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Photochemistry of Benzotriazole: An Unprecedented Tautomer-Selective Intermolecular [2+2] Photocycloaddition

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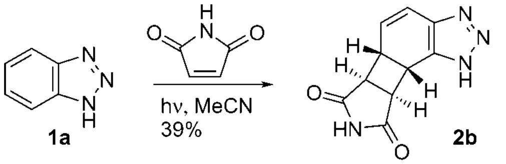
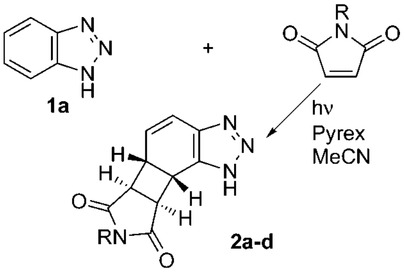
ABSTRACT



Irradiation of benzotriazole with a variety of maleimide derivatives leads to the stereo- and regioselective formation of aryl [2 + 2] photocycloaddition products. Further studies with 2-alkyl benzotriazole derivatives indicates that in the case of the parent benzotriazole this cycloaddition proceeds selectively via the 2*H*-tautomer.

The photochemistry of benzotriazole has long been associated with the extrusion of molecular nitrogen to form reactive diradicals. For example, *N*-aryl-substituted maleimides have been shown to undergo useful carbazole-forming reactions in a sequence known as the photo Graebe−Ullman reaction.[1] As part of a study on the generation and subsequent reactions of diradicals from benzotriazole derivatives we investigated the irradiation of a mixture of maleimide and benzotriazole **1a** using a 125-W medium-pressure Hg lamp as a UV source. Irradiation in a quartz immersion well ($\lambda > 200$ nm) gave an intractable tar. Irradiation in a Pyrex immersion well ($\lambda > 290$ nm) gave a new product. Rather surprisingly, NMR analysis of the product revealed it to be the arene-maleimide [2 + 2] photoadduct **2a** (entry 1, Table 1). The yield of this photoadduct was found to be optimized when 5 equiv of benzotriazole were used. When fewer equivalents of **1a** were employed, substantial amounts of the [2 + 2] maleimide dimer were observed. The reaction was repeated with a variety of *N*-substituted maleimides, with the yields shown in Table 1. In all cases only one diastereoisomer could be

Table 1. Intermolecular [2 + 2] Photocycloaddition of Benzotriazole with Maleimides



entry	R	product	yield (%)
1	H	**2a**	39
2	Me	**2b**	33
3	Et	**2c**	30
4	*t* Bu	**2d**	16

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[1] Katritzky, A. R.; Lan, X. F.; Yang, J. Z.; Denisko, O. V. *Chem. Rev.* **1998**, *98*, 409−548.

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isolated. Detailed NOE studies on **2a** (entry 1) indicate that the stereochemistry of the product is *exo*. Strong NOEs were observed between H_b and H_c, H_c and H_d, and H_a and H_b (Figure 1), whereas relatively weaker NOEs were observed between H_c and H_e and between H_d and H_f. It is reasonable to assume that formation of the *exo* product would be preferred on steric grounds.

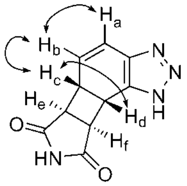
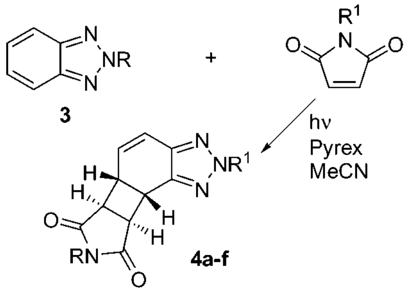


Figure 1. Selected NOE enhancements for **2a**.

In the case of the irradiation of *N*-methyl maleimide with benzotriazole (entry 2), it was possible to identify side products that were the result of conjugate addition of benzotriazole to maleimide. This was found to be a ground state reaction, as the same products were observed in the absence of irradiation. Similar conjugate addition products have been previously observed by Katritzky.[2]

It was hoped that the yield of the [2 + 2] photoproduct could be increased by using a 1-*N*-substituted benzotriazole as the reactant, thus eliminating the possibility of benzotriazole conjugate additions. However, despite several attempts, irradiation of both maleimide and *N*-methyl maleimide with 1-methyl-1*H*-benzotriazole gave *none* of the desired [2 + 2] product, and the only isolable compound was unreacted 1-methyl-1*H*-benzotriazole. This led us to speculate that the difference in reactivity between **1a** and 1-methyl-1*H*-benzotriazole might be a consequence of the former being able to tautomerise to the 2*H* isomer. To test this hypothesis 2-methyl-2*H*-benzotriazole (**3**, R = Me) was irradiated with maleimide, and we were pleased to observe the formation of the aryl [2 + 2] product **4a** in reasonable yield. The reaction of a number of 2-substituted-2*H*-benzotriazoles[3] with a variety maleimides was then investigated, and the results are shown in Table 2.

Table 2. Intermolecular [2 + 2] Photocycloaddition of 2-Alkyl-2*H*-benzotriazoles with Maleimides



3

4a-f

entry	R	R^1	product	yield (%)
1	Me	H	**4a**	46
2	Me	Me	**4b**	52
3	Me	Et	**4c**	51
4	Me	*t* Bu	**4d**	34
5	Bn	Me	**4e**	47
6	Bn	Et	**4f**	48

Generally the reactions were higher yielding and more consistent than those with the parent benzotriazole. Once again only the *exo*-isomer was formed in each case. 2-benzyl-2*H*-benzotriazole (**3**, R = CH_2Ph) was employed, as this will give us the opportunity to liberate the free triazole unit in the resulting adducts (**4e** and **4f**) by hydrogenolysis after the photolysis step.

Confirmation of the structure and stereochemistry of the products was provided by X-ray crystallography of the *N*-ethyl adduct **4c** (Figure 2).[4]

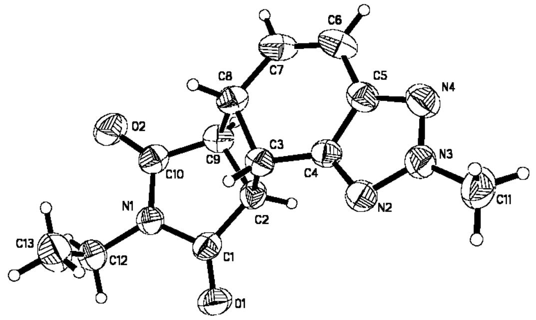
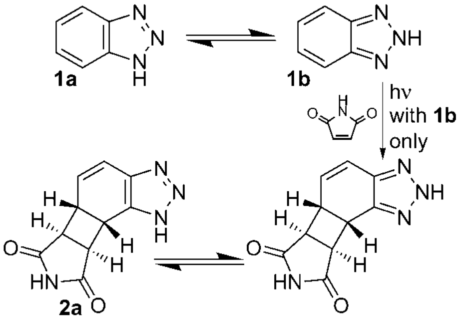


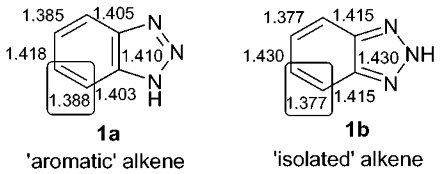
Figure 2. X-ray structure of **4c**.

These remarkable results suggest that the cycloadditions described in Table 1 are a result of the photoexcited maleimide unit undergoing *selective* cycloaddition with the 2*H*-tautomer **1b** as depicted in Scheme 1. This is strongly supported by the fact that 1-methyl-1*H*-benzotriazole fails to undergo photocycloadditon with maleimide. Although aryl [2 + 2] photocycloadditions have been reported previously,[5] as far as we are aware this is the first reported example of such a cycloaddition with benzotriazole. Such a heteroaromatic tautomer-selective cycloaddition would appear to be unprecedented.

Scheme 1. 2*H*-Tautomer-Selective Photocycloaddition



Previously there has been much discussion on the position of the equilibrium between the 1*H*- and 2*H*-benzotriazole tautomers, as well as their relative stabilities. It is generally agreed that 1*H* dominates in solid and solution, whereas the proportion of the 2*H*-tautomer increases in the gas phase.[6] However, the energy difference between the two is very small.[7] Previously both Katritzky[8] and Elguero[9] have published detailed bond length calculations and theoretical studies on the stabilities of the two tautomers **1a** and **1b**. Our own density functional theory calculations at the B3LYP/6-31G* level[10] agree well with those of Katritzky and Elguero and show that the bond lengths in the aryl ring are slightly different in the two tautomers (Figure 3). In **1b** there is a greater difference in bond lengths between the alternating double and single bonds, i.e., the double bonds are shorter and the single bonds are longer in comparison to those of **1a**. Thus, in our opinion,[11] it is fair to assume that this tautomer has more isolated double bond character compared to **1a**.



1a
'aromatic' alkene

1b
'isolated' alkene

Figure 3. Calculated bond lengths (Å) for 1*H*- and 2*H*-benzotriazole (B3LYP/6-31G*).

Therefore it is not unreasonable to postulate that the π-system indicated for **1b** in Figure 3 is able to act as a relatively reactive isolated double bond and thus participate in [2 + 2] cycloaddition with the photoexcited maleimide units. Conversely the π-system indicated in **1a** is more aromatic and less able to participate in cycloaddition.

In conclusion, it has been demonstrated that benzotriazole undergoes an unprecedented intermolecular photochemical [2 + 2] cycloaddition that would appear to proceed selectively via the 2*H*-tautomer. Further studies are concerned with an investigation of the chemistry and reactivity of the highly functionalized photocycloadducts.

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Supporting Information Available: Experimental procedures and characterization for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(2) Katritzky, A. R.; Hitchings, G. J.; Zhao, X. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2371−2377.

(3) Katritzky, A. R.; Kuzmierkiewiecz, W.; Greenhill, J. V *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 369−373.

(4) Crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 177305

(5) (a) Yokoyama, A.; Mizuno K. *Org. Lett.* **2000**, *2*, 3457−3459. (b) Angus, H. J.; Bryce-Smith, D. *Proc. Chem. Soc* **1959**, 326−327.

(6) See: Elguero, J.; Katritzky, A. R.; Denisko, O. V. *Adv. Heterocycl. Chem.* **2000**, *76*, 1−84. Minkin, V. I.; Garnovskii, A. D.; Elguero, J. *Adv. Heterocycl. Chem.* **2000**, *76*, 157−323 and references therein.

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(10) Calculations performed by Professor Roger W. Alder (University of Bristol) using Jaguar 4.1 (Schrödinger Inc., Portland, OR, 2000).

(11) It should be noted that Fischer et al. published calculations for **1a/1b** using three different 6-31G* levels. These authors concluded that the calculated bond lengths from HF were in good agreement for the quinonoid (**1b**) structure. The results from MP2 were less supportive as there was little difference in the calculated bond lengths between **1a** and **1b**. The B3LYP calculations were intermediate between the HF and MP2 results, and in the opinion of these authors, the calculated bond lengths at this level were not strongly supportive of the quinonoid (**1b**) structure**.** Our own B3LYP calculations were in exact agreement with those obtained by the authors: Fischer, G.; Cao, X.; Purchase, R. L. *Chem. Phys. Lett.* **1996**, 689−698.