Stereochemical and electronic features of the [3 + 2] cycloaddition of pentafulvenes with acylnitrones

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A series of mono- and di-substituted pentafulvenes **1**–**3** was reacted with aroylnitrones **4** to afford the corresponding fused bicyclic monoadducts **5**–**9**, generally as a mixture of isomers. The stereochemistry of the addition reaction was established by 1D and 2D NMR spectroscopies or X-ray crystallography. Performance of theoretical calculations has been undertaken in order to rationalize the important differences in regioselectivity displayed by the reaction.

Introduction

Different aspects of the reactivity of pentafulvenes have been reported during the last decades.[1–6] Neuenschwander has reviewed theoretical aspects and synthetic uses of these molecules.[7] These compounds have been mainly utilised in addition reactions. Two, four or six π-electrons of the fulvene structure can be involved, depending on the number of electrons "*n*" furnished by the second reagent. Several papers dealing with [2 + *n*] [4 + *n*] or [6 + *n*] additions have been thus reported. Some studies have described Diels–Alder cycloadditions in which pentafulvenes behave like dienes, but [2 + 4] cycloadditions in which pentafulvenes acted as dienophiles have been more frequently observed.[8–10] In the presence of electron-rich dienes, pentafulvenes may also react *via* their six π-electrons, according to a [6 + 4] addition.[11–13]

The reactions of pentafulvenes with several 1,3-dipoles have been reported. Thus, diazomethane, 3-methyl-2,4-diphenyl-1,3-oxazolium-5-olate, benzonitrile oxide and diarylnitrilimines ($Ar–C^{+}=N–N^{-}–Ar$) are known to undergo cycloaddition successfully with pentafulvenes.[14–18] Chandrasekar *et al.* have reported the cycloaddition of the single 6,6-diphenylfulvene with *C,N*-diphenylnitrone† and proposed a stepwise non-concerted mechanism for this reaction.[19] To the best of our knowledge, however, a more extensive description of the reactivity of pentafulvenes with nitrones has not been reported.

We present here our results concerning the 1,3-dipolar cycloaddition of 6,6-diphenylfulvene **1**, 6-monosubstituted fulvenes **2a**–**d** and 6-methyl-6-phenylfulvene **3** with some *C*-aroyl-*N*-phenylnitrones **4a′**–**d′**. The main results concerning the stereochemical features of the cycloaddition are given first. The reaction is then considered from an electronic point of view; our study proposes several hypotheses concerning the reactivity of the endocyclic carbon–carbon double bonds of the fulvenes.

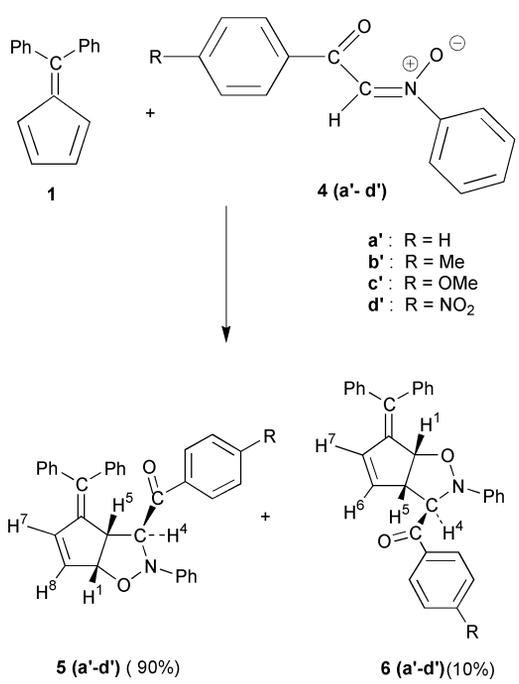
Results

Thermal behaviour of fulvenes: preliminary considerations

The reactions of fulvenes **1**–**3** with acylnitrones **4** usually proceeded with low or moderate isolated yields because of the concomitant polymerisation of these rather unstable dipolarophiles. This phenomenon was clearly proven in a systematic study of the thermal behaviour of fulvenes by differential thermal analysis.[20] Thus, 6,6-diphenylfulvene **1** was reasonably stable upon prolonged *moderate* heating, but 6-monosubstituted fulvenes **2** and 6-methyl-6-phenylfulvene **3** had a propensity to polymerise readily. This was evidenced by the presence of a characteristic broad exothermal peak at temperatures as low as 90–100 °C.

Since no attempt has been made to carry out the cycloadditions at temperatures lower than those indicated here, the reported yields are not optimised.

1 Cycloadditions of 6,6-diphenylfulvene 1. The cycloaddition of fulvene **1** with acylnitrones **4** (110 °C, 24 h) yielded two monoadducts **5** and **6** in a 90 : 10 ratio (Scheme 1). After



Scheme 1

† The IUPAC name for nitrone is alkylideneamine *N*-oxide.

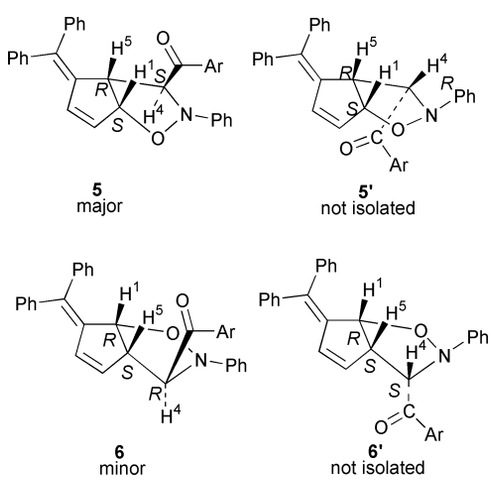
separation by liquid chromatography, the two regioisomers were identified from their ^{1}H NMR spectra.

The *major* adducts were all characterised by a signal (*dd*) around 5.50 ppm, corresponding to the most deshielded proton carried by a sp^3 carbon atom. This proton was therefore located close to the oxygen atom of the isoxazolidine ring (1-H). Moreover, a ^3J coupling constant (≈ 2.3 Hz) was observed in all these adducts, corresponding to the interaction of this 1-H proton with the neighbouring ethylenic hydrogen (8-H). This interpretation was in accordance with a regioselective cycloaddition leading mainly to **5**.

Other ^{1}H NMR information clarified the stereochemistry of the reaction. Thus, the 4-H proton of the isoxazolidine ring was not coupled with the neighbouring 5-H; according to the Karplus rule, the torsion angle 5-H–C-5–C-4–4-H was close to 90°. The preceding observations allowed us to attribute unambiguously the structure of **5** to all *major* adducts.

The ^{1}H NMR spectra of the *minor* adducts were in agreement with a regioisomeric structure coming from the opposite addition of acylnitrones **4** onto fulvene **1**. Indeed, the less shielded proton carried by a sp^3 carbon atom (a doublet at $\delta \approx 5.30$ ppm) was coupled with the most shielded one only. Irradiation of this first proton did not lead to any modification of the signals corresponding to ethylenic protons (6-H or 7-H). The observed doublet should therefore be attributed to 1-H, coupled with 5-H. This latter atom resonated around 4.50 ppm as a complex signal (*ddd*); when irradiated, the simplification of all non-aromatic protons signals was observed. The coupling constant between 4-H and 5-H ($^3J \approx 1.9$ Hz) was in agreement with an *anticlinal* disposition of these atoms (torsion angle around 110°).

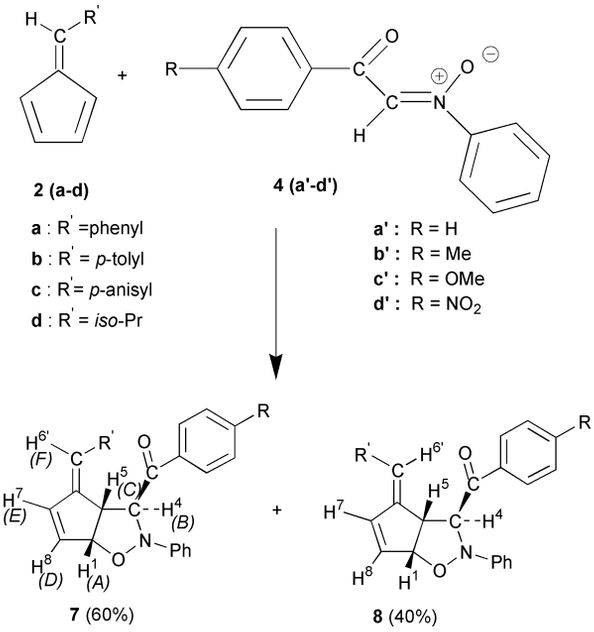
Benzoylnitrones adopt the "*Z*" configuration preferentially (Scheme 1) because of the presence of the two bulky aryl and aroyl groups.[21] Since this arrangement was also encountered in both regioisomers **5** and **6**, there was no *Z*–*E* isomerisation of the acylnitrones during the cycloaddition process and the eventuality of a stepwise non-concerted mechanism should be discarded.[19] The [3 + 2] cycloadditions are stereospecific *cis* additions and the reagents approach in approximately parallel planes. As drawn in Scheme 2, four diastereoisomeric structures



Scheme 2 The different possible adducts resulting from the reaction of 6,6-diphenylfulvene with aroylnitrones.

(strictly *four* couples of enantiomers) should be considered in which the N–Ph and aroyl group are in an *anticlinal* configuration, *i.e.* *rel*-(1*S*,4*S*,5*R*)-**5**, *rel*-(1*S*,4*R*,5*R*)-**5′**, *rel*-(1*R*,4*R*,5*S*)-**6**, and *rel*-(1*R*,4*S*,5*S*)-**6′**. Structures **5** and **6** correspond to the *endo* approach of the reactants, for which interactions between π-systems are maximal. The *exo* approach was not observed; this would have lead to **5′** and **6′**, in which the coupling constant between the 4-H and 5-H protons would have corresponded to a *synclinal* configuration.

2 Cycloadditions of 6- fulvenes 2a–d. The 6- fulvenes **2a–d** have two non-equivalent endocyclic dipolarophilic sites. As depicted in Scheme 3, their cycloaddition with aroylnitrones **4**



Scheme 3

gave two regioisomeric monoadducts **7** and **8**, with almost no selectivity (ratio **7** : **8** of *ca.* 60 : 40, as evaluated by ^{1}H NMR). Separation of the different mixtures of adducts **7** and **8** by preparative TLC was very difficult, because of their similar R_F values. For this reason, total isolated yields were modest. Moreover, although all *major* adducts were isolated, only a small number of *minor* compounds **8** were obtained in a pure form. However, the relative ratio **7** : **8** was easily calculated from the integrations of the 5-H signals in the ^{1}H NMR spectra of the crude mixture of adducts. Indeed, this proton was always disconnected from the others ($\delta \approx 5.00$ ppm for **7**; $\delta \approx 4.50$ ppm for **8**).

1D ^{1}H NMR spectra were often complex and not always sufficient to ascertain the exact structures of compounds **7** and **8**. The use of 2D NMR techniques together with 1D ^{1}H NMR spectroscopy appeared essential for the clear assignment of each proton and stereochemical studies.

The determination of the structures of compounds **7dd′** and **8dd′** (R′ = Pr^i, R = NO$_2$) was representative and is reported here; the method has been generalised for all adducts **7** and **8**. The ^{13}C–^{1}H HSQC spectra of **7dd′** or **8dd′** allowed the distinction of three deshielded hydrogen atoms *A*, *B*, *C* linked to three different sp^3 carbons (beyond the isopropyl group signals) and three ethylenic protons *D*, *E*, *F*. The reactive double bond of **2d** was consequently an endocyclic bond. The very deshielded proton *A* ($\delta \approx 5.50$ ppm) resonated at a field lower than the most shielded ethylenic proton (*F*); it was correlated with the most deshielded *sp*^{3} carbon (≈ 90 ppm). Proton *A* was thus identified as 1-H, whose chemical shift indicated the proximity of the isoxazolidine oxygen atom.

The DQF COSY spectra of **7dd′** and **8dd′** allowed a complete assignment of the six preceding protons. In both adducts, a very strong interaction was noticed between the deshielded proton 1-H (*dd*) and the most shielded proton (*C*), attributed to 5-H. The 1-H atom was also correlated with an ethylenic proton 8-H (*D*). The latter was strongly coupled with another ethylenic proton 7-H (*E*). The two ethylenic protons were almost superimposable in the case of **7dd′**, but were well differentiated for **8dd′**.

In compound **7dd′**, the ^3J spin–spin splitting between 5-H and 4-H (*B*) was very weak (1.2 Hz); it was generally absent for

Table 1 Two dimensional ^{1}H NMR (NOESY experiments, 300 MHz) of adduct **7dd′** [a]

	1-H	4-H	5-H	6′-H	iso-H	7-H	8-H
1-H	/	−	+	−	−	−	+
4-H	−	/	(+)	−	−	−	−
5-H	+	(+)	/	−	**+**	−	−
6′-H	−	−	−	/	−	**+**	−
iso-H	−	−	**+**	−	/	−	−
7-H	−	−	−	**+**	−	/	+
8-H	+	−	−	−	−	+	/

[a] Methyl and aromatic protons excluded; 'iso-H' refers to the isopropyl proton. '+' = strong NOE effect; '(+)' = weak NOE effect; '−' = no correlation; '**+**' indicates the determining ^{1}H–^{1}H correlations through space for **7dd′**.

Table 2 Two dimensional ^{1}H NMR (NOESY experiments, 300 MHz) of adduct **8dd′** [a]

	1-H	4-H	5-H	6′-H	iso-H	7-H	8-H
1-H	/	−	+	−	−	−	+
4-H	−	/	−	−	−	−	−
5-H	+	−	/	**+**	−	−	−
6′-H	−	−	**+**	/	+	−	−
iso-H	−	−	−	+	/	−	−
7-H	−	−	−	−	−	/	+
8-H	+	−	−	−	−	+	/

[a] Methyl and aromatic protons excluded; 'iso-H' refers to the isopropyl proton. '+' = strong NOE effect; '−' = no correlation; '**+**' indicates the determining ^{1}H–^{1}H correlations through space for **8dd′**.

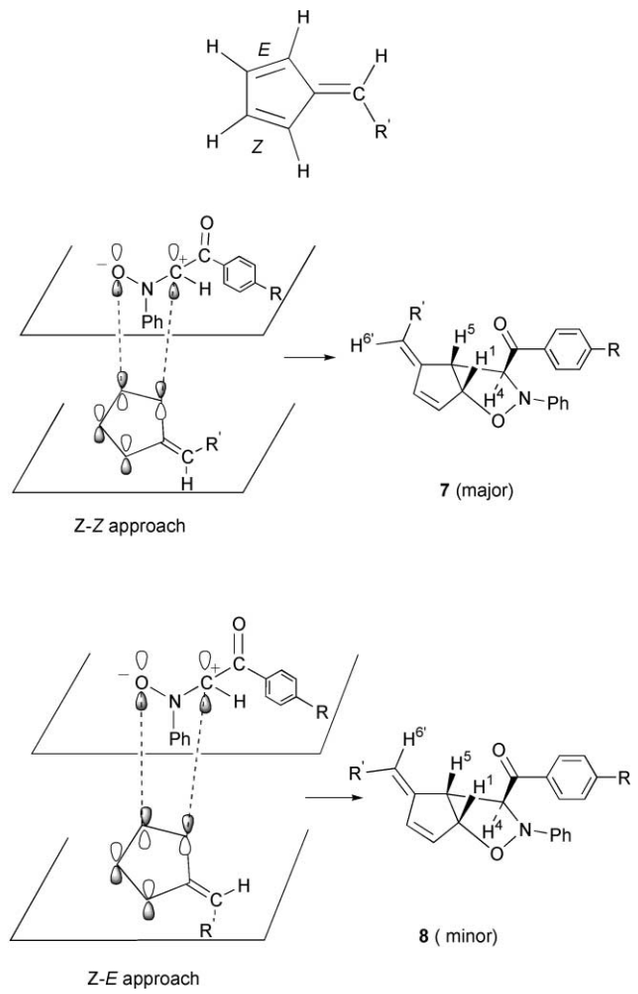
the other adducts **7**. The torsion angle 5-H–C-5–C-4–4-H was therefore close to 90–110° (Karplus rule) with the two protons in an *anticlinal* stereochemical configuration. In adduct **8dd′**, the same hydrogen atoms should be mutually coupled but the ^3J coupling constant was not easy to deduce (complex signal). The measurement was however possible for all other *minor* adducts **8**, the average value of 1.8 Hz corresponding to a torsion angle close to 120° (4-H and 5-H being in an *anticlinal* stereochemical configuration). The last ethylenic proton 6′-H (*F*) was easily identifiable, since it was a single atom in correlation with the isopropyl hydrogen (iso-H).

All spectroscopic data presented until now has remained insufficient to ascribe the *major* structure to **7dd′** or **8dd′**. A ^4J coupling constant (≈ 1.7 Hz) between 5-H and 6′-H was noticeable for the *major* structure but this phenomenon should have also prevailed for the *minor* adduct. Unfortunately, this was not visible because of the complexity of the related signals. However, such a ^4J splitting could be in agreement with a *cisoïd* as well as a *transoïd* allylic linkage between 5-H and 6′-H. More importantly, a long-range coupling between 8-H and 6′-H, $^5J \approx 1.7$ Hz, was observed in *minor* adducts only. This value corresponds to that reported in the literature, concerning the long-range splitting between protons carried by sp^2 carbons of conjugated systems.[22–25] Our observation was compatible with structure **8dd′** exclusively.

Two-dimensional ^{1}H NMR (NOESY experiments) gave the unambiguous stereochemistry of both adducts. Indeed, the long distance correlations between iso-H and 5-H on the one hand, and 6′-H and 7-H on the other hand should associate structure **7dd′** with the *major* adduct (Table 1). Similarly, the long distance correlation between 6′-H and 5-H and the absence of any correlation between iso-H and 5-H should link structure **8dd′** with the *minor* adduct (Table 2).

In order to have further proof of our structure assignments, we have performed X-ray studies on pure adducts **7ca′** (R′ = *p*-methoxyphenyl, R = H) and **8bb′** (R′ = *p*-tolyl, R = CH$_3$). In particular, torsion angles 5-H–C-5–C-4–4-H were 78° for **7ca′** and 87° for **8bb′**. These results were in complete agreement with the general stereochemical features which had emerged from our NMR spectroscopy analyses, attributing the structures **7** to *major* adducts. The two structures have recently been published.[26,27]

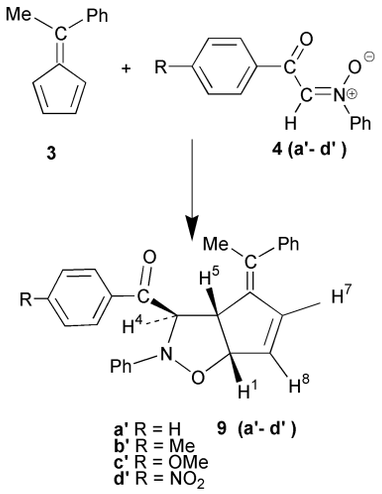
The two possible *endo* approaches of reagents **2a**–**d** and (*Z*)-acylnitrones **4** are represented in Scheme 4. In both adducts, the



Scheme 4 The two *endo* approaches between 6-monosubstituted fulvenes **2** and nitrones **4**.

aroyl group is *exo* towards the envelope built by the two fused rings. The formation of **7** (*major*) came from the approach (noted as Z–*Z*) in which the R′ group in the 6-position of the fulvene and the aroyl group of the nitrone were eclipsed. This interaction should be somewhat unfavoured for steric reasons. The very slight regioselectivity of the addition, favouring the most bulky side of the dipolarophile, was at first thought to be caused by a stabilising π–π interaction, a possible event during the approach between the 6-*aryl*fulvenes **2a**–**c** and the acylnitrones. However, this hypothesis lapsed when 6-isopropylfulvene **2d**–which *did not* carry any aryl group–reacted in a similar way to the dipolarophile.

3 Cycloadditions of 6-methyl-6-phenylfulvene 3. This fulvene was unsymmetrically substituted on C-6 and it was interesting to examine the influence of the methyl group on the orientation of the addition reaction with aroylnitrones **4**. The crude reaction mixture was first analysed by ^{1}H NMR spectroscopy and only adduct **9** was observed (Scheme 5). However, an extremely slight spot, very close to the intense one corresponding to **9**, has been indicated by TLC and might be compatible with the presence of a trace of the regioisomeric adduct (addition onto the phenyl side). As previously mentioned, the regiochemistry of the addition was easily established by ^{1}H NMR



Scheme 5

spectroscopy. The 1-H atom (around 5.50 ppm) was close to the oxygen of the isoxazolidine ring and, moreover, the presence of the ^3J coupling constant of 1.9 Hz between 1-H and 8-H corroborated the assignment of structure **9** for all adducts.

The absence of any spin–spin interaction between the 4-H and 5-H atoms revealed the existence of a torsion angle (5-H–C-5–C-4–4-H) of *ca.* 90°. Thus a *synclinal* stereochemical configuration of the 5-H–C-5–C-4–4-H linkage was excluded. The structure of **9** was fully confirmed from the analysis of the typical ^{1}H–^{1}H NOESY spectrum of **9c′**, reported in Fig. 1. It

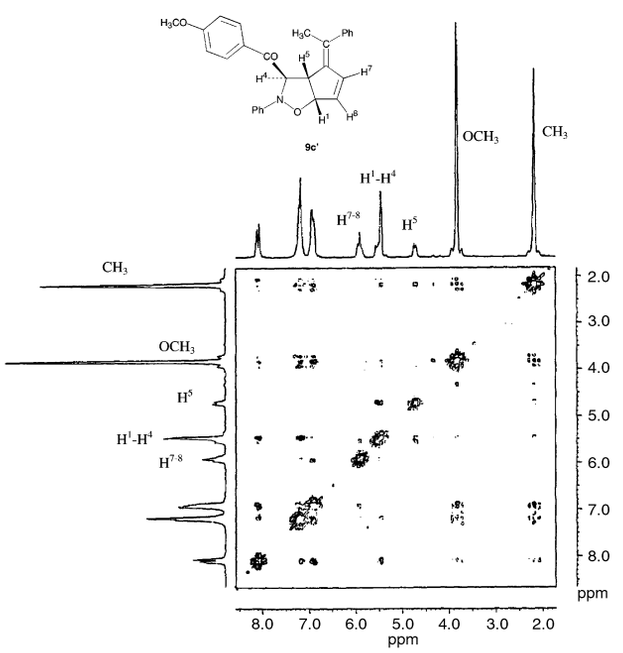


Fig. 1 ^{1}H–^{1}H NOESY spectrum of compound **9c′**.

showed strong through space correlations between the methyl group carried by the exocyclic carbon–carbon double bond and both 5-H (4.70 ppm) and 4-H (5.45 ppm). There was no correlation between the methyl group and ethylenic protons 7-H or 8-H.

The reaction occurred with a very high regioselective character on the dipolarophile side opposite to the phenyl group. This result definitively eliminated the hypothesis of a significant π–π stabilising interaction between both reagents during their approach, which in any case would lead to notable amounts of the second regioisomer.

On the basis of these results, we looked for the possible electronic and/or steric factors, which might control the regiochemistry of the cycloaddition.

Discussion

Prior work has demonstrated the existence of a dipole moment in pentafulvenes, indicating the intramolecular electronic transfer from the exocyclic double bond to the ring.[28,29] The zwitterionic character of these hydrocarbons is increased by the presence of electron-donating groups on C-6.[30,31] More recently, a complete *ab initio* study of the structure of the parent, non-substituted pentafulvene has been published, which tends to minimise the importance of the dipolar character of this molecule.[32] However, because of the presence of electron-releasing groups, the mono- or di-substituted fulvenes used in our work should be regarded as rather electron-rich structures.[7] Indeed, they are known to react with electrophiles,[33] and aroylnitrones **4** display this property through the carbon atom of the dipolar linkage, which attaches preferentially to C-1 or C-4.[7]

In order to rationalize the regiochemistry of the [3 + 2] cycloaddition of acylnitrones with fulvenes, reagents **1**–**3** and **4** were modelled throughout by two methods: *ab initio* computation at the Hartree–Fock (HF) level using the Gaussian 98 package[34] and PM3 semi-empirical calculations included in the Chem3D Pro. software available from Cambridge Soft Corporation (1996). In the first case, all geometries were fully optimised using the split valence basis set 6-31G* with the Mulliken population analysis at 298.15 K and 1 atmosphere. The Freq keyword was also included in the route section of the Gaussian jobs in order to verify if the optimised geometries were in the global minimum of the potential energy surface (no negative frequency values obtained).

Minimization calculations at the ground state were performed with starting geometries having different torsion angle values; (C–C–C–N) represents the dihedral angle for acylnitrones and θ the twist angle between the π-subsystems of fulvenes. Only results for minimized structures at their global minima are gathered here. (Hartree–Fock: Table 3 and Table 4; PM3: Table 5 and Table 6, for fulvenes and acylnitrones respectively).

In the frontier orbital approach, where the highest occupied and lowest unoccupied MO's of the two compounds (fulvene and nitrone) reacted, we compared results obtained from PM3 and *ab initio* calculations.

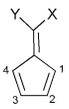
The favoured interaction between FMO (frontier molecular orbitals) during the transition state should be of the type $HOMO_{fulvene}$–$LUMO_{nitrone}$.[35] This feature was successfully demonstrated in the case of the PM3 method, explaining well the preponderant product obtained during the reactions.

Ab initio calculations did not seem to give conclusions which matched well with the experimental results. A medium basis set such as HF/6-31G* was used here in order to have a trade-off between accuracy and computational cost. The results in the minimal STO-3G base, as well as in the more advanced 6-311G** base seemed equally unreliable.

Several points can be given to explain this difference between the PM3 and HF/6-31G* predictions. It is known that activation energies for [3 + 2] cycloadditions of typical nitrones to alkenes are in the range 60–80 kJ mol^{-1} and activation energies obtained by HF calculations are clearly overestimated.[36] Better results should be attained by taking into account the electron correlation.

Apart from the choice of the basis set, the frontier orbital approach employed in this paper was an over-simple approach for explaining such cycloadditions but was in good agreement with the PM3 results. On the other hand, *ab initio* calculations (which must take into account electron correlation effect) should be carried out for excited state molecules in the frontier orbital approach or, should be treated by the mean of the IRC

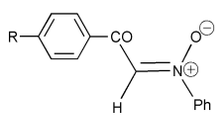
Table 3 HF/6-31G* Eigenvalues C_i for HOMO and partial charges qC_i (e) of atom i for fulvenes



	X	Y	HOMO/eV	LUMO/eV	μ/D	C_1	C_2	C_3	C_4	qC_1	qC_2	qC_3	qC_4	$\|\theta\|$/°
1	Ph	Ph	−7.94	1.90	1.34	−0.02	−0.23	−0.23	−0.02	−0.188	−0.223	−0.223	−0.188	45°
2a	Ph	H	−8.17	1.89	1.00	0.09	−0.12	−0.20	−0.13	−0.198	−0.218	−0.222	−0.186	42°
2c	Ar[a]	H	−7.72	2.01	2.50	−0.01	0.32	0.36	0.07	−0.199	−0.219	−0.224	−0.186	36°
2d	Pr^i	H	−8.19	2.49	1.14	0.69	0.47	−0.48	−0.70	−0.195	−0.218	−0.195	−0.185	—
3	Ph	Me	−8.13	2.32	1.28	−0.40	−0.31	0.32	0.42	−0.185	−0.226	−0.219	−0.191	62°

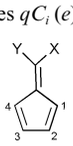
[a] Ar = p–MeO–C_6H_4–

Table 4 HF/6-31G* Eigenvalues C_i for LUMO and partial charges qC_i (e) of atom i for acylnitrones



	HOMO/eV	LUMO/eV	μ/D	C_C	C_N	C_O	qC_C	qC_N	qC_O	Dihedral angle (C–C–C–N)/°
4a	−9.00	1.23	2.95	−0.482	0.618	−0.396	−0.041	−0.044	−0.617	−0.01
4b	−5.33	1.58	11.4	−0.115	0.021	0.118	−0.212	−0.230	−0.723	−8.69
4c	−8.50	1.79	3.07	0.122	0.408	−0.025	−0.095	−0.018	−0.601	55.82
4d	−9.55	0.57	8.43	−0.333	0.504	−0.336	−0.044	−0.039	−0.614	−0.11

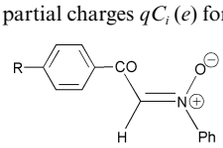
Table 5 Orbital coefficients C_i in fulvene's HOMO and partial charges qC_i (e) for atoms i calculated by PM3



	X	Y	HOMO/eV	LUMO/eV	μ/D	C_1	C_2	C_3	C_4	qC_1	qC_2	qC_3	qC_4	$\|\theta\|$/°
1	Ph	Ph	−9.11	−0.88	1.11	0.57	0.41	−0.42	−0.57	−0.130	−0.116	−0.116	−0.130	45
2a	Ph	H	−9.02	−1.03	1.03	0.06	0.28	0.27	0.04	−0.135	−0.110	−0.117	−0.132	32
2c	Ar[a]	H	−8.73	−0.99	1.33	−0.04	−0.26	−0.25	−0.03	−0.134	−0.112	−0.120	−0.130	32
2d	Pr^i	H	−9.12	−0.61	0.94	0.57	0.41	−0.42	−0.57	−0.133	−0.113	−0.118	−0.129	—
3	Ph	Me	−9.06	−0.74	1.25	−0.58	−0.44	0.39	0.57	−0.121	−0.113	−0.112	−0.136	65

[a] Ar = p-MeO–C_6H_4-

Table 6 Orbital coefficients C_X in acylnitrone's LUMO and partial charges qC_i (e) for atoms i calculated by PM3



	HOMO/eV	LUMO/eV	μ/D	C_C	C_N	C_O	qC_C	qC_N	qC_O
4a	−9.68	−0.95	6.35	−0.24	0.30	−0.21	−0.70	1.13	−0.58
4b	−9.54	−0.96	6.64	−0.25	0.31	−0.22	−0.69	1.13	−0.57
4c	−9.25	−1.06	5.37	0.26	−0.30	0.21	−0.70	1.14	−0.59
4d	−10.0	−1.52	7.82	−0.15	0.24	−0.17	−0.72	1.15	−0.57

(intrinsic reaction coordinates) method connecting the different starting and ending transition structures. This will be done in a forthcoming paper.

As an hypothesis for the observed regiochemistries, the different cycloadditions might proceed under charge control. The endocyclic double bonds of C-6-substituted fulvenes are not equivalent (except for **1**), and the most polarised bond should be on the side bearing the electron-releasing group (essentially alkyl, and to a lesser extent aryl). Cycloadditions of 6-methyl-6-phenylfulvene **3** could illustrate this hypothesis.

The calculated twist angle between the phenyl group and the fulvene ring of **3** was 62° (*ab initio* computation), very close to the angle calculated from the PM3 function (65°). This substituent had therefore no peculiar donating effect towards the C-1–C-2 bond, the conjugation being largely hampered.[37] Considering the two possible *endo* approaches between **3** and any acylnitrone **4**, it was patent that no steric effect promoted the formation of **9** rather than the second (very minor) isomer. The very high selectivity of the reaction should be caused by the exclusive influence of the 6-methyl group. However, this

consequence remained somewhat unexpected, given the results concerning 6-isopropylfulvene **2d**, a dipolarophile which also carries a strong electron-donating group.

Finally, for 6-monosubstituted fulvenes **2**, the electron-releasing character of the aryl groups was too weak to induce significant regioselectivity.

Conclusion

Aroylnitrones added to only one of the endocyclic carbon–carbon double bonds of the pentafulvenes, yielding 1 : 1 adducts by a [3 + 2] cycloaddition, which competed with the usually easy polymerisation of the dipolarophiles. The symmetrical 6,6-diphenylfulvene **1** furnished two isomeric monoadducts, with high regioselectivity. The reaction gave the aroyl group in the *exo* position, directed towards the envelope built by the two fused rings. This stereochemistry was encountered in all categories of cycloadducts and conformed with the favoured *endo* approach of the two reagents. The 6-aryl substituted fulvenes **2a**–**c** gave regioisomeric cycloadducts. The addition proceeded with almost no selectivity, with a very slight tendency to react with the double bond in the *cisoïd* position with respect to the exocyclic substituent. The hypothesis of a stabilising π–π interaction between reagents during their approach—as envisaged at one point—was discarded, in the light of the results concerning the 6-isopropylfulvene **2d**, which behaved similarly to 6-arylfulvenes. Very high regioselectivity was observed when 6-methyl-6-phenylfulvene **3** was reacted as the dipolarophile. The nitrone approached this fulvene almost entirely on the strong electron-releasing methyl group side. The regioselectivity of the reaction might be dependent on the strength of the electron-releasing nature of the substituents carried by the carbon atom in the 6-position. This feature could induce differently polarised endocyclic double bonds, the cycloaddition proceeding preferentially onto the more polarised side.

Experimental

General

Melting points were carried out on an Electrothermal IA 9200 instrument and are uncorrected. IR spectra (KBr) were recorded on a Bio-Rad FTS-7 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC200 spectrometer [200.13 MHz (^{1}H) and 50.32 MHz (^{13}C)]. Two-dimensional ^{1}H–^{1}H spectroscopy (DQF COSY and NOESY experiments) were carried out on a Bruker Avance 300 spectrometer at 300.13 MHz. All compounds were dissolved in $CDCl_3$ with 0.1% TMS as an internal reference. The ^{13}C NMR spectra were obtained from proton-noise decoupled spectra. Chemical shifts are in ppm on the δ scale and coupling constants J are given in Hz. In ^{1}H and ^{13}C NMR spectra, hydrogen and carbon atoms are numbered according to the IUPAC nomenclature rules. All liquid chromatographies were performed in 2.5 cm inside diameter Pyrex columns packed with Kieselgel 60, particle size of 0.063–0.200 mm, from Merck (art. 1.07734.1000). Preparative TLC were carried out on silica gel 60 PF_{254}. Toluene was dried over sodium wire before use.

The acylnitrones **4** were prepared according to ref. 38. Fulvene **1** was synthesized by condensation of freshly prepared cyclopentadiene with benzophenone in the presence of sodium methoxide.[39] All other fulvenes were prepared according to Stone and Little.[40]

Cycloadducts 5–9; general procedure

A mixture of 10 mmol of fulvene **1**–**3** and 10 mmol of nitrone **4** in toluene (60 mL) was refluxed with stirring for 15–24 h. After evaporation of the solvent, the crude mixture was purified by chromatography on silica gel (eluent: CH_2Cl_2–petroleum ether (bp: 40–60 °C), 80 : 20 for cycloadducts **5**–**8**) or preparative TLC (eluent $CHCl_3$–hexane, 90 : 10 for cycloadducts **9**). Analytical samples were obtained after recrystallisation from EtOH.

Substituted 6-diphenylmethylene-2-oxa-3-azabicyclo[3.3.0]-oct-7-enes 5 and 8-diphenylmethylene-2-oxa-3-azabicyclo[3.3.0]-oct-6-enes 6. *4-Benzoyl-6-diphenylmethylene-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene* ***5a′***. Yield 70%. Mp: 187 °C. IR (KBr) cm^{-1}: 1685 ν (C=O). ^{1}H NMR: δ = 4.95 (1H, d, J = 6.8 Hz, 5-H), 5.00 (1H, s, 4-H), 5.50 (1H, dd, J = 6.8 and 2.2 Hz, 1-H), 6.05 (1H, d, J = 5.6 Hz, 7-H), 6.15 (1H, dd, J = 5.6 and 2.2 Hz, 8-H), 6.50–7.80 (20H, m, aromatic). ^{13}C NMR: δ = 49.6 (C-5), 68.5 (C-4), 88.7 (C-1), 110.0–150.0 (ethylenic and aromatic), 195.7 (C=O) (Found: C, 84.5; H, 5.5; N, 3.1. $C_{32}H_{25}NO_2$ requires C, 84.4; H, 5.5; N, 3.1%).

4-Benzoyl-8-diphenylmethylene-3-phenyl-2-oxa-3-azabicyclo-[3.3.0]oct-6-ene ***6a′***. Yield 7%. Mp: 190 °C. IR (KBr) cm^{-1}: 1680 ν (C=O). ^{1}H NMR: δ = 4.50 (1H, dddd, J = 6.0, 1.9, 1.8 and 1.8 Hz, 5-H), 5.25 (1H, d, J = 1.8 Hz, 4-H), 5.35 (1H, d, J = 6.0 Hz, 1-H), 5.90 (1H, dd, J = 5.6 and 1.8 Hz, 7-H), 6.05 (1H, dd, J = 5.6 and 1.9 Hz, 6-H), 6.50–8.00 (20H, m, aromatic). ^{13}C NMR: δ = 56.2 (C-5), 69.8 (C-4), 83.1 (C-1), 110.0–155.0 (ethylenic and aromatic), 195.4 (C=O) (Found: C, 84.1; H, 5.6; N, 2.9. $C_{32}H_{25}NO_2$ requires C, 84.4; H, 5.5; N, 3.1%).

6-Diphenylmethylene-4-(4-methylbenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***5b′***. Yield 70%. Mp: 173 °C. IR (KBr) cm^{-1}: 1660 ν (C=O). ^{1}H NMR: δ = 2.40 (3H, s, CH_3), 4.95 (1H, d, J = 6.9 Hz, 5-H), 5.00 (1H, s, 4-H), 5.50 (1H, dd, J = 6.9 and 2.3 Hz, 1-H), 6.05 (1H, d, J = 5.6 Hz, 7-H), 6.15 (1H, dd, J = 5.6 and 2.3 Hz, 8-H), 6.90–7.60 (19H, m, aromatic). ^{13}C NMR: δ = 21.4 (CH_3), 49.6 (C-5), 68.5 (C-4), 88.6 (C-1), 110.0–150.0 (ethylenic and aromatic), 195.2 (C=O) (Found: C, 84.5; H, 5.8; N, 2.9. $C_{33}H_{27}NO_2$ requires C, 84.4; H, 5.8; N, 3.0%).

8-Diphenylmethylene-4-(4-methylbenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-6-ene ***6b′***. Yield 8%. Mp: 180 °C. IR (KBr) cm^{-1}: 1680 ν (C=O). ^{1}H NMR: δ = 2.40 (3H, s, CH_3), 4.45 (1H, dddd, J = 6.2, 1.9, 1.9 and 1.8 Hz, 5-H), 5.20 (1H, d, J = 1.9 Hz, 4-H), 5.30 (1H, d, J = 6.2 Hz, 1-H), 5.90 (1H, dd, J = 5.8 and 1.8 Hz, 7-H), 6.05 (1H, dd, J = 5.8 and 1.8 Hz, 6-H), 6.80–8.00 (19H, m, aromatic). ^{13}C NMR: δ = 21.5 (CH_3), 56.1 (C-5), 70.7 (C-4), 82.8 (C-1), 110.0–151.0 (ethylenic and aromatic), 195.2 (C=O) (Found: C, 84.3; H, 5.9; N, 3.1. $C_{33}H_{27}NO_2$ requires C, 84.4; H, 5.8; N, 3.0%).

6-Diphenylmethylene-4-(4-methoxybenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***5c′***. Yield 50%. Mp: 153 °C. IR (KBr) cm^{-1}: 1675 ν (C=O). ^{1}H NMR: δ = 3.80 (3H, s, OCH_3), 5.00 (1H, d, J = 6.8 Hz, 5-H), 5.00 (1H, s, 4-H), 5.50 (1H, dd, J = 6.8 and 2.0 Hz, 1-H), 6.15 (1H, d, J = 5.8 Hz, 7-H), 6.20 (1H, dd, J = 5.8 and 2.0 Hz, 8-H), 6.50–7.80 (19H, m, aromatic). ^{13}C NMR: δ = 49.7 (C-5), 55.2 (OCH_3), 68.1 (C-4), 88.7 (C-1), 113.0–165.0 (ethylenic and aromatic), 193.3 (C=O) (Found: C, 82.0; H, 5.6; N, 3.1. $C_{33}H_{27}NO_3$ requires C, 81.6; H, 5.8; N, 2.9%).

8-Diphenylmethylene-4-(4-methoxybenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-6-ene ***6c′***. Yield 7%. Mp: 160 °C. IR (KBr) cm^{-1}: 1680 ν (C=O). ^{1}H NMR: δ = 3.80 (3H, s, OCH_3), 4.50 (1H, dddd, J = 6.2, 2.0, 1.8 and 1.8 Hz, 5-H), 5.15 (1H, d, J = 2.0 Hz, 4-H), 5.30 (1H, d, J = 6.2 Hz, 1-H), 5.90 (1H, dd, J = 5.9 Hz, J = 1.8 Hz, 7-H), 6.05 (1H, dd, J = 5.9 and 1.8 Hz, 6-H), 6.70–8.00 (19H, m, aromatic). ^{13}C NMR: δ = 55.0 (OCH_3), 56.5 (C-5), 69.5 (C-4), 82.9 (C-1), 110.0–152.0 (ethylenic and aromatic), 194.5 (C=O) (Found: C, 81.9; H, 5.5; N, 2.9. $C_{33}H_{27}NO_3$ requires C, 81.6; H, 5.7; N, 2.9%).

6-Diphenylmethylene-4-(4-nitrobenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***5d′***. Yield 50%. Mp: 153 °C. IR (KBr) cm^{-1}: 1675 ν (C=O). ^{1}H NMR: δ = 5.00 (1H, d, J = 6.6 Hz, 5-H), 5.00 (1H, s, 4-H), 5.50 (1H, dd, J = 6.6 and 2.2 Hz,

1-H), 6.15 (1H, d, J = 5.8 Hz, 7-H), 6.15 (1H, dd, J = 5.8 and 2.2 Hz, 8-H), 6.50–8.20 (19H, m, aromatic). ^{13}C NMR: δ = 49.6 (C-5), 69.1 (C-4), 88.6 (C-1), 113.0–151.0 (ethylenic and aromatic), 194.7 (C=O) (Found: C, 77.0; H, 4.8; N, 5.7. $C_{32}H_{24}N_2O_4$ requires C, 76.8; H, 4.8; N, 5.6%).

8-Diphenylmethylene-4-(4-nitrobenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-6-ene ***6d′***. Yield 6%. Mp: 190 °C. IR (KBr) cm^{-1}: 1675 ν (C=O). ^{1}H NMR: δ = 4.50 (1H, dddd, J = 6.1, 1.9, 1.9 and 1.8 Hz, 5-H), 5.20 (1H, d, J = 1.9 Hz, 4-H), 5.40 (1H, d, J = 6.1 Hz, 1-H), 5.90 (1H, dd, J = 5.9 and 1.8 Hz, 7-H), 6.00 (1H, dd, J = 5.9 and 1.8 Hz, 6-H), 6.60–8.20 (19H, m, aromatic). ^{13}C NMR: δ = 56.7 (C-5), 69.8 (C-4), 83.0 (C-1), 110.0–155.0 (ethylenic and aromatic), 195.7 (C=O) (Found: C, 76.9; H, 4.9; N, 5.4. $C_{32}H_{24}N_2O_4$ requires C, 76.8; H, 4.8; N, 5.6%).

(*E*) and (*Z*)-4-Aroyl-6-arylidene-3-phenyl-2-oxa-3-azabicyclo-[3.3.0]oct-7-enes 7 and 8 (Scheme 3, R′ = aryl). *(E)-4-Benzoyl-6-benzylidene-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene* ***7aa′*** *(R′ = Ph, R = H).* Yield 15%. Mp: 130 °C. IR (KBr) cm^{-1}: 1680 ν (C=O). ^{1}H NMR: δ = 5.05 (1H, dd, J = 6.6 and 1.7 Hz, 5-H), 5.35 (1H, s, 4-H), 5.65 (1H, dd, J = 6.6 and 1.6 Hz, 1-H), 6.00 (1H, d, J = 5.5 Hz, 7-H), 6.05 (1H, dd, J = 5.5 and 1.6 Hz, 8-H), 6.35 (1H, d, J = 1.7 Hz, 6′-H), 6.80–8.00 (15H, m, aromatic). ^{13}C NMR: δ = 47.7 (C-5), 68.2 (C-4), 90.5 (C-1), 113.0–151.0 (ethylenic and aromatic), 195.0 (C=O) (Found: C, 82.6; H, 5.4; N, 3.7. $C_{26}H_{21}NO_2$ requires C, 82.3; H, 5.6; N, 3.7%).

(E)-6-Benzylidene-4-(4-methylbenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7ab′*** *(R′ = Ph, R = Me).* Yield 30%. Mp: 136 °C. IR (KBr) cm^{-1}: 1680 ν (C=O). ^{1}H NMR: δ = 2.40 (3H, s, CH_3), 5.05 (1H, dd, J = 6.7 and 1.8 Hz, 5-H), 5.35 (1H, s, 4-H), 5.60 (1H, dd, J = 6.7 and 1.8 Hz, 1-H), 6.00 (1H, d, J = 5.5 Hz, 7-H), 6.05 (1H, dd, J = 5.5 and 1.8 Hz, 8-H), 6.35 (1H, d, J = 1.8 Hz, 6′-H), 6.80–8.00 (14H, m, aromatic). ^{13}C NMR: δ = 21.5 (CH_3), 47.6 (C-5), 68.3 (C-4), 90.4 (C-1), 113.0–151.0 (ethylenic and aromatic), 195.8 (C=O) (Found: C, 82.6; H, 6.0; N, 3.3. $C_{27}H_{23}NO_2$ requires C, 82.4; H, 5.9; N, 3.5%).

(E)-6-Benzylidene-4-(4-methoxybenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7ac′*** *(R′ = Ph, R = OMe).* Yield 30%. Mp: 130 °C. IR (KBr) cm^{-1}: 1675 ν (C=O). ^{1}H NMR: δ = 3.80 (3H, s, OCH_3), 5.05 (1H, dd, J = 6.7 and 1.8 Hz, 5-H), 5.35 (1H, s, 4-H), 5.65 (1H, dd, J = 6.7 and 1.8 Hz, 1-H), 6.00 (1H, d, J = 5.5 Hz, 7-H), 6.05 (1H, dd, J = 5.5 and 1.8 Hz, 8-H), 6.40 (1H, d, J = 1.8 Hz, 6′-H), 6.70–8.00 (14H, m, aromatic). ^{13}C NMR: δ = 47.7 (C-5), 55.3 (OCH_3), 68.1 (C-4), 90.5 (C-1), 113.0–151.0 (ethylenic and aromatic), 194.2 (C=O) (Found: C, 78.9; H, 5.6; N, 3.6. $C_{27}H_{23}NO_3$ requires C, 79.2; H, 5.7; N, 3.4%).

(E)-6-Benzylidene-4-(4-nitrobenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7ad′*** *(R′ = Ph, R = NO$_2$).* Yield 25%. Mp: 138 °C. IR (KBr) cm^{-1}: 1690 ν (C=O). ^{1}H NMR: δ = 5.05 (1H, dd, J = 6.5 and 1.7 Hz, 5-H), 5.25 (1H, s, 4-H), 5.65 (1H, dd, J = 6.5 and 1.7 Hz, 1-H), 5.95 (1H, d, J = 5.5 Hz, 7-H), 6.00 (1H, dd, J = 5.5 and 1.7 Hz, 8-H), 6.40 (1H, d, J = 1.7 Hz, 6′-H), 6.80–8.00 (15H, m, aromatic). ^{13}C NMR: δ = 47.6 (C-5), 68.3 (C-4), 90.4 (C-1), 113.0–147.0 (ethylenic and aromatic), 195.8 (C=O) (Found: C, 73.8; H, 5.0; N, 6.4. $C_{26}H_{20}N_2O_4$ requires C, 73.5; H, 4.7; N, 6.6%).

(E)-4-Benzoyl-6-(4-methylbenzylidene)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7ba′*** *(R′ = p-tolyl, R = H).* Yield 30%. Mp: 156 °C. IR (KBr) cm^{-1}: 1682 ν (C=O). ^{1}H NMR: δ = 2.30 (3H, s, CH_3), 5.05 (1H, dd, J = 6.8 and 1.7 Hz, 5-H), 5.35 (1H, s, 4-H), 5.65 (1H, dd, J = 6.8 and 1.7 Hz, 1-H), 5.90–6.05 (2H, m, 7-H and 8-H), 6.35 (1H, d, J = 1.7 Hz, 6′-H), 6.80–8.10 (14H, m, aromatic). ^{13}C NMR: δ = 21.0 (CH_3), 47.7 (C-5), 68.3 (C-4), 90.5 (C-1), 113.0–151.0 (ethylenic and aromatic), 195.9 (C=O) (Found: C, 82.6; H, 6.0; N, 3.7. $C_{27}H_{23}NO_2$ requires C, 82.4; H, 5.9; N, 3.5%).

(E)-4-(4-Methylbenzoyl)-6-(4-methylbenzylidene)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7bb′*** *(R′ = p-tolyl, R = Me).* Yield 30%. Mp: 143 °C. IR (KBr) cm^{-1}: 1682 ν (C=O). ^{1}H NMR: δ = 2.30 (3H, s, CH_3), 2.35 (3H, s, CH_3), 5.05 (1H, dd, J = 6.7 and 1.8 Hz, 5-H), 5.35 (1H, s, 4-H), 5.60 (1H, dd, J = 6.7 and 1.8 Hz, 1-H), 5.95 (2H, m, 7-H and 8-H), 6.30 (1H, d, J = 1.8 Hz, 6′-H), 6.80–8.00 (13H, m, aromatic). ^{13}C NMR: δ = 21.5 (2 CH_3), 47.7 (C-5), 68.3 (C-4), 90.5 (C-1), 113.0–151.0 (ethylenic and aromatic), 195.5 (C=O) (Found: C, 82.7; H, 6.0; N, 3.3. $C_{28}H_{25}NO_2$ requires C, 82.5; H, 6.2; N, 3.4%).

(Z)-4-(4-Methylbenzoyl)-6-(4-methylbenzylidene)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***8bb′*** *(R′ = p-tolyl, R = Me).* Yield 20%. Mp: 133 °C. IR (KBr) cm^{-1}: 1675 ν (C=O). ^{1}H NMR: δ = 2.30 (3H, s, CH_3), 2.40 (3H, s, CH_3), 4.50 (1H, ddd, J = 6.7, 1.8 and 1.8 Hz, 5-H), 5.45 (1H, d, J = 1.8 Hz, 4-H), 5.55 (1H, dd, J = 6.7 and 1.8 Hz, 1-H), 6.15 (1H, ddd, J = 6.0, 1.7 and 1.7 Hz, 8-H), 6.50 (2H, m, 6′-H and 7-H), 6.80–8.00 (13H, m, aromatic). ^{13}C NMR: δ = 21.0 (CH_3), 21.5 (CH_3), 51.9 (C-5), 72.5 (C-4), 87.7 (C-1), 114.0–151.0 (ethylenic and aromatic), 195.5 (C=O) (Found: C, 82.4; H, 6.4; N, 3.5. $C_{28}H_{25}NO_2$ requires C, 82.5; H, 6.2; N, 3.4%).

(E)-4-(4-Methoxybenzoyl)-6-(4-methylbenzylidene)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7bc′*** *(R′ = p-tolyl, R = OMe).* Yield 24%. Mp: 113 °C. IR (KBr) cm^{-1}: 1675 ν (C=O). ^{1}H NMR: δ = 2.30 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 5.05 (1H, dd, J = 6.7 and 1.7 Hz, 5-H), 5.35 (1H, s, 4-H), 5.65 (1H, dd, J = 6.7 and 1.8 Hz, 1-H), 6.00 (2H, m, 7-H and 8-H), 6.30 (1H, d, J = 1.7 Hz, 6′-H), 6.80–8.00 (13H, m, aromatic). ^{13}C NMR: δ = 20.9 (CH_3), 47.7 (C-5), 55.2 (OCH_3), 68.0 (C-4), 90.5 (C-1), 113.0–151.0 (ethylenic and aromatic), 194.2 (C=O) (Found: C, 79.1; H, 5.9; N, 3.4. $C_{28}H_{25}NO_3$ requires C, 79.4; H, 6.0; N, 3.3%).

(E)-4-(4-Nitrobenzoyl)-6-(4-methylbenzylidene)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7bd′*** *(R′ = p-tolyl, R = NO$_2$).* Yield 35%. Mp: 120 °C. IR (KBr) cm^{-1}: 1690 ν (C=O). ^{1}H NMR: δ = 2.30 (3H, s, CH_3), 5.05 (1H, dd, J = 6.7 and 1.7 Hz, 5-H), 5.35 (1H, s, 4-H), 5.65 (1H, dd, J = 6.7 and 1.8 Hz, 1-H), 5.95 (2H, m, 7-H and 8-H), 6.30 (1H, d, J = 1.7 Hz, 6′-H), 6.80–8.30 (13H, m, aromatic). ^{13}C NMR: δ = 21.0 (CH_3), 47.7 (C-5), 68.8 (C-4), 90.5 (C-1), 113.0–151.0 (ethylenic and aromatic), 195.1 (C=O) (Found: C, 74.1; H, 5.0; N, 6.5. $C_{27}H_{22}N_2O_4$ requires C, 73.9; H, 5.1; N, 6.4%).

(E)-4-Benzoyl-6-(4-methoxybenzylidene)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7ca′*** *(R′ = p-anisyl, R = H).* Yield 30%. Mp: 230 °C. IR (KBr) cm^{-1}: 1680 ν (C=O). ^{1}H NMR: δ = 3.75 (3H, s, OCH_3), 4.95 (1H, dd, J = 6.8 and 1.6 Hz, 5-H), 5.30 (1H, s, 4-H), 5.55 (1H, dd, J = 6.8 and 1.8 Hz, 1-H), 5.95 (2H, m, 7-H and 8-H), 6.35 (1H, d, J = 1.6 Hz, 6′-H), 6.80–8.00 (14H, m, aromatic). ^{13}C NMR: δ = 47.6 (C-5), 55.1 (OCH_3), 68.3 (C-4), 90.6 (C-1), 113.0–159.0 (ethylenic and aromatic), 196.1 (C=O) (Found: C, 79.0; H, 5.7; N, 3.5. $C_{27}H_{23}NO_3$ requires C, 79.2; H, 5.6; N, 3.4%).

(E)-6-(4-Methoxybenzylidene)-4-(4-methylbenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7cb′*** *(R′ = p-anisyl, R = Me).* Yield 41%. Mp: 164 °C. IR (KBr) cm^{-1}: 1680 ν (C=O). ^{1}H NMR: δ = 2.40 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 5.00 (1H, dd, J = 6.8 and 1.8 Hz, 5-H), 5.35 (1H, s, 4-H), 5.65 (1H, dd, J = 6.8 and 1.8 Hz, 1-H), 6.00 (2H, m, 7-H and 8-H), 6.30 (1H, d, J = 1.8 Hz, 6′-H), 6.80–7.80 (13H, m, aromatic). ^{13}C NMR: δ = 21.5 (CH_3), 47.6 (C-5), 55.1 (OCH_3), 68.3 (C-4), 90.6 (C-1), 13.0–159.0 (ethylenic and aromatic), 195.7 (C=O) (Found: C, 79.6; H, 6.1; N, 3.5. $C_{28}H_{25}NO_3$ requires C, 79.4; H, 5.9; N, 3.3%).

(Z)-6-(4-Methoxybenzylidene)-4-(4-methylbenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***8cb′*** *(R′ = p-anisyl, R = Me).* Yield 27%. Mp: 104 °C. IR (KBr) cm^{-1}: 1675 ν (C=O). ^{1}H NMR: δ = 2.40 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 4.45 (1H, ddd, J = 6.6, 1.7 and 1.7 Hz, 5-H), 5.45 (1H, d, J = 1.7 Hz, 4-H), 5.55 (1H, dd, J = 6.6 and 1.6 Hz, 1-H), 6.10 (1H, ddd, J = 5.7, 1.6 and 1.6 Hz, 8-H), 6.45 (2H, m, 7-H and 6′-H), 6.80–8.50 (13H, m, aromatic). ^{13}C NMR: δ = 21.5 (CH_3), 51.5 (C-5), 55.3 (OCH_3), 71.0 (C-4), 87.9 (C-1), 113.0–151.0 (ethylenic and aromatic), 194.9 (C=O) (Found: C, 79.3; H, 5.9; N, 3.4. $C_{28}H_{25}NO_3$ requires C, 79.4; H, 5.9; N, 3.3%).

(E)-4-(4-Methylbenzoyl)-6-(4-methoxybenzylidene)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7cc′*** *(R′ = p-anisyl, R = OMe).* Yield 40%. Mp: 100 °C. IR (KBr) cm^{-1}: 1670 *ν* (C=O). ^{1}H NMR: *δ* = 3.75 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 5.05 (1H, dd, *J* = 6.7 and 1.7 Hz, 5-H), 5.35 (1H, s, 4-H), 5.65 (1H, dd, *J* = 6.7 and 1.8 Hz, 1-H), 6.00 (2H, m, 7-H and 8-H), 6.30 (1H, d, *J* = 1.7 Hz, 6′-H), 6.80–8.10 (13H, m, aromatic). ^{13}C NMR: *δ* = 47.6 (C-5), 55.1 (OCH_3), 55.3 (OCH_3), 68.1 (C-4), 90.6 (C-1), 113.0–164.0 (ethylenic and aromatic), 194.5 (C=O) (Found: C, 76.7; H, 5.7; N, 2.9. $C_{28}H_{25}NO_4$ requires C, 76.5; H, 5.7; N, 3.2%).

(E)-6-(4-Methoxybenzylidene)-4-(4-nitrobenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***7cd′*** *(R′ = p-anisyl, R = NO$_2$).* Yield 25%. Mp: 121 °C. IR (KBr) cm^{-1}: 1695 *ν* (C=O). ^{1}H NMR: *δ* = 3.80 (3H, s, OCH_3), 5.00 (1H, dd, *J* = 6.6 and, 1.6 Hz, 5-H), 5.30 (1H, s, 4-H), 5.60 (1H, dd, *J* = 6.6 and 1.6 Hz, 1-H), 6.00 (2H, m, 7-H and 8-H), 6.30 (1H, d, *J* = 1.6 Hz, 6′-H), 6.80–8.30 (13H, m, aromatic). ^{13}C NMR: *δ* = 47.6 (C-5), 55.1 (OCH_3), 68.8 (C-4), 90.5 (C-1), 113.0–160.0 (ethylenic and aromatic), 195.4 (C=O) (Found: C, 70.9; H, 4.8; N, 6.3. $C_{27}H_{22}N_2O_5$ requires C, 71.3; H, 4.8; N, 6.2%).

(*E*)- and (*Z*)-6-(2-Methylpropylidene)-4-(4-nitrobenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-enes 7dd′ and 8dd′ (Scheme 3, R′ = isopropyl, R = NO$_2$). *(E)-6-(2-Methylpropylidene)-4-(4-nitrobenzoyl)-3-phenyl-2-oxa-3-azabicyclo-[3.3.0]oct-7-ene* ***7dd′***. Yield 24%. Mp: 172 °C. IR (KBr) cm^{-1}: 1680 *ν* (C=O). ^{1}H NMR: *δ* = 1.00 (3H, d, *J* = 6.7 Hz, CH_3), 1.10 (3H, d, *J* = 6.7 Hz, CH_3), 2.50 (1H, ddd, *J* = 6.7, 6.7 and 10.4 Hz, iso-H), 4.55 (1H, ddd, *J* = 6.7, 1.8 and 1.2 Hz, 5-H), 5.20 (1H, d, *J* = 1.2 Hz, 4-H), 5.25 (1H, dd, *J* = 10.4 and 1.8 Hz, 6′-H), 5.50 (1H, dd, *J* = 6.7 and 1.2 Hz, 1-H), 5.85 (2H, m, 7-H and 8-H), 6.80–8.50 (9H, m, aromatic). ^{13}C NMR: *δ* = 22.7 (CH_3), 23.0 (CH_3), 29.3 (CH_{iso}), 47.0 (C-5), 72.8 (C-4), 89.7 (C-1), 113.0–160.0 (ethylenic and aromatic), 195.6 (C=O) (Found: C, 71.1; H, 5.8; N, 7.0. $C_{23}H_{22}N_2O_4$ requires C, 70.7; H, 5.6; N, 7.2%).

(Z)-6-(2-Methylpropylidene)-4-(4-nitrobenzoyl)-3-phenyl-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***8dd′***. Yield 16%. Mp: 104 °C. IR (KBr) cm^{-1}: 1685 *ν* (C=O). ^{1}H NMR: *δ* = 0.85 (3H, d, *J* = 6.7 Hz, CH_3), 0.95 (3H, d, *J* = 6.7 Hz, CH_3), 2.45 (1H, ddd, *J* = 6.7, 6.7 and 10.0 Hz, iso-H), 4.35 (1H, m, 5-H), 5.30 (2H, m, 4-H and 6′-H), 5.45 (1H, dd, *J* = 6.7 and 1.8 Hz, 1-H), 5.95 (1H, ddd, *J* = 6.1, 1.8 and 1.6 Hz, 8-H), 6.15 (1H, d, *J* = 6.1 Hz, 7-H), 6.80–8.50 (9H, m, aromatic). ^{13}C NMR: *δ* = 22.9 (2 CH_3), 28.6 (CH_{iso}), 49.7 (C-5), 73.1 (C-4), 88.6 (C-1), 113.0–150.0 (ethylenic and aromatic), 195.2 (C=O) (Found: C, 70.7; H, 5.7; N, 7.1. $C_{23}H_{22}N_2O_4$ requires C, 70.7; H, 5.6; N, 7.2%).

All DQF COSY and NOESY experiments for adducts **7dd′** and **8dd′** are summarised in Tables 1 and 2.

4-Aroyl-3-phenyl-6-(1-phenylethylidene)-2-oxa-3-azabicyclo-[3.3.0]oct-7-enes 9. *4-Benzoyl-3-phenyl-6-(1-phenylethylidene)-2-oxa-3-azabicyclo[3.3.0]oct-7-ene* ***9a′***. Yield 28%. Mp: 92–94 °C. IR (KBr) cm^{-1}: 1680 *ν* (C=O). ^{1}H NMR: *δ* = 2.20 (3H, s, CH_3), 4.70 (1H, d, *J* = 6.6 Hz, 5-H), 5.35 (1H, s, 4-H), 5.60 (1H, dd, *J* = 6.6 and 1.6 Hz, 1-H), 5.85 (1H, dd, *J* = 5.7 and 1.6 Hz, 8-H), 5.90 (1H, d, *J* = 5.7 Hz, 7-H), 6.90–8.20 (15H, m, aromatic). ^{13}C NMR: *δ* = 21.5 (CH_3), 48.9 (C-5), 70.8 (C-4), 89.3 (C-1), 113.0–151.0 (ethylenic and aromatic), 196.0 (C=O) (Found: C, 82.6; H, 6.2; N, 3.5. $C_{27}H_{23}NO_2$ requires C, 82.4; H, 5.9; N, 3.5%).

4-(4-Methylbenzoyl)-3-phenyl-6-(1-phenylethylidene)-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***9b′***. Yield 30%. Mp: 93 °C. IR (KBr) cm^{-1}: 1685 *ν* (C=O). ^{1}H NMR: *δ* = 2.20 (3H, s, CH_3), 2.40 (3H, s, CH_3), 4.70 (1H, d, *J* = 6.9 Hz, 5-H), 5.45 (1H, s, 4-H), 5.55 (1H, dd, *J* = 6.9 and 1.8 Hz, 1-H), 5.85 (1H, dd, *J* = 6.0 and 1.8 Hz, 8-H), 5.95 (1H, d, *J* = 6.0 Hz, 7-H), 6.80–8.00 (14H, m, aromatic). ^{13}C NMR: *δ* = 21.5 (CH_3), 49.0 (C-5), 70.8 (C-4), 89.2 (C-1), 113.0–151.0 (ethylenic and aromatic), 195.6 (C=O) (Found: C, 82.7; H, 6.3; N, 3.6. $C_{28}H_{25}NO_2$ requires C, 82.5; H, 6.2; N, 3.4%).

4-(4-Methoxybenzoyl)-3-phenyl-6-(1-phenylethylidene)-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***9c′***. Yield 21%. Mp: 144 °C. IR (KBr) cm^{-1}: 1660 *ν* (C=O). ^{1}H NMR: *δ* = 2.20 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 4.70 (1H, d, *J* = 6.8 Hz, 5-H), 5.45 (1H, s, 4-H), 5.50 (1H, dd, *J* = 6.8 and 1.9 Hz, 1-H), 5.85 (1H, dd, *J* = 5.8 and 1.9 Hz, 8-H), 5.95 (1H, d, *J* = 5.8 Hz, 7-H), 6.80–8.20 (14H, m, aromatic). ^{13}C NMR: *δ* = 21.5 (CH_3), 49.1 (C-5), 55.3 (OCH_3), 70.8 (C-4), 89.2 (C-1), 113.0–151.0 (ethylenic and aromatic), 194.5 (C=O) (Found: C, 79.1; H, 5.9; N, 3.5. $C_{28}H_{25}NO_3$ requires C, 79.4; H, 5.9; N, 3.3%).

4-(4-Nitrobenzoyl)-3-phenyl-6-(1-phenylethylidene)-2-oxa-3-azabicyclo[3.3.0]oct-7-ene ***9d′***. Yield 37%. Mp: 164 °C. IR (KBr) cm^{-1}: 1690 *ν* (C=O). ^{1}H NMR: *δ* = 2.20 (3H, s, CH_3), 4.70 (1H, d, *J* = 6.4 Hz, 5-H), 5.45 (1H, s, 4-H), 5.55 (1H, dd, *J* = 6.4 and 1.7 Hz, 1-H), 5.85 (1H, dd, *J* = 5.8 and 1.7 Hz, 8-H), 5.95 (1H, d, *J* = 5.8 Hz, 7-H), 6.80–8.40 (14H, m, aromatic). ^{13}C NMR: *δ* = 21.5 (CH_3), 48.9 (C-5), 71.5 (C-4), 89.4 (C-1), 113.0–151.0 (ethylenic and aromatic), 195.4 (C=O) (Found: C, 74.2; H, 5.1; N, 6.3. $C_{27}H_{22}N_2O_4$ requires C, 73.9; H, 5.0; N, 6.4%).

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References

1 W. Friedrichsen and W. D. Schröer, *Liebigs Ann. Chem.*, 1981, 476.
2 W. Friedrichsen and H. G. Oeser, *Liebigs Ann. Chem.*, 1978, 1161.
3 R. Huston, M. Rey and A. S. Dreiding, *Helv. Chim. Acta*, 1982, **65**, 451.
4 R. Allmann, T. Debaerde-Maeker, W. Friedrichsen, H. J. Jürgens and M. Betz, *Tetrahedron*, 1976, **32**, 147.
5 B. Uebersat and M. Neuenschwander, *Chimia*, 1981, **35**, 400.
6 E. P. Kohler and J. Kable, *J. Am. Chem. Soc.*, 1935, **57**, 1917.
7 M. Neuenschwander, *The Chemistry of Functional Groups, Supplement A, The Chemistry of Double Bonded Functional Groups*, ed. S. Patai, Wiley, Chichester, 1989, vol. 2, pp. 1131–1268.
8 T. Gillmann and H. Hartke, *Chem. Ber.*, 1986, **119**, 2859.
9 K. N. Houk and L. J. Luskus, *J. Org. Chem.*, 1973, **38**, 3836.
10 V. Nair, S. Kumar, G. Anilkumar and J. Somarajan, *Tetrahedron*, 1995, **51**, 9155.
11 T. Susaki, K. Kanematsu and K. Lizuha, *J. Org. Chem.*, 1976, **41**, 1105.
12 H. Takeshito, A. Mori, S. Sano and J. Fujise, *Bull. Chem. Soc. Jpn.*, 1975, **48**, 1661.
13 L. C. Dunn, J. M. Chang and K. N. Kouk, *J. Am. Chem. Soc.*, 1976, **98**, 7095.
14 K. N. Houk and L. J. Luskus, *Tetrahedron Lett.*, 1970, **39**, 4029.
15 V. Alder, R. Praden and H. Flock, *Chem. Ber.*, 1961, **94**, 456.
16 P. Caramella, P. Frattini and P. Grünanger, *Tetrahedron Lett.*, 1971, **41**, 3817.
17 D. N. Dhar and R. Ragunathan, *Tetrahedron*, 1984, **40**, 1585.
18 F. Djapa, M. Msaddek, K. Ciamala, J. Vebrel and C. Riche, *Eur. J. Org. Chem.*, 2000, 1271.
19 S. Chandrasekhar, M. Ravindranath, B. S. Neela, S. Ramakumar and M. A. Viswamitra, *J. Chem. Res. (S)*, 1989, 252.
20 P. Goncalo, Thèse de Chimie Physique, Université de Besançon, 1999, 129.
21 M. Joucla, D. Grée and J. Hamelin, *Tetrahedron*, 1972, **28**, 2315.
22 F. Bohlmann, P. Herbst, C. Arndt, H. Schönowsky and H. Gleinig, *Chem. Ber.*, 1961, **94**, 3193.
23 F. Bohlmann, W. von Kap-Herr, L. Fanghänel, C. Arndt, K. M. Kleine and S. Köhn, *Chem. Ber.*, 1965, **98**, 1411.
24 P. R. Wells, *Aust. J. Chem.*, 1963, **16**, 165.
25 L. M. Jackman and S. Sternhell, in *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, ed. D. H. R. Barton and W. Doering, Pergamon Press, London, 2nd edn., 1969, pp. 332.
26 M. M. Kubicki, O. Blacque, F. Djapa, K. Ciamala and J. Vebrel, *Acta Crystallogr., Sect. C*, 1998, **54**, 1027.
27 F. Djapa, K. Ciamala, J. Vebrel, M. M. Kubicki and O. Blacque, *Acta Crystallogr., Sect. C*, 1999, **55**, 677.
28 J. Thiec and J. Wiemann, *Bull. Soc. Chim. Fr.*, 1958, 207.
29 C. J. Abelt and H. D. Roth, *J. Am. Chem. Soc.*, 1985, **107**, 6814.
30 E. D. Bergmann, *Chem. Rev.*, 1968, **68**, 41.

31 P. Yates, *Adv. Alicyclic Chem.*, 1968, **2**, 59.
32 A. P. Scott, I. Agranat, P. U. Biedermann, N. V. Riggs and L. Radom, *J. Org. Chem.*, 1997, **62**, 2026.
33 K. Hafner, *Angew. Chem.*, 1962, **79**, 499.
34 Gaussian 98, Revision A.9, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle and J. A. Pople, Gaussian, Inc., Pittsburgh, PA, 1998.
35 V. Ondrus, L. Fisera, K. Polborn, P. Ertl and N. Pronayova, *Monatsh. Chem.*, 1995, **126**, 961.
36 A. Baranski, *Wiad. Chem.*, 2000, **54**, 53.
37 D. J. Sardella, C. M. Keane and P. Lemonias, *J. Am. Chem. Soc.*, 1984, **106**, 4962.
38 F. Kröhnke, *Chem. Ber.*, 1938, **71**, 2583.
39 J. Thiele, *Chem. Ber.*, 1900, **33**, 666.
40 K. J. Stone and R. D. Little, *J. Org. Chem.*, 1984, **49**, 1849.