Pergamon

Tetrahedron Letters 39 (1998) 4717–4720

TETRAHEDRON LETTERS

1,3-Diazaanthracenes: photochemical [4π+4π] cycloadditions with cyclopenta-1,3-diene and dimerisations to new *bis*-pyrimidines [1]

Ronald N. Warrener,* Mirta Golic, Douglas N. Butler

Centre for Molecular Architecture, Central Queensland University, Rockhampton, Qld, 4702, Australia

Fax: +61 7 4930 9917; email: r.warrener@cqu.edu.au

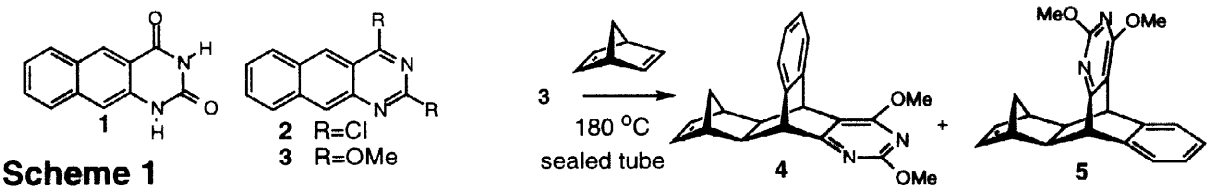
Received 20 March 1998; accepted 21 April 1998

Abstract:

Ultra-violet irradiation of 2,4-dichloro-1,3-diazaanthracene **2** or 2,4-dimethoxy-1,3-diazaanthracene **3** with cyclopentadiene yields single [4π+4π] cycloadducts, which can be transformed into the fused uracil and related pyrimidines by chemical modification of the chlorine or methoxy substituents; **[4π+4π] head to head** *anti*-dimers **17** and head to tail *anti*-dimers **19** are the exclusive products from solution irradiation of **2** or **3**, whereas only *anti*-dimers **19** are formed in the solid state. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords: cycloadditions; photochemistry; uracils; stereoselection

An important objective in some of our recent studies on rigid macrostructure assembly, has been to prepare polycyclic alkenes containing nucleic acid pyrimidine bases for use as building BLOCKs [2] to provide access to rigid framework structures containing one or more pyrimidine base components [3]. We recently reported that the Diels-Alder activity of 1,3-diazaanthracenes (DAAs) **1-3** was poor and that **3** alone reacted with norbornadiene (NBD). The resultant adducts **4** and **5** (Scheme 1) were the first of the fused norbornene building BLOCKs containing naturally occurring pyrimidine components [4] and we have used them to produce multifunctionalised framework structures [5].

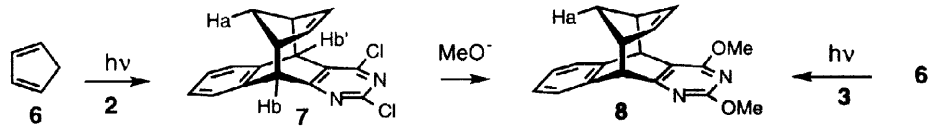


Scheme 1

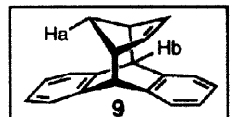
In practice, nucleophilic displacement of the methoxy groups in **4** and **5** was difficult, eg conversion to the respective uracil required fusion with solid NaOH. Accordingly, we sought derivatives of 2,4-dichloro-DAA **2** which could serve as alkene BLOCKs, since they should be more amenable to pyrimidine functional group transformations.

0040-4039/98/$19.00 © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)00865-X

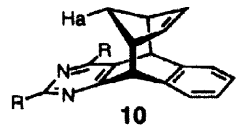
This led us to the present study of the photochemistry of 1,3-diazaanthracenes[1] **1-3**, where we find that both 2,4-dichloro-DAA **2** and 2,4-dimethoxy-DAA **3** undergo [4π+4π] reaction with cyclopenta-1,3-diene **6** to yield respectively single adduct **7**[2] {mp 136-137 °C, 44% yield, ^{1}H NMR δ 1.34 (d, J = 11.5 Hz, 1H), 1.89 (dd, J = 11.5, 2.9 Hz, 1H), 2.95 (m, 2H), 4.18 (d, J = 9.0 Hz, 1H), 4.37 (d, J = 9.0 Hz, 1H), 5.80 (dd, J = 5.5, 2.9 Hz, 1H), 5.87 (dd, J = 5.5, 2.9 Hz, 1H), 7.21 (m, 2H), 7.26 (m, 2H)) and adduct **8** (mp 105-107 °C, 95% yield, ^{1}H NMR δ 1.28 (d, J = 11.3 Hz, 1H), 1.81 (dd, J = 11.3, 4.4 Hz, 1H), 2.84 (m, 2H), 3.95 (s, 6H), 3.99 (d, J = 9.0 Hz, 1H), 4.21 (d, J = 9.0 Hz, 1H), 5.74 (dd, J = 5.5, 3.0 Hz, 1H), 5.84 (dd, J = 5.5, 3.0 Hz, 1H), 7.12 (m, 2H), 7.18 (m, 2H)} (Scheme 2). No evidence for [4π+2π] co-products of the type reported to occur in the photoaddition of cyclopentadiene to anthracene [7-10], although some self dimerisation of DDA **2** and DAA **3** was observed (*vide infra*).



Cmpd	Ha	Hb (Hb')	J
7	1.34	4.18, 4.37	9.0 Hz
8	1.28	3.99, 4.21	9.0 Hz
9	1.19 (ref 6)	3.92	9.0 Hz
	1.25 (ref 9)	3.95	9.0 Hz
	1.27 (this study)	**3.98**	**8.8 Hz**



not observed



Scheme 2

Two important chemical features of these adducts are:

a) the chlorine substituents on the pyrimidine ring of 7 are smoothly displaced by hydroxide, ammonia, alkoxide, or amines.

b) the alkene component in the tricyclo[4.2.2.1^{2,5}]undeca-3-ene ring-systems has norbornene-like reactivity and can be used in BLOCK construction.

Ultra-violet irradiation (benzene, 300 nm, Rayonet) of a solution of 2,4-dichloro-DAA **2** in cyclopenta-1,3-diene **6** produced a *single* 1:1-photoadduct in 44% yield. The gross structure was supported by spectral data (Scheme 2 and Table) and the choice between stereostructures **7** and **10** (R=Cl) was made on the basis of chemical shift data and local symmetry arguments. The known anthracene adduct **9** [6-9], where only benzene rings are present, gave the first evidence in favour of **7**. Here, the chemical shift of the methylene bridge proton Ha in **9** occurred at δ 1.27,[3] similar to that in **7** at δ 1.34 implying benzenoid-ring shielding in both cases. The final decision in favour of **7** followed from nOe data on the derived cyclobutene diester **14** (see Scheme 4) where one of the methylene bridge protons (Ha) was correlated with the benzenoid ring-protons. The 2,4-dimethoxy-DAA **3** also formed a single photoadduct with cyclopenta-1,3-diene **6** and this is assigned structure **8** in view of its independent synthesis from the dichloro-adduct **7** on treatment with sodium methoxide (see Scheme 2). Adduct **8** also revealed a methylene bridge resonance Ha at δ 1.28 again attesting to the proposed structure.

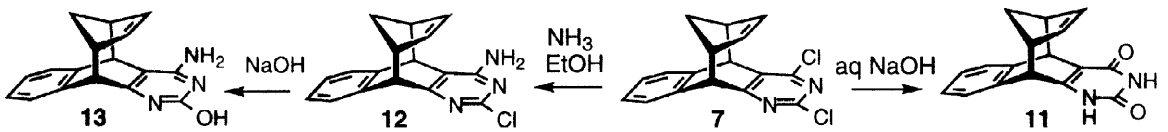
Hydrolysis of photoadduct **7** (2M NaOH/dioxan, 60 °C) yielded the uracil **11** {mp >340 °C, 49% yield, ^{1}H NMR δ1.14 (d, J = 11.4 Hz, 1H), 1.77 (td, J = 11.4, 4.4 Hz, 1H), 2.79 (brs, 2H), 3.74 (d, J = 8.7 Hz, 1H), 4.09 (d, J = 8.7 Hz, 1H), 6.07 (narrow m, 2H), 7.15 (m, 4H), 10.09 (brs, 1H), 11.00 (brs, 1H)} (Scheme 3). The structure of **11** was supported by alkene proton

[1] The photochemistry of azaanthracenes have been reported [6], but this is the first example of 1,3-diazaanthracene participation.

[2] All compounds displayed ^{13}C NMR, MS and/or analytical data consistent with structure.

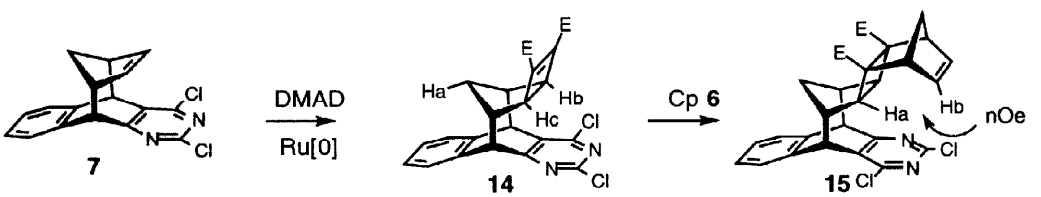
[3] There are disparate chemical shifts reported [7, 10] for **9**. We have remade compound **9** and our data are included in Scheme 2.

resonances at δ 6.07 (narrow multiplet), methylene bridge protons at δ 1.14 and δ 1.77 and the pyrimidine component by the retention of the bisbenzylic bridgehead protons at δ 3.74 and δ 4.09 (J = 8.7 Hz), NH resonances at δ 10.09 and δ 11.0 and ^{13}C resonances at 162.0 and 162.5 (amide carbonyls). The mass spectrum of **11** showed a strong parent ion at *m/z* 278 and major ions for naphthyluracil (*m/z* 212) and cyclopentadiene (*m/z* 66), possibly implicating rearrangement to a [4π+2π] isomer[4] prior to retro-Diels-Alder cleavage. Compounds **7** (*m/z*=295.1), **8** (*m/z*=306.1), **12** (*m/z*=395.1) and **13** (no M^+) show analogous retro-Diels-Alder fragmentations. Treatment of dichloro-adduct **7** with excess ethanolic NH_3 produced (sealed tube at 115 °C for 3 days) only the 2-chloro-4-amino-pyrimidine **12** {mp 188-190 °C, 68% yield, ^1H NMR δ 1.28 (d, J = 11.4 Hz, 1H), 1.83 (td, J = 11.4, 4.4 Hz, 1H), 2.86 (m, 2H), 3.92 (d, J = 9.0 Hz, 1H), 4.25 (d, J = 9.0 Hz, 1H), 5.04 (brs, 2H), 5.84 (m, 1H), 5.88 (m, 1H), 7.19 (m, 4H)} and preferential nucleophilic displacement at the 4-position is commonly observed in 2,4-dichloropyrimidine chemistry [11]. Preliminary results indicate that the chlorine group in **12** can be displaced with base to give the corresponding cytosine **13** (Scheme 3).



Scheme 3

Further transformations can be conducted on alkene **7**, eg, ruthenium catalysed addition of dimethyl acetylene dicarboxylate [12,13] yields the cyclobutene diester **14** {mp 278-280 °C, 23% yield, ^1H NMR δ 1.25 (d, J = 14.0 Hz, 1H), 1.70 (td, J = 14.0, 4.2 Hz, 1H), 2.70 (m, 2H), 2.81(brs, 1H), 2.88 (brs, 1H), 3.77 (s, 3H), 3.79 (s, 3H), 4.32 (d, J = 9.4 Hz, 1H), 4.55(d, J = 9.4 Hz, 1H), 7.27 (m, 4H)} which can be transformed to the new norbornene system **15** {mp 142-144 °C, 53% yield, ^1H NMR δ 0.99 (d, J = 13.8 Hz, 1H), 1.42 (m, 2H), 1.58 (d, J = 9.0 Hz, 1H), 1.94 (d, J = 9.0 Hz, 1H), 2.06 (td, J = 13.8, 4.2 Hz, 1H), 2.82 (dd, J = 9.4, 4.2 Hz, 1H), 3.08 (dd, J = 9.4, 4.2 Hz, 1H), 3.12 (brs, 1H), 3.16 (brs, 1H), 3.64 (s, 3H), 3.65 (s, 3H), 4.20 (d, J = 9.4 Hz, 1H), 4.40 (d, J = 9.4 Hz, 1H), 6.21 (m, 1H), 6.26 (m, 1H), 7.23 (m, 4H)} by treatment with cyclopenta-1,3-diene **6** (Scheme 4). The stereochemical assignment is based on an nOe between methine proton Ha and vinyl proton Hb in **15** and this *anti*-Alder stereochemistry is well precedented from additions of cyclopentadiene **6** to dimethyl tricyclo[4.2.1.$0^{2,5}$]nona-3,7-dien-3,4-dicarboxylates [14,15].



Scheme 4

Ultraviolet irradiation of dichloro-DAA **2** in solution (benzene, 350 nm, Rayonet) affords a mixture of two dimeric products. There are four possible isomers, two head to head (HH) dimers and two head to tail (HT) dimers; each dimeric type comes in *syn* and *anti* variants (Figure 1). Each dimer is characterised by a pair of doublets (J = 10.9 Hz) in the ^1H NMR, corresponding to vicinal coupling of the bridgehead protons. These are assigned the HH *anti*-dimer **17** (R=Cl) and HT *anti*-dimer **19** (R=Cl) {mp 254-257 °C, 75%

[4] The [4π+2π] adduct from anthracene and cyclopenta-1,3-diene can be made directly under thermal conditions (sealed-tube, 180 °C, 12h). We find that it undergoes retro-Diels-Alder fragmentation under electron impact. The [4π+2π] adduct is formed, together with the [4π+4π] adduct **9**, under photochemical conditions [7-10].

combined yield with **17**, ^{1}H NMR δ 4.66 (d, J = 11.0 Hz, 2H), 4.82 (d, J = 11.0 Hz, 2H), 6.95 (m, 4H), 7.08 (m, 4H)} (boxed in Figure 1) since symmetry considerations for the *syn*-dimers dictate that the vicinal protons are chemically equivalent and must occur as singlets. Solution irradiation of dimethoxy-DAA **3** yielded an inseparable mixture (75% yield) of HH *anti*-dimer **17** (R=OMe) (^{1}H NMR δ 3.90 (s, 6H), 3.93 (s, 6H), 4.52 (d, J = 10.9 Hz, 2H), 4.78 (d, J = 10.9 Hz, 2H), 6.91 (m, 4H), 6.97 (m, 4H)) and HT *anti*-dimer **19** (R=OMe) {^{1}H NMR δ 3.84 (s, 6H), 3.86 (s, 6H), 4.51 (d, J = 10.9 Hz, 2H), 4.75 (d, J = 10.9 Hz, 2H), 6.94 (m, 4H), 7.02 (m, 2H), 7.12 (m, 2H)}.

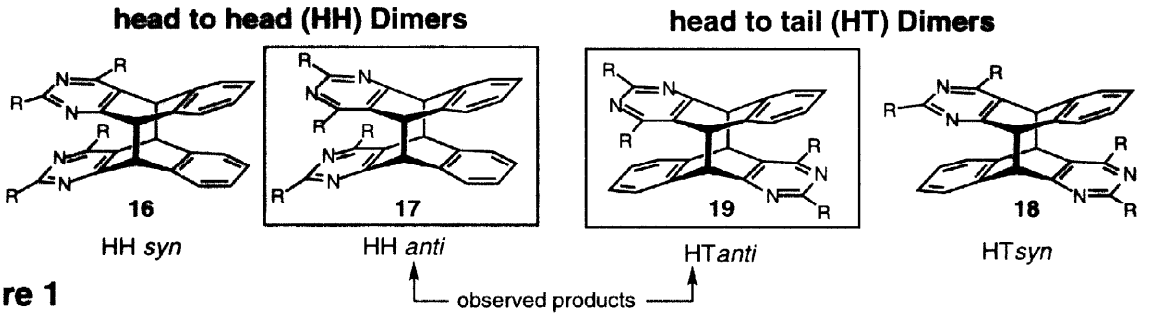


Figure 1

The assignment of exact structures to these dimers rests on symmetry considerations provided by the observed multiplicity of the aromatic protons in their ^{1}H NMR spectra. In one isomer, these resonances occur as three separate sets (the fourth one overlaps with the highest field set) and these are assigned to HT isomer **19** where the aromatic ring is proximate to the unsymmetrical field of the pyrimidine ring; the other isomer has only two sets of aromatic resonances indicating their more symmetrical environment as expected for the HH dimer **17**. Interestingly, single isomers **19** (R = Cl, OMe) were the only photodimers observed as by-products in the photoadditions of cyclopentadiene to diazaanthracenes **2** and **3**. They have also been isolated as the only product of irradiation of **2** and **3** in the solid state. The photoadducts **7** and **8** described herein, have been incorporated into rigid framework structures by BLOCK coupling techniques [2] and these are reported in the accompanying letter [15].

Acknowledgements.

MG thanks the Centre for Molecular Architecture for provision of a PhD Scholarship.

References

[1] Building BLOCKs in Synthesis Part 9; for part 8, see Warrener RN, Amarasekara AS, Russell RA. Tetrahedron Lett. 1998:in press.
[2] Warrener RN, Schultz AC, Butler DN, Wang S, Mahadevan IB, Russell RA. Chem. Commun. 1997:1023-1024.
[3] Warrener RN. Chem. Aust. 1992;59:578-581.
[4] Warrener RN, Golic M, Butler DN. Synlett 1997:1105-1107.
[5] Mustafa A. Chem. Rev. 1952:51:1-23.
[6] Kaupp G, Grüter H-W. Chem Ber. 1980;113:1626-1631.
[7] Kaupp G, Grüter H-W. Angew. Chem Int. Ed. 1979;18:881-882.
[8] Kaupp G, Dyllick-Brenzinger R. Angew. Chem Int. Ed. 1974;13:478-479.
[9] Kaupp G. Angew. Chem Int. Ed. 1972;11:718-719.
[10] Brown DJ. The Pyrimidines, 2. New York. John Wiley & Sons, 1994:372-381.
[11] Mitsudo T, Naruse H, Kondo T, Ozaki Y, Watanabe Y. Angew. Chemie, Int. Ed. Engl. 1994;33:580-581.
[12] Mitsudo T, Kokuryo K, Shinsugi T, Nakagawa Y, Watanabe Y, Takegami Y J. Org. Chem. 1979;44:4492-4496.
[13] Warrener RN, Pitt IG, Butler DN. J. Chem. Soc. Chem. Commun. 1983:1340-1342.
[14] Warrener RN, Butler DN. Aldrichimica Acta 1997;30:119-130.
[15] Warrener RN, Golic M, Butler DN. Tetrahedron Lett. 1998;39:4721-4724.