2.90 (m, 3H)] type splitting pattern for the ketomethylene and bridgehead protons. Based on the above generalizations, the isomer with an ABX pattern should have been assigned the *endo*-methoxy-*exo*-methyl configuration **5a**, and the other isomer with an ABC multiplet the *exo*-methoxy-*endo*-methyl configuration **4a**. However, the shieldings of the C-2 and C-2—CH_3 carbon resonances in the ^{13}C NMR spectra (discussed later) suggested configurational assignments contrary to the above. C-2 isomeric *exo*- and *endo*-hydroxy-2,5-dimethylbicyclo-[3.2.1]octane-6,8-diones **4b** and **5b**, reported by Hajos and Parrish,[1] showed differences in the splitting pattern for the ketomethylene and bridgehead protons, viz. an A_2X type pattern [δ 2.63, 2.85 (3H, J(AX) = 4.50 Hz)] for the *exo*-hydroxy isomer **4b**, and an AMX type pattern [δ 2.55, 3.10, 2.85 (3H, J(AM) = 18 Hz, J(AX) = 7 Hz, J(AM) = 0 Hz)] for the *endo*-hydroxy isomer **5b**. These assignments were in agreement with those independently made by Fedorova *et al.*[20] on the basis of IR spectra (differences in the axial and equatorial C—O stretching vibrations[21]) and chromatographic mobility[21] of these isomeric hydroxybicyclic compounds **4b** and **5b**. The apparent incompatibility of these results with those obtained with phenyl substituents suggests that the anisotropy due to a planar π-electron cloud, and that due to the non-bonding sp^3 electrons on the oxygen atom, affect the bridgehead and the ketomethylene protons differently.

^{13}C NMR SPECTRA: RESULTS

^{13}C NMR spectral data of several C-2 substituted 5-methylbicyclo[3.2.1]octane-6,8-diones **2–5** and **9** are given in Tables 6–9. Most of the assignments of individual carbon resonances were made directly from their off-resonance decoupled spectra (ORDS). The three carbon triplets which appear around δ 23–35, 35–42 and 39–45 are due to the C-3, C-4 and C-7 methylene carbons, respectively. The high-field triplet varied from δ 23 to 35 with changes of alkyl substitution at C-2 (see Table 6). Hence, this carbon resonance was conclusively assigned to the C-3 methylene carbon, which is most susceptible to the β- and γ-effects of the C-2 substituents.[4,6,22] The remaining two methylene carbon resonances, C-4 and C-7, at δ 35–42 and 39–45, respectively, were expected to experience similar γ-effects due to the C-2 substituents. The C-4 carbon is expected to have a greater contribution from the γ-effect than the C-7 carbon.[7,8] Moreover, from these three resonances, the low-field absorption around δ 39–45 always appeared as a very sharp and intense triplet (in all the *endo* isomers **3**, and **4a–c**) or a doublet of doublets (in all the *exo* isomers **2**, the ene-diketones **6** and **5a**), while the remaining two were broad in the ORDS, as well as in the fully coupled spectrum (i.e. decoupler off). The C-7 ketomethylene carbon was expected to show a sharp triplet or a sharp doublet of doublets (being adjacent to only a C-1 bridgehead proton and in a rigid five-membered ring) and experiences a lesser γ-effect due to the C-2 substituents.[7,8] Therefore, the low-field methylene carbon resonance was assigned to C-7, while the broad triplet around δ 35–42 was assigned to C-4 (the broadening is due to the adjacent C-3 methylene carbon in the flexible six-membered ring). These assignments were further confirmed by a selective CW experiment on irradiating the isolated ketomethylene protons in the *endo* bicyclic compound **3j**, which appear at δ 2.35 in the ^{1}H NMR spectrum (Table 3). When this experiment was carried out (irradiated at 9393 Hz with 0.2 W power), the low-field carbon was affected to a greater extent (singlet) than the other methylene carbon triplets.

The two carbonyl carbon singlets due to C-6 and C-8 appeared around δ 209–212 and δ 213–215. The high-field resonance around δ 211 did not undergo any change on going from *exo*-**2** to *endo*-**3**, or on substitution at C-2. On the other hand, the low-field resonance was affected by 1–2 ppm (see Table 6). Comparison of the low-field carbonyl shielding of the 2-ene-bicyclic diketone **9** (at δ 213.3) with either of the C-2 desalkyl isomers *exo*-**2a** (at 215.7) or *endo*-**3a** (at 214.8) revealed that it was shielded by 2.4 and 1.5 ppm in **9** relative to *exo*-**2a** and *endo*-**3a**, respectively. It is known[23,24] that homoconjugative interaction between olefinic and carbonyl bonds results in an upfield shift of carbonyl carbon resonances, and such interactions are expected to be strongly dependent on the relative orientation of the two π bonds. In view of this, the low field carbonyl carbon resonance around δ 213–215 was assigned to C-8, while the constant high field resonance was assigned to C-6. Normally, the C-6 and C-8 carbonyl carbons in bicyclo[3.2.1]octan-6-one and -8-one are reported[4,8,25] to appear at δ 221.4 and 222.9, respectively. It is known that these carbons experience a γ-effect from the γ-substituents. Heumann and Kolshorn[7,8] reported the effect of C-2 substituents in bi-

Table 6. Carbon-13 chemical shifts of C-2 substituted isomeric *exo*- and *endo*-5-methylbicyclo[3.2.1]octane-6,8-diones 2–5 and 9 (skeletal carbons, C-5—$\underline{C}H_3$ and C-2—R_4 substituents)

Bicyclic compound	C-1(d)[a]	C-2(s)	C-3(t)	C-4(t)	C-5(s)	C-6(s)	C-7	C-8(s)	C-9(q)	C-10	Others
exo-**4a**	54.2	84.2	29.7	37.8	57.9	210.9	42.3[b]	212.0	11.8	21.7(q)	49.3(q)
	(0)[d]	(3.3)				(0.1)		(−1.4)		(1.1)	
endo-**5a**	54.2	80.9	31.7	35.8	58.3	210.8	40.6[c]	213.4	11.6	20.6(q)	49.1(q)
exo-**4b**	57.5	80.4	32.2	38.5	58.1	211.0	42.7[b]	213.9	11.8	28.3(q)	—
exo-**4c**	58.4	75.7	35.0	37.7	57.3	209.2	42.9[b]	209.9	11.8	30.8(q)	—
9	48.5	144.6	119.2(d)	45.9	57.1	211.2	50.1[c]	213.3	12.4	—	—
exo-**2a**	52.7	49.3(d)	23.6	41.7	58.9	211.5	39.5[c]	215.7	11.9	—	—
	(1.3)	(−1.7)				(−0.2)		(0.9)			
endo-**3a**	51.4	51.0(d)	23.8	42.3	58.5	211.7	45.2[b]	214.8	12.2	—	—
exo-**2b**	54.7	49.2	29.6	39.3	57.9	211.4	41.9[c]	213.0	11.7	31.2(q)	—
	(−1.1)	(0.8)				(0.1)		(−2.0)		(3.9)	
endo-**3b**	55.8	48.4	29.5	39.1	58.7	211.3	42.4[b]	215.0	11.8	27.3(q)	—
exo-**2c**	53.1	52.8	27.9	39.1	58.5	211.5	41.6[c]	213.2	11.7	35.6(t)	8.0(q)
	(−1.2)	(0.4)				(0.1)		(−1.9)		(4.8)	
endo-**3c**	54.3	52.4	26.8	39.0	58.9	211.4	42.4[b]	215.1	11.8	30.8(t)	8.3(q)
endo-**3d**	55.4	51.2	27.8	39.2	58.4	211.0	42.3[b]	214.6	11.7	37.5(t)	69.4(t), 58.4(q)
exo-**2e**	54.4	52.7	28.9	39.3	58.5	211.3	41.8[c]	212.8	11.7	52.3(t)	24.0(d), 24.8(q), 24.6(q)
	(−1.2)	(0.5)				(0.1)		(−2.0)		(5.8)	
endo-**3e**	55.6	52.2	27.5	39.0	58.9	211.2	42.4[b]	214.8	11.7	46.5(t)	24.6(d), 24.6(q)
exo-**2f**	52.1	50.1	30.3	39.9	58.2	212.6	41.5[c]	214.2	11.7	26.4(q)	—
	(−0.6)	(1.3)				(1.1)		(−1.0)		(3.6)	
endo-**3f**	52.7	48.8	29.8	38.5	58.8	211.5	42.6[b]	215.2	11.8	22.8(q)	—
endo-**3g**	52.9	48.4	30.1	38.6	58.8	211.8	42.6[b]	215.4	11.8	23.0(q)	—
endo-**3m**	55.0	51.1	30.6	39.0	60.1	212.4	43.9[b]	216.0	11.6	22.7(q)	—
exo-**2h**	52.2	53.7	27.6	39.9	58.7	212.6	41.4[c]	214.3	11.7	31.0(t)	8.8(q)
	(−0.1)	(0.9)				(0.5)		(−1.3)		(5.1)	
endo-**3h**	52.3	52.8	26.5	38.6	59.1	212.1	42.7[b]	215.6	11.8	25.9(t)	9.1(q)
exo-**2i**	51.2	55.1	26.8	39.3	58.7	212.2	42.1[c]	213.7	11.7	143.0(d)	113.1(t)
	(−1.1)	(1.0)				(0.4)		(−0.5)		(1.7)	
endo-**3i**	52.3	54.1	28.7	38.5	58.9	211.8	42.5[b]	214.2	11.8	141.3(d)	113.7(t)
exo-**2j**	52.5	52.2	28.9	40.1	58.9	212.2	41.4[c]	213.8	11.7	38.1(t)	69.8(t), 58.4(q)
	(−0.2)	(1.0)				(0.2)		(−1.5)		(5.4)	
endo-**3j**	52.7	51.2	27.6	38.6	59.0	212.0	42.4[b]	215.3	11.8	32.7(t)	70.2(t), 58.3(q)
exo-**2k**	53.1	53.4	29.2	40.3	58.9	212.8	41.4[c]	214.0	11.7	47.8(t)	24.9(d), 24.8(q), 24.4(q)
	(0)	(1.2)				(0.6)		(−1.5)		(6.6)	
endo-**3k**	53.1	52.2	27.0	38.3	58.8	212.2	42.6[b]	215.5	11.7	41.2(t)	25.4(d), 24.4(q)

[a] Letters in parentheses indicate the multiplicity of the signal in ORDS.
[b] Sharp triplet in ORDS.
[c] Sharp doublet of doublet in ORDS.
[d] Values in parentheses refer to $\Delta\delta$(**2**−**3**) for the significant carbon shieldings.

cyclo[3.2.1]octan-8-one and bicyclo[3.3.1]nonan-9-ones and observed a high-field shift for the C-8/C-9 carbonyl carbons, irrespective of the stereochemistry of the functional group at C-2. In the present series of C-2 substituted 5-methylbicyclo[3.2.1]octane-6,8-diones **2**–**5** and **9**, the observed high-field shifts for both C-6 and C-8 carbonyl carbons could be the result of the 1,3-dicarbonyl interactions, in addition to the effects of the C-2 substituents. The corresponding seco-diones **1** also exhibit carbonyl carbon resonances around δ 215. The presence of 1,3-dicarbonyl interactions in **2**–**5**, **9**, and in **1**, were also evident from their IR spectra, which showed the characteristic split carbonyl bands around 1765 and 1725 cm^{-1}.[26]

The individual assignment of the aromatic carbon resonances listed in Tables 7–9 was in agreement with the calculated shielding of the model compounds possessing *tert*-butyl and methoxy substituents on the phenyl ring.[27] It is clearly seen that C-1′, C-2′ and C-6′ are considerably affected with varying C-2 substitution due to β- and γ-shielding of the alkyl substituents, while the chemical shifts of C-3′, C-4′ and C-5′ remain unchanged.

The chemical shift of C-2 alkyl or vinylic substituents (C-10) was found to vary considerably (*ca.* 5 ppm) depending on the phenyl ring orientation (*exo*/*endo*) and also on the *ortho*-methoxy substitution on the phenyl ring (see Tables 6 and 10). The latter also has some effect on the chemical shift of other carbons, as seen in the spectra of **2** and **3**. There is a considerable shielding of the C-10 alkyl substituent (4.3–5.3 ppm) and the C-1 carbon (0.8–3.1 ppm) (see Table 10) on going from *p*-methoxyphenyl to *ortho*-methoxy or 2,4-dimethoxyphenyl substitution. With di-*ortho*-methoxy substitution, however, the C-10 methyl carbon was not affected further, but C-1 and C-2 were deshielded by *ca.* 2 ppm (Table 6). The upfield shift of C-10 and C-1 with *ortho*-substitution is probably due to steric congestion.[28]

It is evident from the ^{13}C NMR data (see Tables

Table 7. Aromatic carbon shieldings of the *p*-methoxyphenyl substituent in bicyclo[3.2.1]octane-6,8-diones 2a–c, e, 3a–e and 9

Compound	C-1′(s)[a]	C-2′ and C-6′ (d)	C-3′ and C-5′ (d)	C-4′ (s)	Ar-OCH_3 (q)
4-Methoxy-*-tert*-butylbenzene	142.5	126.1	113.1	156.7	—
9	130.7	126.7	114.2	159.8	55.3
2a	133.3 (−0.8)[d]	128.0	114.4	159.0	55.4
3a	134.1	128.2	114.2	158.6	55.3
2b	135.9 (−3)	126.9	114.1	158.3	55.2
3b	139.2	126.4	114.3	158.4	55.3
2c	132.9 (−3.5)	128.1	113.9	158.2	55.2
3c	136.4	127.3	114.0	158.3	55.2
3d	136.4	127.3	114.3	158.6	55.4
2e	133.4 (−3.2)	128.1	113.9	158.3	55.2
3e	136.6	127.5	114.0	158.3	55.2

[a,d] See footnotes to Table 6.

6–10) that the significant differences which can be used for distinguishing *exo*/*endo* isomers are in the shieldings of C-10, C-1′ and C-2 and the nature of the C-7 absorption in the ORDS. The C-10 methyl/methylene/olefinic carbon in the *exo* isomers **2** and **4a** was always deshielded compared to the *endo* isomers **3** and **5a** by 1.1–6.6 ppm (see Table 6), in agreement with the well known[29] shieldings of axial/equatorial carbons in various cyclic systems. The C-2 carbon in the *exo* isomers **2b**, **c**, **e**, **f**, **h–k** is deshielded compared with C-2 in the corresponding *endo* isomers. A similar trend is observed for the compounds with hetero substitution at C-2 (**4a** and **5a**) instead of the aromatic ring. For compounds **2a** and **3a**, where the alkyl group is replaced by hydrogens, the trend is reversed.

Table 8. Aromatic carbon shieldings of the 2,4-dimethoxyphenyl substituent in bicyclo[3.2.1]octane-6,8-diones 2h–k and 3g–k

Compound	C-1′(s)[a]	C-2′(s)	C-3′(d)	C-4′(s)	C-5′(d)	C-6′(d)	Ar-OCH_3(q)
2,4-Dimethoxy-*-tert*-butylbenzene	127.5	157.4	98.1	157.7	105.1	126.1	—
3g	126.7	159.9	100.2	158.6	104.1	127.5	55.2 55.1
2h	120.8 (−2.8)[d]	160.0	100.5	159.5	104.1	129.1	55.4 55.2
3h	123.6	160.0	99.9	158.7	104.9	128.4	55.2 55.1
2i	121.8 (−3.0)	160.4	100.9	159.4	104.6	127.6	55.4 55.3
3i	124.8	160.2	100.5	158.2	104.1	127.6	55.4 55.3
2j	120.6 (−2.7)	160.1	100.5	159.4	104.3	128.8	55.4 55.3
3j	123.3	160.2	99.9	158.6	104.1	129.2	55.3 55.1
2k	121.8 (−3.0)	160.4	100.9	159.4	104.6	127.6	55.4 55.3
3k	124.8	160.2	100.6	158.2	104.1	127.6	55.4 55.3

[a,d] See footnotes to Table 6.

Table 9. Aromatic carbon resonances of the *ortho*- and di-*ortho*-methoxyphenyl substituent in bicyclo[3.2.1]octane-6,8-diones 2f, 3f and 3m

Compound	C-1′ (s)[a]	C-2′ (s)	C-3′ (d)	C-4′ (d)	C-5′ (d)	C-6′ (d)	Ar-OCH_3 (q)
2-Methoxy-*-tert*-butylbenzene	135.5	156.4	113.1	126.4	120.1	126.1	—
2f	132.1 (−2.0)[d]	158.4	112.9	126.5	120.8	128.5	55.3
3f	134.1	157.7	112.4	126.9	120.7	128.2	55.1
2,6-Dimethoxy-*tert*-butylbenzene	120.5	157.4	105.1	127.4	105.1	157.4 (s)	—
3m	122.6	160.0	106.5	128.0	106.5	160.0 (s)	55.7

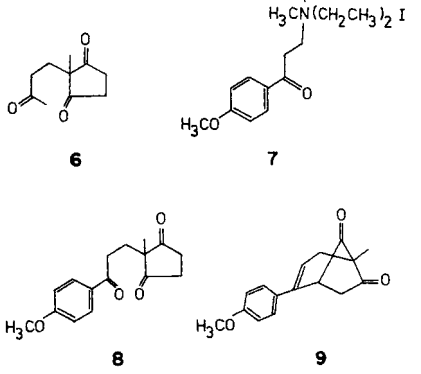
[a,d] See footnotes to Table 6.

Table 10. Effect of methoxy substitution in the phenyl ring on the chemical shifts of C-1 and C-10

Compounds	C-1	C-10	Compounds	C-1	C-10
2b–2f	2.6	4.8	**2c–2h**	0.9	4.6
3b–3f	3.1	4.5	**3c–3h**	2.0	4.9
3b–3g	2.9	4.3	**3d–3j**	2.7	4.8
3b–3m	0.8	4.6	**2e–2k**	1.3	4.5
			3e–3k	2.5	5.3

EXPERIMENTAL

For general procedures, see Ref. 9. The ^1H NMR spectra were recorded at 270 MHz with a Bruker WH-270 FT NMR spectrometer, with TMS as the internal standard and deuterium lock in $CDCl_3$ solution (concentration *c.* 5–10%) at 299 K (probe temperature). Usually 10–20 scans were accumulated with 20K memory, 16K for data and 4K for the program.



6 **7** **8** **9**

A spectra width of 3012 Hz, a pulse width of 5–6 μs and a delay of 3s were employed. ^{13}C NMR spectra were recorded on the same instrument operating at 67.89 MHz containing TMS as internal standard and deuterium lock in $CDCl_3/CHCl_3$ solution (concentration *ca.* 15–20%) at 299 K (probe temperature). For each compound, the broad band decoupled spectrum

was obtained by accumulating approximately 400–600 scans with a spectral width of 17241 Hz, a pulse width of 15 μs, a delay of 2–3 s and a power of 3 W. The ORDS were recorded by single frequency irradiation at *ca.* δ −5, with a decoupler power of *ca.* 2 W, a pulse interval of 3 s and 1500–2000 scans were accumulated. Chemical shifts (both ^{1}H and ^{13}C) are quoted in δ values (ppm) relative to TMS = 0.

The syntheses of C-2 desalkyl bicyclic compounds **2a** and **3a** were achieved by the catalytic hydrogenation of the bicyclo[3.2.1]oct-2-en-6,8-dione **9**. The ene-diketone **9** was reported in a patent,[31] and prepared by the *p*-tosic acid–benzene dehydration of the triketone **8**. The syntheses of the bicyclic compounds **2b, c, e–l, 3b–m, 4a–c** and **5a** have been reported earlier.[1,3,9,19] In the case of the seco-diones **1d** and **1m**, only the corresponding *endo* bicyclic compounds **3d** and **3m** were isolated, along with side products.[9c,30]

2-[3-(4-Methoxyphenyl)-3-ketopropyl]-2-methylcyclopentane-1,3-dione (8)

The triketone **8** was prepared following a patented procedure.[31] A mixture of the Mannich base methiodide **7** (8 g) (prepared from *p*-methoxyacetophenone[32]), 2-methylcyclopentane-1,3-dione (4 g), dry diethyl ether (70 ml) and triethylamine (4.70 ml) was stirred at room temperature for 30 h to give crystalline triketone **8**[31] (6.40 g, 70%), m.p. 101–102 °C (hexane–benzene), IR (Nujol): ν_{max} 1770, 1725, 1675, 1615, 1580 cm^{-1}; NMR (T 60 MHz): δ 1.20 (s, CH_3, 3H), 2.03 (t, —$COCH_2\underline{CH_2}$—, 2H, J = 7 Hz), 2.83 (s, ketomethylenes, 4H), 2.92 (t, —$CO\underline{CH_2}CH_2$—, 2H, J = 7 Hz), 3.83 (s, Ar—OCH_3, 3H), 6.90 (d, Ar—H, 2H, J = 9 Hz), 7.86 (d, Ar—H, 2H, J = 9 Hz). (Found: C, 69.68; H, 6.87. Calculated for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61%).

2-(4-Methoxyphenyl)-5-methylbicyclo[3.2.1]oct-2-en-6,8-dione (9)

Reaction of the triketone **8** (1.38 g) in refluxing benzene (60 ml) with *p*-tosic acid (0.60 g) for 4 h gave the unsaturated bicyclic diketone **9**[31] (0.71 g, 55%), m.p. 129–130 °C, IR (Nujol): ν_{max} 1765, 1725, 1605 cm^{-1}; NMR (T 60 MHz): δ 1.25 (s, CH_3, 3H), 2.78 (d, allylic —CH_2—, 2H, J = 4 Hz), 2.85–3.10 (AB multiplet, —$COCH_2$—, 2H), 3.56 (dd, —C-1—H, 1H, $J \approx 2$ Hz, J = 7 Hz), 3.77 (s, Ar—OCH_3, 3H), 5.72 (t, C-3-vinylic H, 1H, J = 4 Hz), 6.80 (d, Ar—H, 2H, J = 9 Hz), 7.25 (d, Ar—H, 2H, J = 9 Hz); MS: $[M]^{+\cdot}$: m/z 256 (base peak). (Found: C, 74.69; H, 6.57. Calculated for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29%).

Catalytic hydrogenation of 9

Hydrogenation of the bicyclic ene-diketone **9** (0.26 g) in ethanol (30 ml) in the presence of 10% Pd–C catalyst (30 mg) was carried out in an atmosphere of hydrogen until no further absorption occurred. The catalyst was filtered off and the solvent removed. The crude product obtained was subjected to preparative thin-layer chromatography (silica gel) using a 4:1 hexane–ethyl acetate solvent mixture, and separated into two fractions. *Fraction* 1: The less polar fraction 1 (166 mg) on crystallization from hexane–benzene afforded 2-*exo*-(4-methoxyphenyl)-2-*endo*-hydro-5-methylbicyclo[3.2.1]octane-6,8-dione (**2a**), m.p. 116 °C; IR (Nujol): ν_{max} 1760, 1723 cm^{-1}; NMR: δ 1.12 (s, CH_3, 3H), 1.88–2.10 (m, —CH_2CH_2—, 4H), 2.44 (dd, 1H, J = 7.72 Hz, 19.48 Hz), 2.70 (d, 1H, J = 19.48 Hz), 3.02 (dd, 1H, J = 1.80 Hz, 7.72 Hz), 3.51 (bd, 1H, J = 9.56 Hz), 3.80 (s, Ar—OCH_3, 3H), 6.89 (m, Ar—H, 2H, J = 2.20 Hz, 8.82 Hz), 7.19 (m, Ar—H, 2H, J = 2.20 Hz, 8.82 Hz); MS: $[M]^{+\cdot}$: m/z: 258 (24%), 147 (100), 134 (76). (Found: C, 74.30; H, 6.93. Calculated for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02%). *Fraction* 2: The more polar fraction 2 (96 mg) on crystallization from hexane–benzene gave 2-*endo*-(4-methoxyphenyl)-2-*exo*-hydro-5-methylbicyclo-[3.2.1]octane-6,8-dione (**3a**), m.p. 111–112 °C; IR (Nujol): ν_{max} 1762, 1725 cm^{-1}; NMR: δ 1.05 (s, 3H), 2.02–2.30 (m, 4H), 2.80–2.82 (AB multiplet, 2H), 3.20 (quintet, 1H, J = 2.53 Hz, 3.30 Hz, 5.88 Hz), 3.66 (bs, 1H), 3.79 (s, 3H), 6.86 (m, 2H, J = 2.20 Hz, 8.82 Hz), 7.22 (m, 2H, J = 2.20 Hz, 8.82 Hz); MS: $[M]^{+\cdot}$: m/z: 258 (35%), 147 (100), 134 (64). (Found: C, 74.30; H, 7.05. Calculated for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02%).

All the bicyclic compounds **2b, c, e–h** and **3b–h** exhibited the split IR (Nujol) absorption bands around 1765 and 1725 cm^{-1}, indicating the presence of a cyclopenta-1,3-dione system.[26] The NMR data (excluding those tabulated in Tables 1–5) are given below for each isomer.

2b: δ 1.62–1.97 (m, —CH_2CH_2—, 3H), 2.32 (bd, C-3 or C-4 methylene H, 1H, J = 14.70 Hz), 3.79 (s, Ar—OCH_3, 3H), 6.89 (d, Ar—H, 2H, J = 8.82 Hz), 7.33 (d, Ar—H, 2H, J = 8.82 Hz).

3b: δ 1.84–2.20 (m, 4H), 3.80 (s, 3H), 6.88 (m, 2H, J = 3.30 Hz, 8.82 Hz), 7.19 (m, 2H, J = 3.30 Hz, 8.82 Hz).

2c: δ 0.56 (t, —$CH_2\underline{CH_3}$, 3H, J = 7.35 Hz), 1.56–1.76 (m, 3H), 1.86–1.91 (m, 2H), 2.38 (bd, C-3 or C-4—H, 1H, J = 15.07 Hz), 3.80 (s, 3H), 6.89 (m, 2H, J = 3.31 Hz, 8.82 Hz), 7.28 (m, 2H, J = 3.31 Hz, 8.82 Hz).

3c: δ 0.58 (t, 3H, J = 7.35 Hz), 1.57–2.20 (m, 6H), 3.81 (s, 3H), 6.88 (m, 2H, J = 3.31 Hz, 8.82 Hz), 7.12 (m, 2H, J = 3.31 Hz, 8.82 Hz).

3d: 25% yield, b.p. 195–205 °C at 1–2 mmHg, δ 1.70–2.25 (m, 6H), 2.90–3.16 (m, —$CH_2\underline{CH_2}OCH_3$, 2H), 3.13 (s, aliphatic OCH_3, 3H), 3.81 (s, 3H), 6.89 (m, 2H, J = 3.31 Hz, 8.82 Hz), 7.15 (m, 2H, J = 3.31 Hz, 8.82 Hz). (Found: C, 72.04; H, 7.48. Calculated for $C_{19}H_{20}O_4$: C, 72.11; H, 7.60%).

2e: δ 0.55 (d, $CH_3CH\underline{CH_3}$, 3H, J = 6.62 Hz), 0.70 (d, $\underline{CH_3}CHCH_3$, 3H, J = 6.62 Hz), 1.26–1.37 [m, $CH_2\underline{CH}(CH_3)_2$], 1.51–1.94 (m, 5H), 2.42 (bd, C-3 or C-4—H, 1H, J = 14.70 Hz), 3.80 (s, 3H), 6.88 (d, 2H, J = 9.91 Hz), 7.30 (d, 2H, J = 9.19 Hz).

3e: δ 0.55 (d, 3H, J = 6.62 Hz), 0.67 (d, 3H, J = 6.62 Hz), 1.24–1.30 (m, 1H), 1.24–1.78 (m, 2H), 1.99–2.10 (m, 4H), 3.81 (s, 3H), 6.87 (d, 2H, J = 9.19 Hz), 7.15 (d, 2H, J = 9.19 Hz).

2f: δ 1.74–2.14 (m, 3H), 2.35 (dd, C-3 or C-4—H,

1H, $J = 4.78$ Hz, 15.44 Hz), 3.90 (s, 3H), 6.90 (m, 1H, $J = 1.10$ Hz, 7.90 Hz), 6.97 (dd, 1H, $J = 1.10$ Hz, 7.90 Hz), 7.15 (dd, 1H, $J = 1.10$ Hz, 7.90 Hz), 7.25 (m, 1H, $J = 1.10$ Hz, 7.90 Hz).

3f: δ 1.69–2.20 (m, 4H), 3.86 (s, 3H), 6.92 (dd, 1H, $J = 1.47$ Hz, 8.09 Hz), 6.93 (m, 1H, $J = 1.47$ Hz, 8.09 Hz), 7.16 (dd, 1H, $J = 1.47$ Hz, 8.09 Hz), 7.26 (m, 1H, $J = 1.47$ Hz, 8.09 Hz).

2g: δ 1.70–2.11 (m, 3H), 2.31 (dd, C-3 or C-4—H, 1H, $J = 4.41$ Hz, 15.81 Hz), 3.79, 3.87 (2s, 6H), 6.41 (dd, 1H, $J = 2.57$ Hz, 8.45 Hz), 6.54 (d, 1H, $J = 2.57$ Hz), 7.05 (d, 1H, $J = 8.45$ Hz).

3g: δ 1.88–2.17 (m, 4H), 3.80, 3.83 (2s, 6H), 6.44 (dd, 1H, $J = 2.57$ Hz, $J = 8.82$ Hz), 6.49 (d, 1H, $J = 2.57$ Hz), 7.06 (d, 1H, $J = 8.82$ Hz).

2h: δ 0.53 (t, $CH_2\underline{CH}_3$, 3H, $J = 7.35$ Hz), 1.54–2.16 (m, 5H), 2.45 (bd, C-3 or C-4—H, 1H, $J = 16.54$ Hz), 3.79, 3.85 (2s, 6H), 6.41 (dd, 1H, $J = 2.57$ Hz, 8.45 Hz), 6.52 (d, 1H, $J = 2.57$ Hz), 6.99 (d, 1H, $J = 8.45$ Hz).

3h: δ 0.49 (t, 3H, $J = 7.35$ Hz), 1.54–1.97 (m, 6H), 3.80 (s, 6H), 6.41–6.47 (m, 2H), 6.99 (d, 1H, $J = 8.09$ Hz).

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