Photoreaction of 2-morpholinoacrylonitrile with substituted 1-acetonaphthones. Part II†

Hamid R. Memarian,*[a] Masoud Nasr-Esfahani[a] and Dietrich Döpp[b]

[a] *Department of Chemistry, Faculty of Sciences, University of Esfahan, 81744 Esfahan, Iran. Fax +98 (31) 689 732*

[b] *Institut für Synthesechemie, Gerhard-Mercator-Universität-GH-Duisburg, D-47048 Duisburg, Germany. Fax +49 (203) 379 4192*

Received (in Montpellier, France) 16th August 2000, Accepted 4th December 2000
First published as an Advance Article on the web 7th February 2001

Photochemical reactions of substituted 1-acetonaphthones in the presence of 2-morpholinoacrylonitrile were investigated. The type of reaction, photocycloaddition *vs.* photosubstitution, is dependent on the nature of the additional substituent. The location of the additional substituent on the ring also affects the type of addition, [2 + 2] *vs.* [4 + 2].

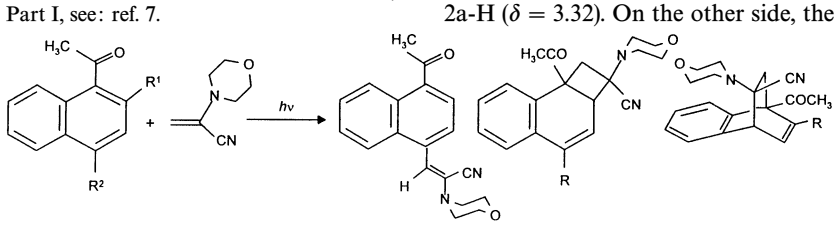
In the course of our studies on the photochemical behaviour of acylnaphthalenes,[1–6] especially substituted 1-acetonaphthones **1b–e**,[7] towards captodative alkenes,[8] especially 2-morpholinoacrylonitrile, **2**, we investigated the photochemical reactions of further substituted 1-acetonaphthones. Our earlier studies showed the occurrence of two types of reactions: *photosubstitution* and *photoaddition*, which is dependent on the nature of the additional substituent on the naphthalene ring of 1-acetonaphthone. Our earlier results also indicated that the type of addition, [2 + 2] *vs.* [4 + 2], is dependent on the location of the additional substituent on the ring.[7] Only in the case of the 4-bromo derivative **1b**, has photosubstitution of bromine been observed.[7] In continuation of this work, we prepared 4-chloro-, 4-fluoro-, 4-methyl- and 2-methylsubstituted 1-acetonaphthones **1f–i**, respectively, and investigated their photochemical behaviour in the presence of **2**, to ascertain the effect of an additional substituent on the type of reaction.

Results and discussion

Irradiation ($\lambda \geqslant 280$ nm) of equimolar solutions of ketones **1f–i** with **2** resulted in the occurrence of one or both reactions, depending on the type of substituent. Whereas in the cases of 4-chloro **1f** only photosubstitution and 4-fluoro **1g** both reactions were observed, irradiation of 4-methyl **1h** and 2-methyl **1i** derivatives in the presence of **2** resulted in the addition of **2** to the naphthalene skeleton of **1h** and **1i**. IR, ^{1}H NMR and UV data gave useful information for the structural assignment of the photoproducts. Characterization of the photosubstitution product **3** in the case of **1f** and **1g** was achieved by comparison of its physical and spectroscopic data with those of **3** obtained upon irradiation of the 4-bromo derivative **1b** in the presence of **2**.[7] Irradiation of a mixture of **1g** and **1i** with **2** causes the formation of [2 + 2]-cycloadducts **4d** and **4e**, respectively. ^{1}H NMR spectra of **4d** and **4e** showed the resonance of an acetyl group at 2.04 and 1.99 ppm, respectively, which indicates the attachment of this group to the cyclobutane ring.[4,7] This observation is also supported by comparison of the ^{1}H NMR data of **4d** and **4e** with those of **4a–c**, which are summarized in Table 1. The UV spectra (in chloroform solution) exhibit intense (lg $\varepsilon = 3.73$ and 3.52) absorptions at 276 nm for **4d** and **4e**, respectively, consistent with 1,2-adducts with styrene-type conjugation of the benzoid ring and a residual double bond.

The *exo* orientation of the morpholino group was confirmed by exact analysis of the 500 MHz ^{1}H NMR spectrum of compound **4d**. The 1-CH_2 protons form an AX pattern with $\delta_A = 3.28$ (*endo*-1-H), $\delta_X = 2.67$ (*exo*-1-H) and a geminal coupling of 12.17 Hz, the high-field portion of which is additionally split by 0.73 Hz due to a long range (W type) interaction with 2a-H ($\delta = 3.32$). On the other side, the anisotropic effect of the

† Taken in part from the doctoral thesis work of M. Nasr-Esfahani, University of Esfahan. For Part I, see: ref. 7.



1	R^1	R^2
a	H	H
b	H	Br
c	H	CN
d	H	OCH_3
e	OCH_3	H
f	H	Cl
g	H	F
h	H	CH_3
i	CH_3	H

4	R
a	H
b	CN
c	OCH_3
d	F
e	CH_3

5	R
a	H
b	OCH_3
c	CH_3

 DOI: 10.1039/b006835g

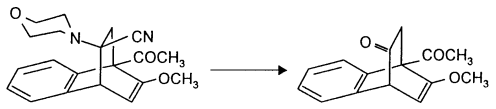
Table 1 Structurally relevant ^{1}H NMR chemical shifts (δ values) and ^{1}H, ^{1}H coupling J (Hz) of **4d** and **4e** in comparison with **4a**, **4b** and **4c**

	CH_3CO	2a-H	3-H	4-H	$J_{2a\text{-}3}$
4a	2.01	3.24	5.67	6.73	5.7
4b	2.00	3.40	6.59	—	6.15
4c	2.00	3.30	4.74	—	6.41
4d	2.04	3.32	5.36	—	6.30
4e	1.99	3.24	5.62	—	5.61

cyano group *cis* to the *endo*-1-H causes a deshielding effect on this proton, which consequently shows this signal at a lower field in comparison to the *exo*-1-H, which is *cis* to the morpholino group. A four-spin system was also observed for 2a-H, 3-H, 4-F and 1-H_{exo}. The resonance for 2a-H shows a vicinal coupling of 6.30 Hz with 3-H, coupling with 4-F (4.73 Hz) and long-range coupling with 1-H_{exo} (0.73 Hz). These data indicate that the X part of the AX system at higher field is *cis* to the morpholino group, which displays an *exo* orientation of the morpholino group. Such an orientation has also been observed earlier in the case of **4c** by an X-ray crystal structure analysis as well as by an NOE signal intensity difference determination for **4b**.[7]

The formation of the [4 + 2]-cycloadduct **5c** was observed upon irradiation of a mixture of **1i** and **2**. Since the structures of **5a** and **5b** have been unambiguously determined an earlier from X-ray structural analysis[1] and by a NOE signal intensity difference determination experiment,[7] respectively, the assignment for **5c** was based on comparison of its ^{1}H chemical shifts and couplings with those obtained for **5a** and **5b** (Table 2) and on its UV spectrum. The resonance of the CH_3CO group at 2.53 ppm, compared with the same resonance for **5a** and **5b**, and also the AX pattern for 3-H and 4-H with a vicinal coupling of 6.32 Hz indicate 1,4-addition of **2** to **1i**. The UV spectrum (in chloroform solution) exhibits absorption, lg $\varepsilon = 2.86$ and 3.27, at 273 and 242 nm, respectively, indicative of a non-conjugated benzoid ring and residual double bond and formation of the 1,4-ethanonaphthalene skeleton. Most of the cycloadducts are thermally unstable and undergo retro-cleavage to the starting material on heating. Our new results on cycloaddition support the formation of an exciplex intermediate, which we proposed earlier.[7]

Product **5b** was hydrolyzed to give the 1,4-diketone **6** following a published procedure.[9] The IR spectrum of **6** showed a broad band for both CO groups at 1714 cm^{-1} and the loss of the CN group. The ^{1}H NMR spectrum also supports the hydrolysis of **5b** and formation of **6**.



5b **6**

An interesting result was obtained upon irradiation of **5b** at 253.8 nm. Whereas upon irradiation photoisomerization of **5a** into a dihydrobenzosemibullvalene product[4] by a di-π-methane rearrangement[10,11] has been reported, a retro photo-Diels–Alder reaction was observed on irradiation of **5b**. The

Table 2 Structurally relevant ^{1}H NMR chemical shifts (δ values) and ^{1}H, ^{1}H coupling J (Hz) of **5c** in comparison with **5a** and **5b**

	CH_3CO	2-H	3-H	4-H	$J_{3,4}$
5a	2.53	6.93	6.77	4.45	7.8
5b	2.53	—	5.32	4.31	7.16
5c	2.53	—	[a]	4.41	6.32

[a] Overlapped by aromatic hydrogen.

^{1}H NMR spectrum of a crude reaction mixture after 12 h irradiation showed only peaks characteristic of both compounds **1e** and **2**.

Experimental

All melting points were determined with a Stuart Scientific SMP2 and are uncorrected. IR spectra were obtained on a Shimadzu IR-435 and Perkin–Elmer 983 spectrometers. UV spectra were recorded on a Shimadzu UV-160. ^{1}H NMR spectra were collected on Bruker AW 80 (80 MHz), Bruker WM 300 (300 MHz), and Bruker drx 500 (500 MHz) apparatus. ^{13}C NMR spectra were recorded on a Bruker drx 500 (500 MHz) spectrometer; the DEPT technique was employed for compound **4d**. MS (EI and FD mode) spectra were obtained on an AMD 604. Elemental analyses were run on Heraeus CHN-O-RAPID and Carlo Erba 1106 CHN analyzers. Preparative layer chromatography (PLC) was carried out on 20 × 20 cm^2 plates, coated with a 1 mm layer of Merck silica gel PF_{254}, prepared by applying the silica as a slurry and drying in air.

All irradiations were carried out in a pyrex cell ($\lambda > 280$ nm) using a 400 W high pressure Hg vapour lamp from NARVA (with a 150 W high pressure mercury burner from Philips in the case of **1g**) through a water-cooled immersion well made of Duran glass. A solution of 1 mmol of each of the ketones **1f**, **h**, **i** and **2** was irradiated in 15 mL dry benzene ($c = 0.067$ M) and in the case of **1g** in 20 mL acetonitrile ($c = 0.05$ M) and continuously purged with a stream of argon for the times given below.

Irradiation of 4-chloro-1-acetonaphthone 1f in the presence of 2-morpholinoacrylonitrile 2

The solution was irradiated for 8 h. The solvent was evaporated and PLC of the residue (toluene–ethyl acetate, 7 : 1) gave zone 1 ($R_f = 0.45$, 170 mg of **1f**), zone 2 ($R_f = 0.42$, 120 mg of **2**) and zone 3 ($R_f = 0.36$, 39 mg of **3**; 13% based on **1f** used, 74% based on **1f** consumed). The latter was recrystallized from *n*-hexane–ethyl acetate (10 : 1), m.p. 186–187 °C (lit. m.p.,[7] 186–187 °C).

Irradiation of 4-fluoro-1-acetonaphthone 1g in the presence of 2

The solution was irradiated for 15 h. The solvent was evaporated and PLC of the residue (toluene–ethyl acetate, 10 : 1) gave zone 1 ($R_f = 0.67$, 125 mg of **1g**), zone 2 ($R_f = 0.49$, 12 mg of **2**) and zone 3 ($R_f = 0.36$, 28 mg of **3**), which was recrystallized from *n*-hexane–ethyl acetate (10 : 1), m.p. 186–187 °C (18% based on **1g** used) and zone 4 ($R_f = 0.12$, 44 mg of **4d**), which was recrystallized from *n*-hexane–ethyl acetate (5 : 1), m.p. 189–190 °C (27% based on **1g** used).

***rel*-(2*R*,2a*S*,8b*S*)-8b-Acetyl-4-fluoro-1,2,2a,8b-tetrahydro-2-morpholinocyclobuta[*a*]naphthalene-2-carbonitrile, 4d.** IR (KBr): ν 2220 (CN), 1705 (CO) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.04 (s, 3H, CH_3), 2.38 (m_c, 2H, $CH_{ax}N$), 2.50 (m_c, 2H, $CH_{eq}N$), 2.67 (dd, $|^2J| = 12.17$, $^4J_{1,2a} = 0.72$, 1-*exo*-H), 3.28 (d, $|^2J| = 12.17$, 1-*endo*-H), 3.32 (ddd, $^3J_{2a,3} = 6.30$, $^4J_{2a,F} = 4.73$, $^4J_{2a,1\text{-exo-H}} = 0.72$, 2a-H), 3.72 [$m_c$, 4H, $(CH_2)_2O$], 5.36 (dd, $^3J_{3,F} = 12.81$, $^3J_{3,2a} = 6.30$ Hz, 3-H), 6.98 (m_c, 1H, 8H), 7.34 (m_c, 2H, 6- and 7-H), 7.56 (m_c, 1H, 5-H). ^{13}C NMR ($CDCl_3$): δ 25.13 (CH_3), 42.40 (C-1), 45.51 and 45.58 ($|^3J_{C,F}| = 9.47$, C-2a), 47.19 [$(CH_2)_2N$], 48.17 (C-8b), 63.45 and 63.48 ($|^4J_{C,F}| = 3.98$, C-2), 66.57 [$(CH_2)_2O$], 97.50 and 97.66 ($|^2J_{C,F}| = 20.43$, C-3), 116.33 (CN), 122.84 and 122.90 ($|^3J_{C,F}| = 6.49$, C-5), 127.07 (C-8a), 127.24 and 127.28 ($|^4J_{C,F}| = 4.49$, C-6), 128.92 and 130.84 (C-7, C-8), 135.32 and 135.37 ($|^2J_{C,F}| = 6.49$, C-4a), 158.50 and 160.54 ($|^1J_{C,F}| = 257.43$ Hz, C-4), 204.56 (CO). EI-MS (70 eV,

150 °C): *m/z* (%) 325 [$M^+ - 1$, (0.05), 299 [M^+ − HCN] (0.8), 283 [$M^+ - COCH_3$] (8), 196 [M^+ − morpholine − $COCH_3$] (9), 188 [M^+ − **2**] (22), 173 [$M^+ - 2 - CH_3$] (81), 145 [$M^+ - 2 - COCH_3$] (25), 138 [M^+ − **1g**] (100). UV ($CHCl_3$): λ_{max} (lg ε) 276 (3.73), 268 nm (3.74). Anal. calc. for $C_{19}H_{19}N_2O_2F$ (326.368): C, 69.92; H, 5.87; N, 8.58%. Found: C, 69.72; H, 5.92; N, 8.61%.

Irradiation of 4-methyl-1-acetonaphthone 1h in the presence of 2

The solution was irradiated for 8 h. The solvent was evaporated and PLC of the residue (toluene–ethyl acetate, 3 : 1) gave zone 1 ($R_f = 0.73$, 168 mg of **1h**), zone 2 ($R_f = 0.6$, 110 mg of **2**), and zone 3 ($R_f = 0.49$, 35 mg of **4e**; 11% based on **1h** used, 80% based on **1h** consumed). The latter was recrystallized from *n*-hexane–ethyl acetate (10 : 1), m.p. 138–139 °C (decomp.).

***rel*-(2*R*,2a*S*,8b*S*)-8b-Acetyl-4-methyl-1,2,2a,8b-tetrahydro-2-morpholinocyclobuta[*a*]naphthalene-2-carbonitrile, 4e.** IR (KBr): *ν* 2220 (CN), 1710 (CO) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.99 (s, 3H, $COCH_3$); 2.22 (s, 3H, CH_3); 2.41–2.54 [m, 4H, $(CH_2)_2N$]; AX ($\delta_A = 2.64$, $\delta_X = 3.29$, $|^2J_{AX}| = 12.07$, 1-CH_2), 3.73–3.75 [m, 4H, $(CH_2)_2O$]; AX ($\delta_A = 3.24$, $\delta_X = 5.62$, $^3J_{AX} = 5.61$ Hz; 2a-H, 3-H); 6.95–7.41 (m, 4H, aromatics). EI-MS (70 eV, 125 °C): *m/z* (%) 295 [M^+ − HCN] (0.35), 279 [$M^+ - COCH_3$] (2.25), 264 [$M^+ - COCH_3 - CH_3$] (0.45), 236 [M^+ − morpholine] (0.1), 221 [M^+ − morpholine − CH_3] (0.31), 209 [M^+ − morpholine − HCN] (0.71), 184 [M^+ − **2**] (73), 169 [**1h** − CH_3] or [$M^+ - 2 - CH_3$] (100), 141 [**1h** − $COCH_3$] or [$M^+ - 2 - COCH_3$] (19), 138 [M^+ − **1c**] (16). UV ($CHCl_3$): λ_{max} (lg ε) 276 (3.52), 246 nm (3.59). Anal. calc. for $C_{20}H_{22}N_2O_2$ (322.395): C, 74.51; H, 6.87; N, 8.69%. Found: C, 73.97; H, 6.94; N, 8.74%.

Irradiation of 2-methyl-1-acetonaphthone 1i in the presence of 2

The solution was irradiated for 12 h. The solvent was evaporated and PLC of the residue (toluene–ethyl acetate, 3 : 1) gave zone 1 ($R_f = 0.76$, 165 mg of **1i**), zone 2 ($R_f = 0.61$, 120 mg of **2**), and zone 3 ($R_f = 0.47$, 25 mg of **5c**; 8% based on **1i** used, 72% based on **1i** consumed). The latter was recrystallized from *n*-hexane–ethyl acetate 10 : 1), m.p. 140–141 °C (decomp.).

***rel*-(1*S*,4*R*,9*R*)-1-Acetyl-1,4-dihydro-2-methyl-9-morpholino-1,4-ethanonaphthalene-9-carbonitrile, 5c.** IR (KBr): *ν* 2210 (CN), 1705 (CO) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ AB ($\delta_A = 1.90$, $\delta_B = 2.20$, $|^2J_{AB}| = 12.52$, 2H, 10-CH_2); 2.33 (s, 3H, CH_3); 2.53 (s, 3H, $COCH_3$); 2.55 (m_c, 2H, $CH_{ax}N$); 2.74 (m_c, 2H, $CH_{eq}N$); 3.50 (m_c, 2H, $CH_{ax}O$); 3.59 (m_c, 2H, $CH_{eq}O$); AX ($\delta_A = 4.41$, δ_X = overlapped with aromatic Hs, $^3J_{AX} = 6.32$ Hz); 6.72–7.20 (m, 5H, aromatic H and 3-H). EI-MS (70 eV, 100 °C); *m/z* (%) 322 [M^+] (0.17), 307 [$M^+ - CH_3$] (0.8), 295 [M^+ − HCN] (0.28), 279 [$M^+ - COCH_3$] (0.55), 226 [$M^+ - COCH_3 - CN$] (1.58), 211 [$M^+ - COCH_3 - CN - CH_3$] (0.71), 198 (1.89), 184 [$M^+ - 2$] (55), 169 [$M^+ - 2 - CH_3$] 100), 155 (22), 141 [$M^+ - 2 - COCH_3$] (36), 138 [$M^+ - 1i$] (4), 115 [$M^+ - 2 - COCH_3 - CN$] (26). FD-MS (0.005 V): *m/z* (%) 322 [M^+] (100), 226 (33), 184 (52), 138 (14). UV ($CHCl_3$): λ_{max} (lg ε) 273 (2.86), 242 nm (3.27). Anal. calc. for $C_{20}H_{22}N_2O_2$ (322.395): C, 74.51; H, 6.87; N, 8.69%. Found. C, 73.77; H, 6.78; N, 8.34%.

Irradiation of 5b

A solution of 50 mg (0.15 mmol) of **5b** in 3 mL of acetonitrile ($c = 0.05$) contained in a quartz cell was irradiated in a Rayonet reactor at 253.8 nm for 12 h. The reaction was followed by TLC. TLC showed the retro-Diels–Alder reaction of **5b** and formation of **1e** and **2**. Solvent was evaporated. ^1H NMR of the residue showed characteristic peaks of **1e** and **2**.

Hydrolysis of 5b

In adaptation of a published procedure, a suspension of 60 mg (0.23 mmol) of $CuSO_4 \cdot 5H_2O$ and 16 mg (0.005 mmol) of $Na_2HPO_4 \cdot 12H_2O$ in 1 mL of water, 1.5 mL of methanol and 1.5 mL of acetone was stirred for 10 min, then 50 mg (0.15 mmol) of **5b** was added, the mixture stirred for 6 h, and a further 11 mg (0.003 mmol) of $Na_2HPO_4 \cdot 12H_2O$ was added. After stirring for 72 h at room temperature, the organic material was extracted with 5 mL of chloroform, the extract was dried with $MgSO_4$ and concentrated to give 40 mg of **6**. PLC, toluene–ethyl acetate, (7 : 1), $R_f = 0.36$, gave 32 mg (90%) of **6** as a viscose oil.

***rel*-(1*R*,4*R*)-1-Acetyl-1,4-dihydro-2-methoxy-1,4-ethanonaphthalene-9-one, 6.** IR (film): *ν* 1714 cm^{-1} (CO, br). ^1H NMR (80 MHz, $CDCl_3$): δ AB ($\delta_A = 2.15$, $\delta_B = 2.60$, $|^2J_{AB}| = 18$, 2H, CH_2); 2.51 (s, 3H, $COCH_3$); 3.60 (s, 3H, OCH_3); AX ($\delta_A = 4.21$, $\delta_X = 5.32$, $^3J_{AX} = 6.4$ Hz, 3-H, 4-H), 7.01–7.30 (m, 4H, aromatic H).

Acknowledgements

We are thankful to the Esfahan University Research Council for partial support of this work. H. R. M. is indebted to the German Academic Exchange Service (DAAD) for a scholarship during the period July–August 1998.

References

1 D. Döpp, C. Krüger, H. R. Memarian and Y.-H. Tsay, *Angew. Chem.*, 1985, **97**, 1059; D. Döpp, C. Krüger, H. R. Memarian and Y. H. Tsay, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 1048.

2 D. Döpp and H. R. Memarian, in *Substituent Effects in Radical Chemistry*, ed. H. G. Viehe, Z. Janousek and R. Merenyi, D. Reidel Publishing Co., Dordrecht, Germany, 1986, pp. 383–385.

3 D. Döpp, H. R. Memarian, C. Krüger and E. Raabe, *Chem. Ber.*, 1989, **122**, 585.

4 D. Döpp and H. R. Memarian, *Chem. Ber.*, 1990, **123**, 315.

5 D. Döpp, J. Bredehorn, A. W. Erian, A. Jung, H. Lanfermann, H. R. Memarian, B. Mühlbacher and M. Pies, *Proc. Indian Acad. Sci.*, 1993, **105**, 583.

6 D. Döpp, *Proc. Indian Acad. Sci.*, 1995, **107**, 863.

7 H. R. Memarian, M. Nasr-Esfahani, R. Boese and D. Döpp, *Liebigs Ann./Recueil*, 1997, 1023.

8 H. G. Viehe, Z. Janousek, R. Merenyi and L. Stella, *Acc. Chem. Res.*, 1985, **18**, 148.

9 G. Büchi, P. H. Liang and H. Wüest, *Tetrahedron Lett.*, 1978, 2763.

10 D. Döpp and H. E. Zimmerman, in *Methoden der Organischen Chemie*, ed. E. Müller, Georg Thieme, Stuttgart, Germany, 1975, vol. IV, ch. 5, pp. 413–432.

11 S. S. Hixon, P. S. Mariano and H. E. Zimmerman, *Chem. Rev.*, 1973, **73**, 531.