Pergamon

Tetrahedron 55 (1999) 6961–6970

TETRAHEDRON

Substituted 1-Benzyl-4-(benzylidenimino)-4-phenylazetidin-2-ones: Synthesis, Thermal and Photochemical Reactions.

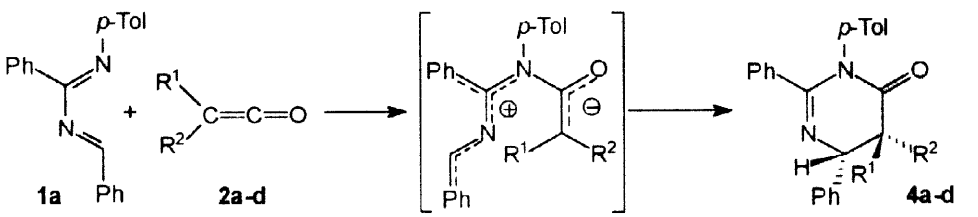
Elisabetta Rossi*, Giorgio Abbiati, Elena Pini

Istituto di Chimica Organica, Facoltá di Farmacia, Universitá degli Studi di Milano, Via Venezian, 21, I-20133 Milano, Italy. E-mail: Elisabetta.Rossi@unimi.it

Received 14 December 1998; revised 25 March 1999; accepted 8 April 1999

Abstract: The title compounds were synthesised from 1,3-diazabuta-1,3-dienes and ketenes. Thermal and photochemical ring expansion reactions to 5,6-dihydro-3*H*-pyrimidin-4-ones are also described.

Recently we reported that cycloaddition reactions of 1-(4-methylphenyl)-1,3-diazabuta-1,3-diene **1a** with ketenes **2a-d**, obtained *in situ* from the corresponding acyl chlorides and triethylamine, proceed directly to [4+2] cycloaddition products, the formation of [2+2] adducts being forbidden for steric reasons (Scheme 1).[1]



2,4	R¹	R²
a	H	Ph
b	Ph	Ph
c	H	Cl
d	H	COOEt

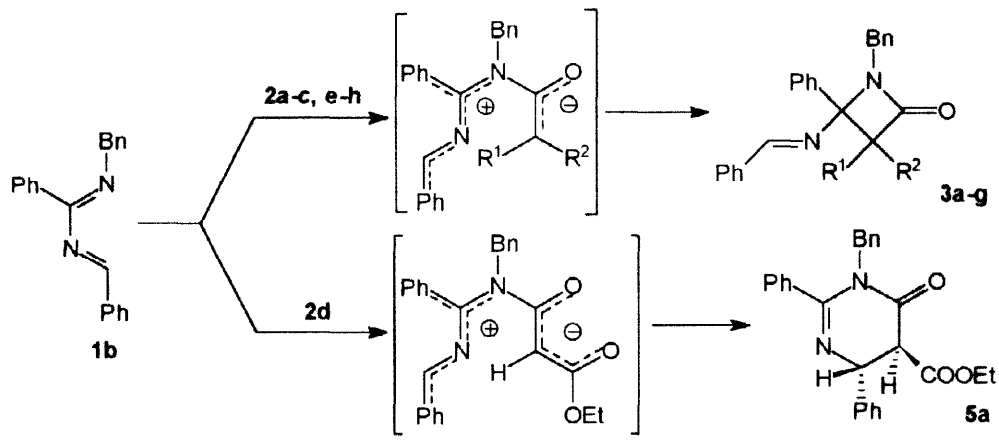
Scheme 1

Starting from 1-benzyl-1,3-diazabuta-1,3-diene **1b** the reactions performed with ketenes **2a-c** resulted in the isolation of [2+2] cycloaddition products and only the reaction with ethoxycarbonylketene **2d** gave the [4+2] adduct **5a**. Probably, in the latter case, the greater stability of the zwitterionic intermediate, related to the presence of an ethoxycarbonyl substituent on the ketene moiety, is responsible for the formation of the thermodynamically controlled cycloadduct **5a** (Scheme 2).

Moreover, the formation of azetidinones **3** is under kinetic control and these compounds rearranged partially into the more stable 5,6-dihydro-3*H*-pyrimidin-4-ones **5** when the reaction mixtures were allowed to stand for a few days or when the reactions were performed using a stoichiometric amount of triethylamine.[1]

In this work we investigated more closely the reactivity of **1b** with ketenes in order to obtain the isomeric dihydropyrimidin-4-ones **5** and to achieve a better understanding about the mechanism involved. Therefore we extended our study to vinyl, dimethyl, methoxy and dichloroketenes **2e-h** which react, under standard conditions,[1] with 1,3-diazadiene **1b** to give the expected azetidin-2-ones **3d-g** (Scheme 2).

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00325-7



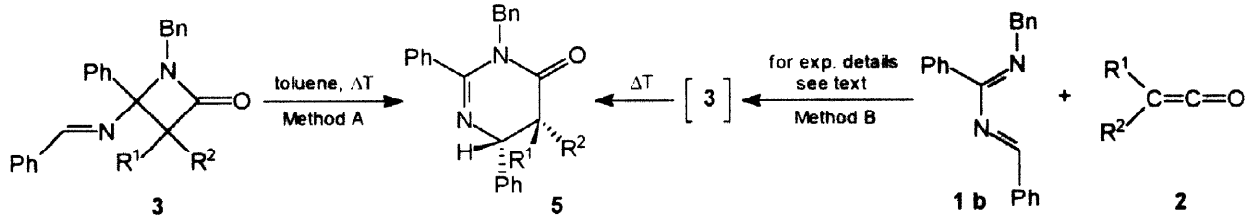
2	3	R^1	R^2
a	a	H	Ph
b	b	Ph	Ph
c	c	H	Cl
d	-	H	COOEt
e	d	H	CH_2=CH
f	e	Me	Me
g	f	H	OMe
h	g	Cl	Cl

Scheme 2

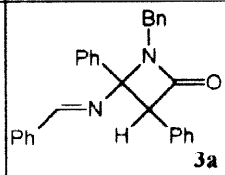
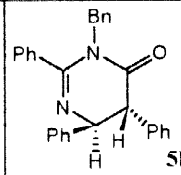
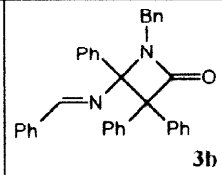
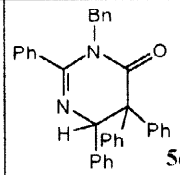
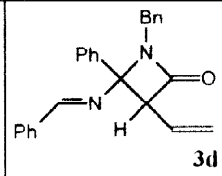
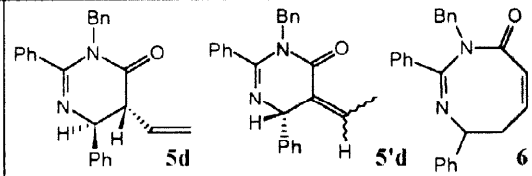
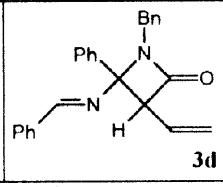
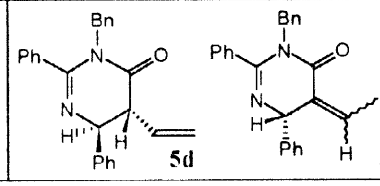
Diastereoselectivity for cycloaddition reactions involving monosubstituted ketenes was demonstrated by ^{1}H-NMR spectra analysis and NOE-difference experiments performed for azetidinones **3a,c,d,f** showing the presence of a single diastereoisomer with *cis* relationship between the benzylideneimino group at C-4 and the hydrogen at C-3. As expected, HPLC analysis of compounds **3a,c,d,f** on a Chiralcel OD column is consistent with the presence of two enantiomers in 1:1 ratio.

Moreover, we tested the case of rearrangement of azetidin-2-ones **3** to dihydropyrimidin-4-ones **5** by heating under reflux in dry toluene the pure isolated **3** (method A) or in a one-pot reaction starting from azadiene **1b**, acyl chlorides and triethylamine in a molar ratio of 1 : 1,1 : 1 and heating the mixtures under reflux, using tlc analysis to show the disappearance of **1b** and the formation of **3** (method B). The complete transformation of **3** into **5** occurs for azetidin-2-ones **3a** and **3b** with both methods (Table 1, entry 1-2). Entry 3-4 report the behaviour of **3d** from which the 4,5-dihydropyrimidin-4-one **5d** was isolated beside its quinoid isomer **5'd** in ratio 1 : 5 when the reaction was performed with method B, whereas with method A the 1,3-diazacyclooctadienone **6** was isolated as the main product beside small quantities of **5d** and **5'd**. Apparently 1,3-diazacyclooctadienone **6** is formed directly from azetidinones **3d**, since heating a mixture of **5d** and **5'd** in toluene under reflux resulted only in the isomerization of dihydropyrimidin-4-one **5d** into the methylene derivative **5'd**. On the other hand, compounds **3c,e-g** were quantitatively recovered when heated in dry toluene or, in poorer yields than under the standard conditions, in the one-pot reactions. Thermolysis of compound **3g** was performed at higher temperature (tetralin at reflux) with the same results. The *trans* configuration of the 5,6-dihydro-3*H*-pyrimidin-4-ones **5b** and **5d** was assigned by analysis on the basis of the ^{1}H-NMR coupling constants reported[2,3] for such systems ($J_{trans} > J_{cis}$) and by comparison with the *cis* isomers isolated in the photochemical reactions (see below). Theoretical calculation based on Karplus equation applied to the *cis* and *trans* stereoisomers of compounds **5** are in agreement with the experimental results.

Table 1. Thermal behaviour of azetidin-2-ones **3**.



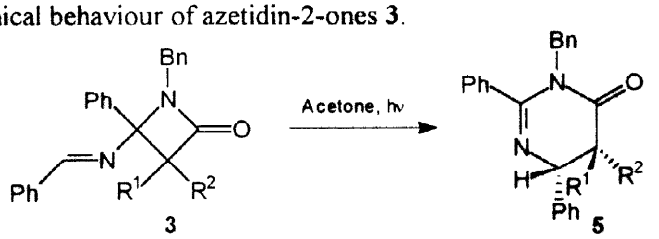
3 **5** **1 b** **2**

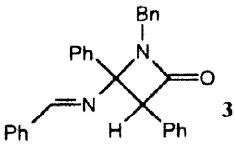
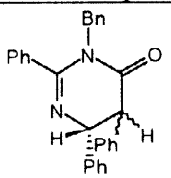
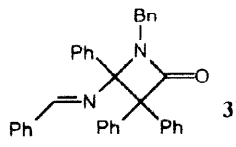
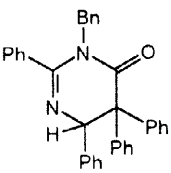
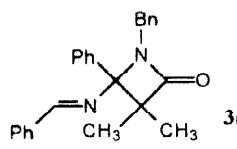
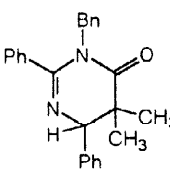
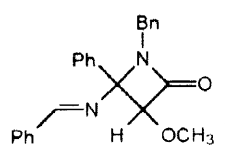
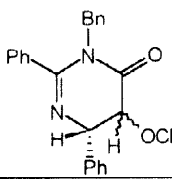
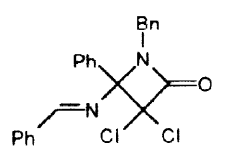
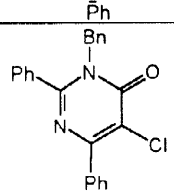
Entry	3	Method	Reaction products	Purification	Yield
1	 **3a**	A / B	 **5b**	A: Crystallisation: *i*-Pr_2O B: Chromatography: PE/AcOEt 9:1	A = 75 B = 65
2	 **3b**	A / B	 **5c**	A: Crystallisation: PE B: Chromatography: PE/AcOEt 9:1	A = 90 B = 76
3	 **3d**	A	 **5d** **5'd** **6**	Chromatography: PE/AcOEt 9:1	**5d** = 16 **5'd** = 25 **6** = 59
4	 **3d**	B	 **5d** **5'd**	Chromatography: PE/AcOEt 9:1	**5d** = 10 **5'd** = 51

PE = petroleum ether

These results prompted us to extend our investigations to the photochemical behaviour of azetidinones **3** which were irradiated for 8-12 h in dry acetone solution at room temperature with a high pressure mercury lamp. The results are collected in Table 2. Under these conditions, azetidinones **3a,b,e,f,g** yield the corresponding dihydropyrimidin-4-ones **5b,c,e,f** and pyrimidin-4-one **5g**, whereas compounds **3c,d** gave more complex reaction mixtures in which pyrimidinones **5** were detected by ^{1}H-NMR analysis beside other unidentified products. The *cis* and *trans* isomers of the 5,6-dihydro-3*H*-pyrimidin-4-ones **5b** and **5f** were separated by flash chromatography and identified from their ^{1}H-NMR coupling constants between H-5 and H-6.[2] Furthermore, *cis/trans* isomerization was not observed when pure *cis* and *trans* **5f** were irradiated for 15h in dry acetone solution, demonstrating that the isomers are formed during the ring expansion step.

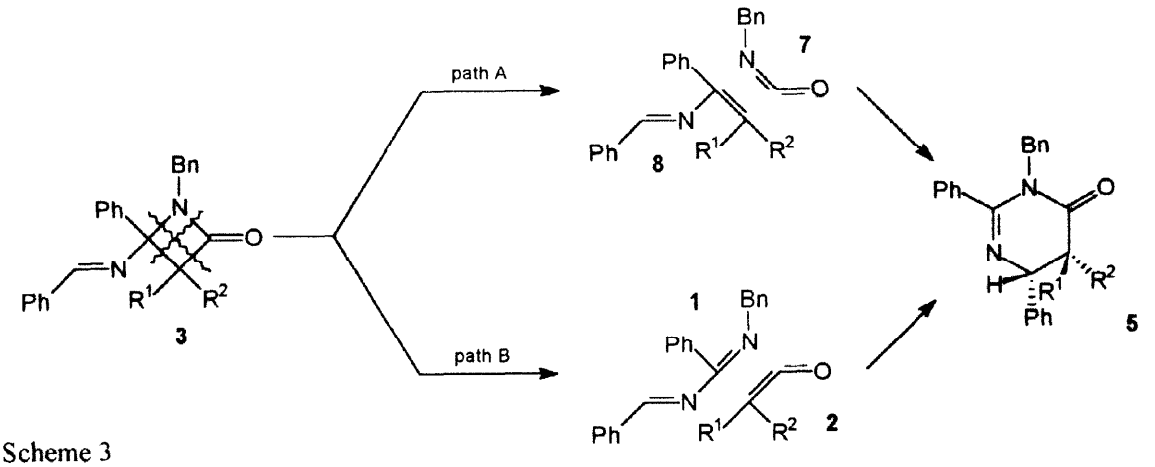
Table 2. Photochemical behaviour of azetidin-2-ones **3**.



Entry	3	Reaction products	Purification	Yield
1	 **3a**	 **5b**	Chromatography: PE/AcOEt 9:1	70 *cis/trans* mixture 30:70
2	 **3b**	 **5c**	Crystallisation: PE	Quant.
3	 **3e**	 **5e**	Crystallisation: PE	Quant.
4	 **3f**	 **5f**	Chromatography: PE/AcOEt 9:1	Quant. *cis/trans* mixture 65:35
5	 **3g**	 **5g**	Crystallisation: PE	Quant.

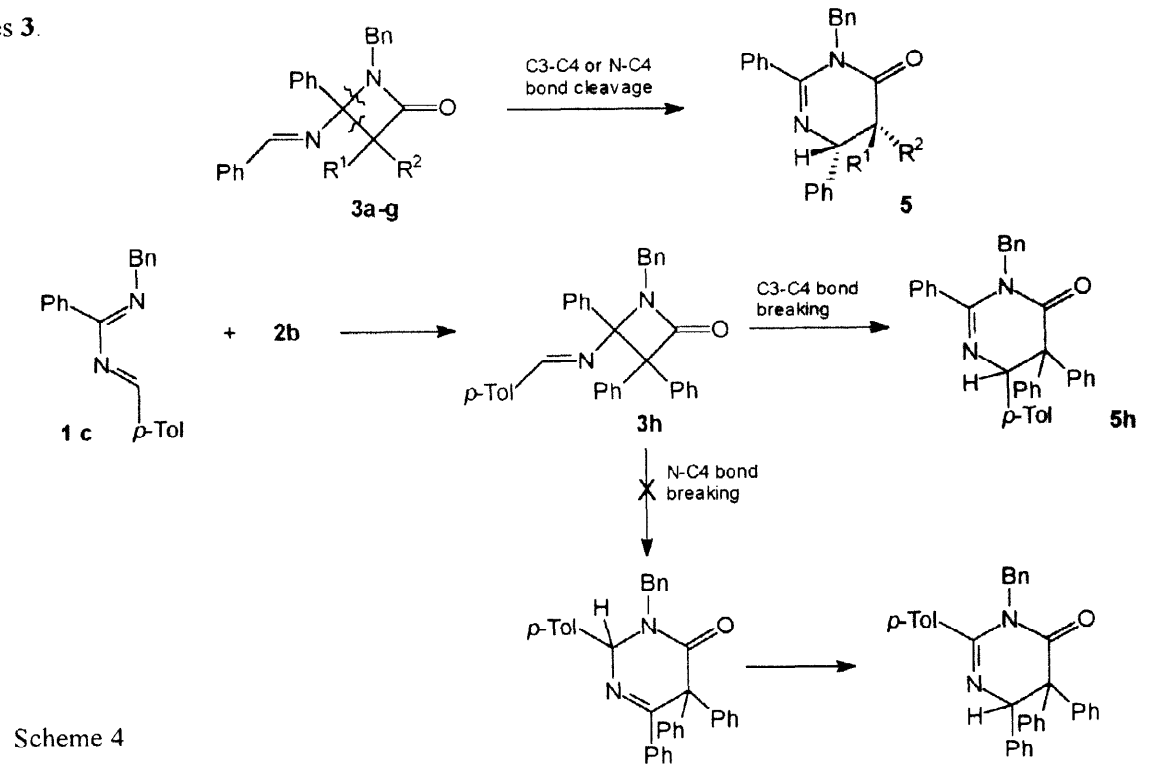
PE = petroleum ether

It is known[4] that thermal and photochemical cleavage of the azetidin-2-one ring may follow two different pathways A and B giving rise to alkenes and isocyanates or ketenes and imines (Scheme 3). It was also reported that photolysis favours path A and thermolysis path B and in many cases the isocyanate and/or ketene products were trapped as urea and/or carbamate by reaction with amine or alcohol.[5] Through these cycloreversion reactions the azetidin-2-ones **3** could regenerate the starting compounds **1** and **2** or give benzylisocyanate **7** and the 2-azabutadiene **8**; consequently [4+2] cycloaddition reaction could afford the pyrimidin-4-ones **5** (Scheme 3). However all attempts to detect ureic or carbamic derivatives in the thermal and photochemical reactions of azetidin-2-ones **3** performed in the presence of diethylamine, dipropylamine or methanol failed, and pyrimidin-6-ones **5** were the sole isolable products.



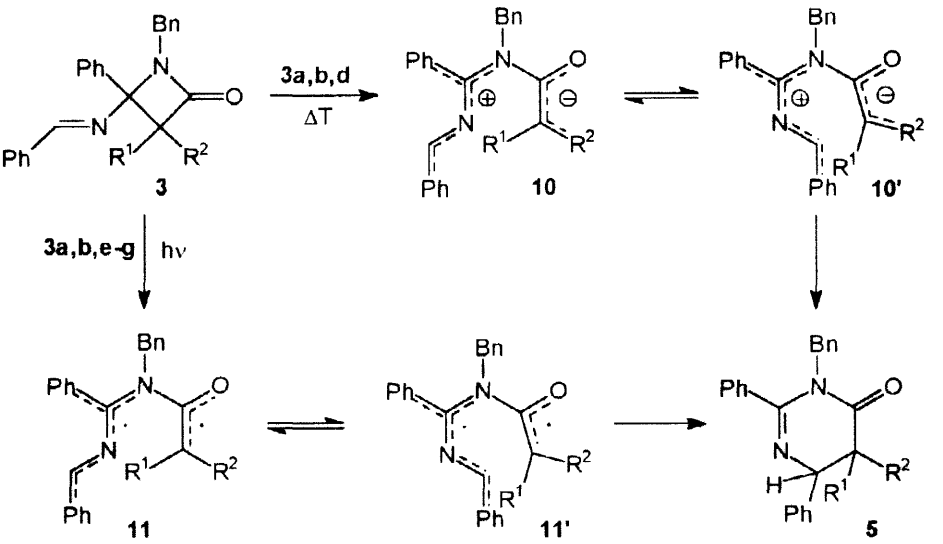
Scheme 3

More probably a stepwise ionic or radical mechanism was involved in the ring enlargement. Some examples of reactions involving cleavage of N-C4[6] or C3-C4[7] bonds and rearrangement of a polar intermediate are reported in the literature, although few of these involve vinyl or azomethine substituted azetidin-2-ones.[8] Starting from azetidin-2-ones **3**, cleavage of either N-C4 or C3-C4 bond followed by ring closure gave pyrimidin-4-ones **5** (Scheme 4). First, in order to determine which bond was cleaved in the ring expansion, we performed thermal and photochemical reactions with the azetidin-2-one **3h**, which was obtained in the usual way by reaction of 1-benzyl-2-phenyl-4-*p*-tolyl-1,3-diazabuta-1,3-diene **1c** with diphenylketene **2b**. As depicted in Scheme 4, the pyrimidin-4-one **5h** was isolated in quantitative yield in both photochemical and thermal reactions and this demonstrates that the ring enlargement proceeds by breaking of the C3-C4 bond of azetidin-2-ones **3**.



Scheme 4

We can reasonably postulate that in both ionic and radical mechanisms the driving force for the ring opening reactions of azetidin-2-ones **3** is the formation of a highly stabilised 2-aza-allyl cation or radical intermediate, which can exist in two forms **10/10'** and **11/11'**, respectively, with a small barrier for the rotation about the C-N bond (ΔH ca. 13-21 kJ/mole) (Scheme 5). Thus, probably the mechanism of the thermolysis is essentially the inverse of the two-step [2+2] cycloaddition described in Scheme 1, which occurs only when the anionic centre of the zwitterionic intermediate **10/10'** is stabilised by resonance within an adjacent unsaturated system (azetidin-2-ones **3a,b,d**). This hypothesis also accounts for the formation of diazaoctadienone **6** from **3d** by cyclization between the terminal carbon atom of the vinylic system and the imine moiety. Instead the diradical **11/11'** is involved in the photolytic reactions, in which azetidin-2-ones **3a,b,e,f,g** gave pyrimidin-4-ones **5** in high yields whereas **3c,d** gave more complex reaction mixtures. The behaviour of compounds **3c,d** could be explained by competitive hydrogen atom abstraction at C-3 giving rise to the formation of a number of side products and could account also for the lower yield of dihydropyrimidin-4-one **5b** observed for **3a**, such reaction being negligible for 3-methoxy substituted azetidin-2-one **3f**. The behaviour[9] of **3f** compared to **3a,c,d** could be related to the C3-H bond dissociation energy[10], to the thermochemical stabilization energy of the radical center[11] and also to the opposite character, nucleophilic for **3f** and electrophilic for **3a,c,d**, of the forming radicals[12].



Scheme 5

EXPERIMENTAL

All chemicals and solvents are commercially available and were used after distillation or treatment with drying agents. Photochemical reactions were performed with a high pressure mercury vapour lamp Philips HPK 125 watt. Merck silica gel 60 F_{254} thin-layer plates were employed for thin layer chromatography. Merck silica gel (230-400 mesh) was employed for flash column chromatography. Melting points, measured with a Büchi or a Stuart Scientific SMP3 apparatus, are uncorrected. Infrared spectra were recorded on a FT-IR Perkin Elmer 16

PC spectrophotometer, using KCl disks or KBr tablets. ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50.3 MHz) spectra were recorded in $CDCl_3$, with a Varian-Gemini 200 spectrometer.
1-Benzyl-2,4-diphenyl-1,3-diaza-1,3-butadiene **1b** is a known compound.[1] 1-Benzyl-2-phenyl-4-*p*-tolyl-1,3-diaza-1,3-butadiene **1c** is new and was prepared as reported in Ref.1.
PE = petroleum ether; TEA = triethylamine

1c: purified by flash chromatography (PE/TEA 95:5); white solid; m.p. 95-98°C (*i*-Pr_2O); yield 35%; ^{1}H-NMR ($CDCl_3$, δ, Hz): 2.46 (s, 3H, CH_3), 4.63 (s, 2H, CH_2), 7.22-7.43 (m, 10H, arom.), 7.79 (d, 2H, arom. *p*-tolyl, J 8.1), 7.86-7.91 (dd, 2H, arom.), 8.16 (s, 1H, CH); ^{13}C-NMR ($CDCl_3$, δ): 22.2 (CH_3), 53.7 (CH_2), 126.9, 128.2, 128.3, 128.7, 128.8, 129.5, 130.2, 130.7 (CH arom.), 132.9, 136.5, 141.8, 143.6 (C arom.), 162.3 (CH), 164.5 (N=C-N); IR (KBr, cm^{-1}): 1574, 1606, 1638 (ν C=N and ν C=C); elem. anal., found (calcd for $C_{22}H_{20}N_2$): C 84.21 (84.58) H 6.27 (6.45) N 8.58 (8.97).

Azetidinones **3a-c**[1] and ketenes **2a-h**[13] are known compounds and were prepared according to described methods. Azetidinones **3d-h** are new and were prepared by the method reported in Ref. 1 (time of reaction 3-48 h).

3d: purified by flash chromatography (PE/EtOAc 9:1); white solid; m.p. 107-108°C (*i*-Pr_2O); yield 78%; ^{1}H-NMR ($CDCl_3$, δ, Hz): Second order system: 3.84 (m, 1H, H<u>C</u>-CH=CH_2), 3.92 and 4.94 (AX system, 2H, CH_2, J 15.1), 5.10 (m, 1H, HC-CH=C<u>H</u>$_2$), 5.26-5.52 (m, 2H, HC-C<u>H</u>=C<u>H</u>$_2$) 7.27-7.60 (m, 15H, arom.), 7.95 (s, 1H, Ph-CH=N); ^{13}C-NMR ($CDCl_3$, δ): 45.5 (CH_2), 69.8 (H<u>C</u>-CH=CH_2), 87.1 (N-C-N), 121.1 (HC-CH=<u>C</u>H$_2$) 128.2, 128.7, 128.9, 129.0, 129.1, 129.2, 129.3, 129.6, 129.8, 131.8 (CH arom. and HC-<u>C</u>H=CH_2), 135.9, 137.4, 137.5 (C arom.), 158.7 (Ph-CH=N), 168.7 (C=O); IR (KBr, cm^{-1}): 1648 (ν C=N), 1756 (ν C=O); elem. anal., found (calcd for $C_{25}H_{22}N_2O$): C 81.88 (81.94) H 6.08 (6.05) N 7.54 (7.64).

3e: purified by flash chromatography (PE/EtOAc 9:1); white solid; m.p. 115°C (PE); yield 54%; ^{1}H-NMR ($CDCl_3$, δ, Hz): 0.96 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 3.88 and 5.02 (AX system, 2H, CH_2, J 15.2), 7.26-7.48 (m, 13H, arom.), 7.61-7.65 (dd, 2H, arom.), 7.74 (s, 1H, Ph-CH=N); ^{13}C-NMR ($CDCl_3$, δ): 19.9 (CH_3), 20.5 (CH_3), 45.5 (CH_2), 62.5 (CH_3-<u>C</u>-CH_3), 90.7 (N-C-N), 128.2, 128.6, 128.7, 128.8, 128.9, 129.0, 129.4, 129.6, 131.6 (CH arom.), 136.0, 138.2, 139.3 (C arom.), 158.8 (Ph-CH=N), 175.8 (C=O); IR (KBr, cm^{-1}): 1648 (ν C=N), 1748 (ν C=O); elem. anal., found (calcd for $C_{25}H_{24}N_2O$): C 81.24 (81.49) H 6.38 (6.46) N 7.40 (7.60).

3f: purified by flash chromatography (PE/TEA 9:1); white solid; m.p. 111°C (PE); yield 73%; ^{1}H-NMR ($CDCl_3$, δ, Hz): 3.12 (s, 3H, OCH_3), 3.75 and 4.84 (AX system, 2H, CH_2, J 14.9), 4.22 (s, 1H, CH_3O-C<u>H</u>-C=O), 7.26-7.53 (m, 13H, arom.), 7.69-7.71 (dd, 2H, arom.), 7.82 (s, 1H, Ph-CH=N); ^{13}C-NMR ($CDCl_3$, δ): 45.0 (CH_2), 58.8 (CH_3O), 88.3 (N-C-N), 95.7 (CH_3O-<u>C</u>H-C=O), 128.3, 128.7, 129.0, 129.1, 129.1, 129.2, 129.3, 129.8, 131.9 (CH arom.), 135.8, 135.9, 137.1 (C arom.), 159.1 (Ph-CH=N), 167.1 (C=O); IR (KBr, cm^{-1}): 1650 (ν C=N), 1756 (ν C=O); elem. anal., found (calcd for $C_{24}H_{22}N_2O_2$): C 77.54 (77.81) H 5.85 (5.99) N 7.38 (7.56).

3g: purified by flash chromatography (PE/TEA 9:1); white solid; m.p. 158-159°C (*i*-Pr_2O/AcOEt); yield 65%; ^{1}H-NMR ($CDCl_3$, δ, Hz): 3.94 and 5.04 (AX system, 2H, CH_2, J 15.0), 7.31-7.56 (m, 13H, arom.), 7.71-7.76 (dd, 2H, arom.), 7.73 (s, 1H, Ph-CH=N); ^{13}C-NMR ($CDCl_3$, δ): 46.5 (CH_2), 92.7 (N-C-N), 94.0 (Cl-C-Cl), 128.9, 129.0, 129.1, 129.5, 129.6, 129.7, 129.8, 130.2, 132.5 (CH arom.), 135.1, 135.8, 136.2 (C arom.), 162.5 (Ph-CH=N), 163.5 (C=O); IR (KBr, cm^{-1}): 1652 (ν C=N), 1774 (ν C=O); elem. anal., found (calcd for $C_{23}H_{18}N_2OCl_2$): C 67.35 (67.49) H 4.32 (4.43) N 6.65 (6.84).

3h: purified by flash chromatography (PE/AcOEt 95:5); white solid; m.p. 139-141°C (PE/AcOEt); yield 65%; ^{1}H-NMR ($CDCl_3$, δ, Hz): 2.32 (s, 3H, CH_3) 3.66 and 5.00 (AX system, 2H, CH_2, J 14.9), 7.01-7.51 (m, 24H, arom. and 1H, Ph-CH=N); ^{13}C-NMR ($CDCl_3$, δ): 22.0 (CH_3), 45.6 (CH_2), 80.4 (Ph-C-Ph), 90.7 (N-C-N),

126.6, 127.0, 128.1, 128.3, 128.4, 128.6, 128.7, 128.8, 129.1, 129.4, 129.4, 129.7, 139.8, 129.9 (CH arom.), 133.3, 137.7, 139.0, 139.2, 139.4, 141.7 (C arom.), 159.4 (Ph-CH=N), 171.3 (C=O); IR (KBr, cm^{-1}) 1648 (ν C=N), 1754 (ν C=O); elem. anal., found (calcd for $C_{36}H_{30}N_2O$): C 85.12 (85.34) H 5.85 (5.97) N 5.38 (5.53).

Thermal behaviour of azetidinones 3:

Method A: A solution of pure azetidinone **3a-h** (1 mmol) in dry toluene (15-20 ml) was heated under reflux for 5-30 h. The crude reaction mixtures were purified by crystallization, or by flash chromatography when more than one product was detected by tlc. For reaction products, yields and purification data see table 1.

Method B: A solution of appropriate acyl chloride (1.1 mmol) in dry toluene (8 ml) was added slowly (over a period of 1h) to a nitrogen flushed, well stirred and ice-water cooled solution of 1,3-diaza-1,3-butadiene **1b** (1.0 mmol) and triethylamine (1.0 mmol) in dry toluene (14 ml). The reaction mixture was initially stirred at room temperature and heated under reflux (22-48 h) when tlc analysis shown the disappearance of **1b** and the formation of **3**. It was then washed with a saturated solution of $NaHCO_3$ (3 x 15 ml) and the organic layer, dried over anhydrous sodium sulphate, was freed from solvent under reduced pressure at 40°C. The crude products were purified by flash chromatography over silica gel column followed by crystallisation. For reaction products, yields and purification data see Table 1.

Photochemical behaviour of azetidinones 3:

In a quartz test-tube 30 mg of azetidinones **3a-h** were dissolved in 3 ml of acetone. The solutions were irradiated with a mercury vapour lamp for 8-12 h and the crude purified by crystallisation or by flash chromatography when more than one product was detectable by tlc. For reaction products, yields and purification data see Table 2.

5b trans: white solid; m.p. 169-170°C (*i*-Pr_2O); ^{1}H-NMR ($CDCl_3$, δ, Hz): 4.02 and 5.17 (AX system, 2H, CH-CH, J_{trans} 8.3), 4.85 and 4.98 (AB system, 2H, CH_2, J_{gem} 15.5), 6.83 (dd, 2H, arom.), 7.08-7.48 (m, 18H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 47.8 (CH_2), 53.9 (Ph-CH-C=O), 63.9 (Ph-CH-N), 127.7, 127.8, 128.0, 128.1, 128.3, 128.6, 128.9, 128.9, 129.0, 129.1, 129.2, 130.5 (CH arom.), 135.5, 136.8, 137.5, 140.5 (C arom.), 157.0 (N-C=N), 171.3 (C=O); IR (KBr, cm^{-1}): 1644 (ν C=N), 1698 (ν C=O); elem. anal., found (calcd for $C_{29}H_{24}N_2O$): C 83.42 (83.63) H 5.75 (5.81) N 6.60 (6.73).

5b cis: yellowish oil; ^{1}H-NMR ($CDCl_3$, δ, Hz): 4.25 and 5.25 (AX system, 2H, CH-CH, J_{cis} 5.6), 4.68 and 5.32 (AX system, 2H, CH_2, J_{gem} 15.1), 6.90-7.00 (m, 2H, arom.), 7.10-7.49 (m, 18H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 47.7 (CH_2), 53.1 (Ph-CH-C=O), 62.4 (Ph-CH-N), 127.6, 128.0, 128.1, 128.2, 128.6, 128.7, 128.9, 129.0, 129.1, 129.2, 129.8, 130.7 (CH arom.), 133.5, 135.3, 137.7, 138.9 (C arom.), 157.1 (N-C=N), 171.7 (C=O); IR (neat, cm^{-1}): 1636 (ν C=N), 1696 (ν C=O); elem. anal., found (calcd for $C_{29}H_{24}N_2O$): C 83.98 (83.63) H 5.94 (5.81) N 6.95 (6.73).

5c: white solid; m.p. 170-171°C (PE); ^{1}H-NMR ($CDCl_3$, δ, Hz): 4.63 and 5.13 (AX system, 2H, CH_2, J 14.8), 5.60 (s, 1H, Ph-CH-N), 6.54 (dd, 2H, arom.), 6.73 (dd, 2H, arom.) 6.87-7.14 (m, 10H, arom.), 7.19-7.46 (m, 9H, arom.), 7.61 (dd, 2H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 48.4 (CH_2), 61.0 (Ph-C-Ph), 67.9 (Ph-CH-N), 126.8, 127.4, 127.9, 128.1, 128.3, 128.4, 128.8, 128.8, 128.9, 128.9, 129.1, 129.1, 129.6, 130.2, 130.9 (CH arom.), 135.8, 136.4, 137.2, 140.7, 141.2 (C arom.), 156.0 (N-C=N), 172.0 (C=O); IR (KBr, cm^{-1}): 1662 (ν C=N), 1693 (ν C=O); elem. anal., found (calcd for $C_{35}H_{28}N_2O$): C 85.45 (85.34) H 5.75 (5.73) N 5.70 (5.69).

5d: pale yellow oil; ^{1}H-NMR ($CDCl_3$, δ, Hz): 3.49 (t, 1H, O=C-CH-C=, J_{vic} 7.8), 4.86 (d, 1H, Ph-CH-C, J_{vic} 7.9), 4.87 (s, 2H, Ph-CH_2), 5.12 (dt, 1H, HC=CH_2, J_{trans} 17.1, J_{all} = J_{gem} 1.2), 5.22 (dt, 1H, HC=CH_2, J_{cis} 10.4, J_{all} = J_{gem} 1.1), 5.89 (ddd, 1H, HC=CH_2, J_{trans} 17.1, J_{cis} 10.3, J_{vic} 7.7), 6.78 (dd, 2H, arom.), 6.97-7.46 (m, 13H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 47.5 (Ph-CH_2), 51.9 (CO-CH-C=), 62.6 (Ph-CH-C), 120.3 (HC=CH_2), 126.5 (HC=CH_2), 127.8, 127.9, 128.0, 128.3, 128.9, 129.0, 129.4, 130.6, 132.7, (CH arom.), 136.3, 137.4, 140.2, (C arom.), 157.0 (N-C=N), 171.2 (C=O); IR (neat, cm^{-1}): 1643 (ν C=N), 1697 (ν C=O); elem. anal., found (calcd for $C_{25}H_{22}N_2O$): C 82.15 (81.94) H 6.27 (6.05) N 7.88 (7.64).

5'd: pale yellow solid; m.p. 96-97°C (*i*-Pr_2O); ^{1}H-NMR ($CDCl_3$, δ, Hz): 1.95 (d, 1H, CH_3, J_{vic} 7.3), 4.33 and 5.33 (AX system, 2H, Ph-C$\underline{H}_2$, J 15.3), 5.97 (s, 1H, Ph-C$\underline{H}$-N), 6.49 (dd, 1H, arom.), 6.91-7.10 (m, 3H, arom.), 7.18 (dq, 1H, C=C$\underline{H}$-CH_3, J_{vic} 7.3, J_{all} 1.3), 7.27-7.43 (m, 10H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 14.3 (CH_3), 47.8 (CH_2), 57.9 (Ph-CH-N), 127.1, 127.5, 127.8, 128.4, 128.5, 128.6, 128.8, 129.1, 130.3 (CH arom.), 130.8, 135.7, 137.3 (C arom.), 138.7 (CH_3-$\underline{C}$H=C), 140.6 (CH_3-CH=$\underline{C}$), 156.3 (N-C=N), 165.6 (C=O); IR (KBr, cm^{-1}): 1654 (ν C=N), 1684 (ν C=O); elem. anal., found (calcd for $C_{25}H_{22}N_2O$): C 81.98 (81.94) H 5.92 (6.05) N 7.50 (7.64).

5e: pale yellow solid; m.p. 155-159°C (PE); ^{1}H-NMR ($CDCl_3$, δ, Hz): 1.06 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 4.56 and 5.14 (AX system, 2H, CH_2, J 14.8), 4.59 (s, 1H, Ph-CH-N), 6.96 (dd, 2H, arom.), 7.17-7.50 (m, 13H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 18.6 (CH_3), 23.7 (CH_3), 41.6 (CH_3-$\underline{C}$-CH_3), 47.8 (CH_2), 68.1 (Ph-CH-N), 127.8, 127.9, 128.0, 128.3, 128.4, 128.5, 128.9, 129.5, 130.3, (CH arom.), 135.6, 137.8, 138.7, (C arom.), 156.5 (N-C=N), 176.8 (C=O); IR (KBr, cm^{-1}): 1640 (ν C=N), 1696 (ν C=O); elem. anal., found (calcd for $C_{25}H_{24}N_2O$): C 81.71 (81.49) H 6.58 (6.46) N 7.58 (7.60).

5f trans: white solid; m.p. 128-130°C (PE); ^{1}H-NMR ($CDCl_3$, δ, Hz): 3.45 (s, 3H, OCH_3), 3.89 and 4.80 (AX system, 2H, CH-CH, J_{trans} 10.3), 4.60 and 5.13 (AX system, 2H, CH_2, J_{gem} 14.8), 6.87 (dd, 2H, arom.), 7.18-7.45 (m, 13H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 47.6 (CH_2), 60.4 (CH_3O), 63.1 (Ph-CH-N), 79.8 (CH_3O-$\underline{C}$H), 128.0, 128.1, 128.1, 128.2, 128.7, 128.8, 128.9, 129.0, 130.6, (CH arom.), 135.0, 137.2, 139.2, (C arom.), 156.2 (N-C=N), 170.7 (C=O); IR (KBr, cm^{-1}): 1636 (ν C=N), 1704 (ν C=O); elem. anal., found (calcd for $C_{24}H_{22}N_2O_2$): C 77.90 (77.81) H 5.90 (5.99) N 7.58 (7.56).

5f cis: white solid; m.p. 130-132°C (PE); ^{1}H-NMR ($CDCl_3$, δ, Hz): 3.51 (s, 3H, OCH_3), 4.14 and 5.02 (AX system, 2H, CH-CH, J_{cis} 4.5), 4.81 and 4.91 (AB system, 2H, CH_2, J_{gem} 15.3), 6.80 (dd, 2H, arom.), 7.14-7.44 (m, 13H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 47.5 (CH_2), 59.9 (CH_3O), 61.2 (Ph-CH-N), 79.0 (CH_3O-$\underline{C}$H-C=O), 127.9, 128.0, 128.1, 128.2, 128.4, 128.7, 128.8, 128.9, 130.5, (CH arom.), 135.0, 137.2, 139.2, (C arom.), 156.2 (N-C=N), 170.7 (C=O); IR (KBr, cm^{-1}): 1660 (ν C=N), 1696 (ν C=O); elem. anal., found (calcd for $C_{24}H_{22}N_2O_2$): C 77.56 (77.81) H 5.81 (5.99) N 7.44 (7.56).

5g: white solid; m.p. 186-189°C (PE); ^{1}H-NMR ($CDCl_3$, δ, Hz): 5.30 (s, 2H, CH_2), 6.97-7.02 (m, 2H arom.), 7.22-7.54 (m, 11H, arom.), 7.86-7.91 (m, 2H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 50.7 (CH_2), 119.5 (Cl-$\underline{C}$), 127.9, 128.3, 128.5, 128.7, 129.1, 129.2, 129.9, 130.4, 130.8 (CH arom.), 134.8, 136.2, 136.6, (C arom.), 157.5 (Ph-C-N), 158.0 (N-C=N), 160.4 (C=O); IR (KBr, cm^{-1}): 1662 (ν C=O); elem. anal., found (calcd for $C_{23}H_{17}N_2OCl$): C 73.95 (74.09) H 4.50 (4.60) N 7.48 (7.51).

5h: purified by flash chromatography (PE/AcOEt 95:5); white solid; m.p. 180-182°C (PE/AcOEt); ^{1}H-NMR ($CDCl_3$, δ, Hz): 2.24 (s, 3H, CH_3), 4.62 and 5.13 (AX system, 2H, CH_2, J 15.3), 5.58 (s, 1H, CH), 6.44 (d, 2H, *p*-Tolyl J 8.1), 6.71-7.50 (m, 20H, arom.), 759-7.62 (m, 2H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 21.5 (CH_3), 48.3 (CH_2), 60.9 (Ph-C-Ph), 67.5 (*p*-Tol-CH-N), 126.8, 127.4, 128.1, 128.1, 128.3, 128.8, 128.8, 128.9, 129.0, 129.0, 129.1, 129.5, 130.2, 131.0 (CH arom.), 133.2, 135.8, 137.2, 147.5, 140.7, 141.2 (C arom.), 155.9 (N-$\underline{C}$=N), 172.1 (C=O); IR (KBr, cm^{-1}): 1646 (ν C=N), 1694 (ν C=O); elem. anal., found (calcd for $C_{36}H_{30}N_2O$): C 85.05 (85.34) H 5.80 (5.97) N 5.32 (5.53).

6: pale yellow oil; ^{1}H-NMR ($CDCl_3$, δ, Hz): 2.75 (m, 2H, CH-C$\underline{H}_2$-CH=), 4.51 and 4.70 (AX system, 2H, Ph-C$\underline{H}_2$-, J_{gem} 17.4), 4.84 (dd, 1H, N-C$\underline{H}$Ph-CH_2-, J_{vic} 8.8, 7.3), 6.28 (dt, 1H, O=C-C$\underline{H}$=CH, J_{vic} 9.9, J_{all} 1.8), 6.83 (dt, 1H, CH_2-C$\underline{H}$=CH, J_{vic} 9.9, 4.3), 6.91 (dd, 2H, arom.),7.09 (t, 2H arom.), 7.12-7.45 (m, 11H, arom.); ^{13}C-NMR ($CDCl_3$, δ): 33.0 (CH-$\underline{C}H_2$-CH=), 56.1 (Ph-CH_2), 61.1 (N-$\underline{C}$HPh-CH_2), 125.4, 126.9, 127.6, 128.0, 128.3, 128.4, 128.6, 128.8, 129.0, 130.5, 141.0, (C_{sp2}-H), 136.2, 139.3, 140.7 (C arom.), 152.2 (N-C=N), 163.0 (C=O); IR (neat, cm^{-1}): 1613, 1643 (ν C=N), 1684 (ν C=O); elem. anal., found (calcd for $C_{25}H_{22}N_2O$): C 82.30 (81.94) H 6.32 (6.05) N 7.91 (7.64); ^{1}H-^{1}H COSY crosspeaks: H-5/H-6, H-5/H-7, H-6/H-7, H-7/H-8.

REFERENCES

1. Rossi, E.; Abbiati, G.; Pini, E. *Tetrahedron* **1997**, 41, 14107-14114.
2. Cho, H.; Ueda, M.; Ohnaka, Y.; Hayashimatsu, M. *Heterocycles* **1984**, 1959-1963.
   Veale, C. A.; Steelman, G. B.; Chow, M. M. J. *Org. Chem.* **1993**, 4490-4493.
3. In ref 1 we erroneously assigned a *cis* configuration to 5,6 dihydro-3*H*-pyrimidin-4-ones **4a,c,d** using the Karplus equation. The mistake was related to a wrong detection of the dihedral angle between H-5 and H-6.
4. Mukerjee, A. K.; Singh, A. K. *Synthesis* **1975**, 547-589 (pp 586-587).
   Mukerjee, A. K.; Singh, A. K. *Tetrahedron* **1978**, 34, 1731-1767 (p 1761).
   Davies, D. E.; Storr, R. C. In *Comprehensive Heterocyclic Chemistry*, Katritzky, A.R.; Rees, C.W. Eds.; Pergamon Press: New York, **1984**; Vol. 6, p 249-250.
5. Van Leusen, A. M.; Arens, J. F. *Rec. Trav. Chim. Pays-Bas* **1959**, 78, 551-557.
   Fischer, M. *Chem. Ber.* **1968**, 101, 2669-2678.
   Paquette, L. A.; Wyvratt, M. J.; Allen, G. R. Jr. J. *Am. Chem. Soc.* **1970**, 92, 1763-1765.
6. Mukerjee, A. K.; Singh, A. K. *Synthesis* **1975**, 547-589 (pp 583-584).
   Mukerjee, A. K.; Singh, A. K. *Tetrahedron* **1978**, 34, 1731-1767 (pp 1760-1761).
   Moriconi, E. J.; Jalandoni, C. C. J. *Org. Chem.* **1970**, 35, 3796-3800.
   Effenberger, F.; Fischer, P.; Prossel, G.; Kiefer, G. *Chem. Ber.* **1971**, 104, 1987-2001.
   Barton, T. J.; Rogido, R. J. *Tetrahedron Lett.* **1972**, 37, 3901-3902.
   Barton, T. J.; Rogido, R. J. J. *Chem. Soc., Chem. Commun.* **1972**, 878-879.
   Effenberger, F.; Gerlach, O. *Chem. Ber.* **1974**, 107, 278-298.
7. Mukerjee, A. K.; Singh, A. K. *Synthesis* **1975**, 547-589 (p 583).
   Mukerjee, A. K.; Singh, A. K. *Tetrahedron* **1978**, 34, 1731-1767 (pp 1759-1760).
   Bird, C. W. *Tetrahedron* **1966**, 22, 2489-2491.
   Bose, A. K.; Kugajevsky, I. *Tetrahedron* **1967**, 23, 957-963.
8. Bormann, D. *Angew. Chem. Int. Ed.* **1969**, 8, 892.
   Schabel, H. *Angew. Chem. Int. Ed.* **1969**, 8, 922.
   Bird, C. W.; Twibell, J. D. J. *Chem. Soc. [C]* **1971**, 3155-3158.
   Moriconi, E. J.; Meyer, W. C. J. *Org. Chem.* **1971**, 36, 2841-2849.
   Millership, J. S.; Suschitzky, H. J. *Chem. Soc., Chem. Commun.* **1971**, 1496.
   Barr, J. J.; Storr, R. C. J. *Chem. Soc., Chem. Commun.* **1975**, 788-789.
9. For a general discussion on substituent effects in radical reactions see:
   Carey, F. A.; Sundberg, R. J. In *Advanced Organic Chemistry*, 3rd Ed., Plenum Press, **1990**, Part A, p 674-688.
   Davis, W. H.; Pryor, W. A. *J. Am. Chem. Soc.* **1977**, 99, 6365-6372.
   Davis, W. H.; Gleason, J. H.; Pryor, W. A. *J. Org. Chem.* **1977**, 42, 7-12.
   Pryor, W. A.; Gojon, G.; Church, D. F. *J. Org. Chem.* **1978**, 43, 793-800.
10. Kerr, J. A. *Chem. Rev.* **1966**, 66, 465-499.
    Cao, J. R.; Back, M. H. *Int. J. Chem. Kinet.* **1984**, 16, 961-966.
    Holmes, J. L.; Lossing, F. P. *J. Am. Chem. Soc.* **1988**, 110, 7343-7345.
11. Leroy, C.; Peeters, D.; Wilante, C. *Theochem* **1982**, 5, 217-233.
12. Giese, B. *Angew. Chem: Int. Ed. Eng.* **1983**, 22, 753-764.
    Giese, B.; Horler, H.; Leising, M. *Chem. Ber.* **1986**, 119, 444-452.
13. Luknitskii, F. I.; Vovsi, B. A. *Russian Chem. Rev.* **1969**, 38, 487-494.