

Cycloaddition of phenyl azide to unsymmetrical azabicyclic alkenes

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Dedicated with pleasure to Professor Charles Rees on the occasion of his 75th birthday

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Abstract

Addition of phenyl azide to selected derivatives of the 2-azabicyclo[2.2.1]hept-5-ene, 2-azabicyclo[2.2.1]hept-5-en-3-one and 2-azabicyclo[2.2.2]oct-5-en-3-one ring systems is described. Modest levels of regioselectivity are observed; 100% *exo*-facial selectivity is found in the [2.2.1] systems but *exo*- and *endo*- adducts are formed from the [2.2.2] substrate allowing isolation of all four possible stereoisomers. Photolytic removal of dinitrogen from the triazolines gives aziridines which are potential precursors to stereospecifically functionalised aziridino-cyclopentanes and aziridino-cyclohexanes.

Keywords: Phenyl azide, 1,3-dipolar cycloaddition, triazolines, aziridines, bicyclic amines, lactams

Introduction

The cycloaddition of azides to norbornenes and benzonorbornadienes¹ has been well studied as has the effect of a bridging heteroatom in 7-oxa² and 7-aza³ derivatives of the latter ring systems. Typical benzo-annelated examples demonstrate the characteristic addition from the *exo*-face giving triazolines **1a**; subsequent photolysis of the triazolines yields aziridines **2a** (Figure 1). Analogous addition of diazomethane gives pyrazolines **1b** from which cyclopropanes **2b** are accessible *via* photolytic deazetisation;⁴ epoxides are accessible *via* direct epoxidation of norbornene,⁵ as are the corresponding benzo- derivatives **2c** from 1,4-iminonaphthalenes (benzonorbornadienes) and 1,4-imino-anthracenes.⁶

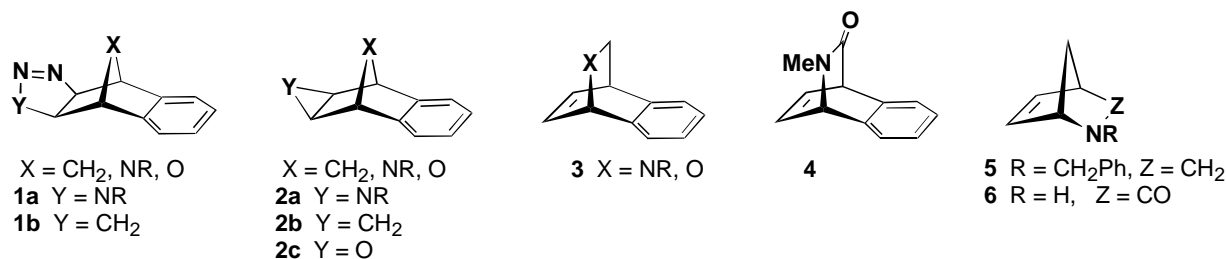
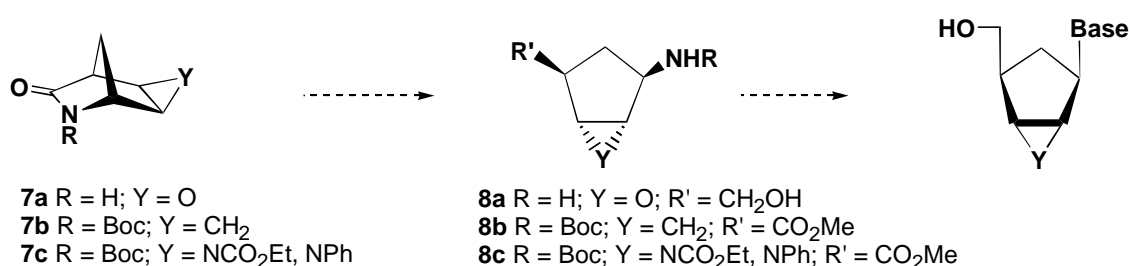


Figure 1

We are not aware of corresponding studies with bicyclic alkenes containing unsymmetrically-placed amino-nitrogen and we have therefore examined azide addition to the strained bicyclic amine **5**. Turning to higher homologues, potential substrates such as the hetero-bicyclo[2.2.2]octenes **3** unfortunately decompose rapidly by retro-Diels-Alder cycloaddition and we were therefore unable, for example, to achieve [4+2] cycloaddition of cyclic dienes to **3**.⁷ However, the alternative cycloaddition of dienes to the lactam **4** proceeds readily and subsequent removal of the carbonyl group using hydride reduction is straightforward.⁷ We have therefore examined the reaction of **4** with phenyl azide in order to probe the potential facial selectivity and regioselectivity offered by this unsymmetrical substrate. We have also included the lactam **6**. This readily-available substrate⁸ has formed the basis for recent syntheses of epoxy⁹ and cyclopropano¹⁰ derivatives of **7** and their conversion into stereospecifically-substituted bicyclo[3.1.0]hexanes **8** which are intermediates in the synthesis of novel nucleoside variants (Scheme 1). We are prompted to report our results by the developing activity in this area and also by a recent report of the formation of the aziridines **7c** by cycloaddition of azides to **6** (in its *N*-Boc-protected form) using high pressure, followed by deazetisation.¹¹



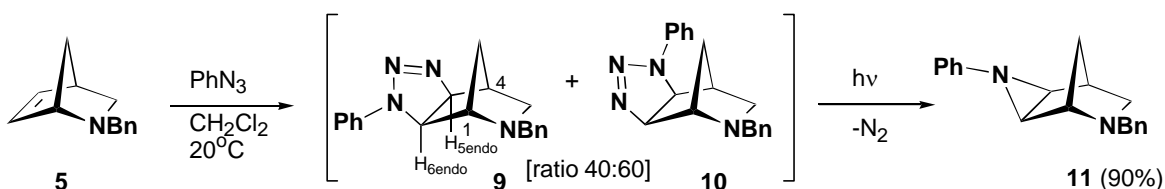
Scheme 1

Whilst we expected attack to occur exclusively from the *exo*-face of **5** and **6**, we were mindful of a report that *endo*-addition has been observed in epoxidation of **6**.⁸ We expected both faces of the double bond in **4** to be accessible to cycloaddition on the basis of our earlier work on the addition of cyclic dienes.⁷ There has been disagreement concerning the influence of the homoallylic nitrogen in analogues of **5** on the regioselectivity of addition to the double bond¹²

and we wished to determine whether nitrogen could exert a significant influence on the regiochemistry of azide cycloadditions.

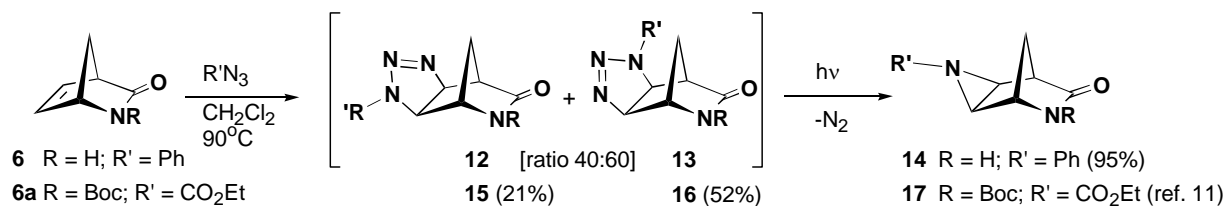
Results and Discussion

The amine **5** was treated with phenyl azide in dichloromethane solution at room temperature; the reaction was followed by IR spectroscopy and was complete within 5 days (Scheme 2).



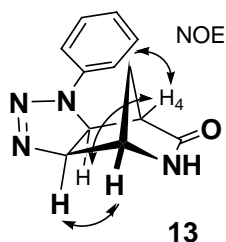
Scheme 2

A quantitative yield of triazolines **9** and **10** was obtained in a 40:60 ratio as measured by NMR integration. The *exo*- stereochemistry was assigned on the basis of the small coupling constants $J_{1,6}$ and $J_{4,5}$ (< 1 Hz). Early work with norbornene/phenyl azide adducts established that the proton adjacent to $\text{N}=\text{N}$ was further downfield than that next to the *N*-phenyl substituent;¹ this distinction was evident in all of the adducts obtained in the present study and formed a consistent basis for assignment of ^1H NMR signals. Clearly, the bridgehead proton H_1 always appears downfield of H_4 but the amino-nitrogen at the 2-position exerts an additional influence in a variety of 2-alkyl-2-azabicyclo-[2.2.1]heptane and -[2.2.2]octane derivatives, causing $\text{H}_{6\text{-endo}}$ to appear downfield of $\text{H}_{5\text{-endo}}$ (Scheme 2) by between 0.2 and 0.5 ppm.¹³ Despite the complexity of the spectrum of the mixture of triazolines **9** and **10**, two downfield doublets were resolved at δ 4.91 (major) and 4.65 (minor) and these signals were therefore assigned to $\text{H}_{6\text{-endo}}$ in **10** and $\text{H}_{5\text{-endo}}$ in **9** respectively, consistent with the assignment of **10** as the major component. The cycloadducts could not be separated and the mixture of **9** and **10** was photolysed in acetone solution in a quartz vessel using a medium pressure mercury lamp. Conversion into the single aziridine **11** was complete within 4 hours and gave a yield of 90% after chromatography on silica (Scheme 2).



Scheme 3

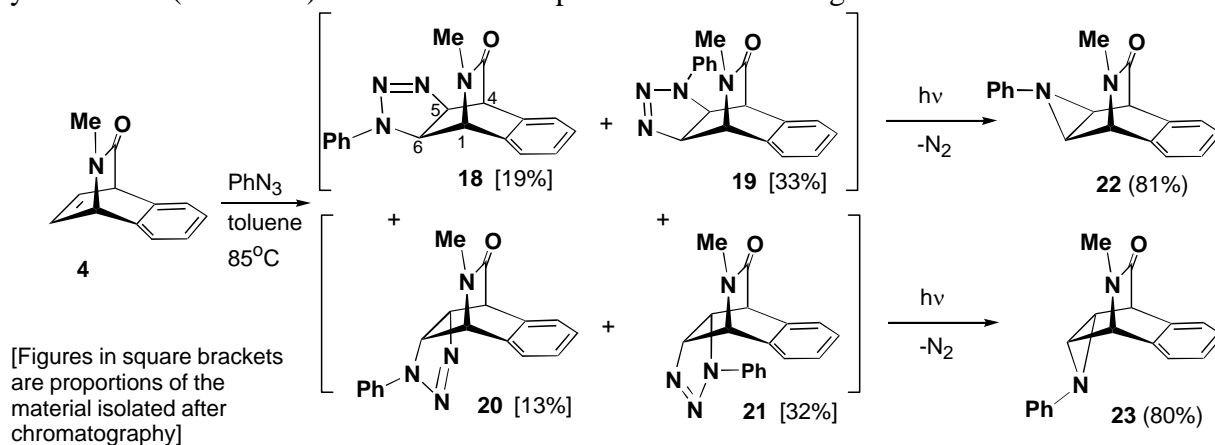
The corresponding reaction of phenyl azide with the lactam **6** (Scheme 3) occurred more slowly but was complete on heating overnight in dichloromethane in a sealed tube at 90°C. Attempts to perform the reaction at higher temperatures in toluene led to substantial decomposition. Similar cycloadditions of azides to the *N*-Boc-protected lactam **6a** were reported to require high pressure;¹¹ the use of a secondary lactam in our study may be significant in making the reaction easier but we did not investigate this question further. The *exo*-selectivity in attack on **6** was maintained, as was the 40:60 ratio of cycloadducts **12:13** [the ratio of regioisomers **15:16** from **6a** is based on isolated yields¹¹ and is included in Scheme 3 for comparison].



The assignments for **12** and **13** were confirmed by considering the major and minor signals at δ 3.13 and 3.22 due to the bridgehead protons H_4 (adjacent to the amide carbonyl group). Examination of bridgehead proton signals in the compounds produced in this work shows that the bridgehead proton (H_1 or H_4) on the same side as the $N=N$ bond of the triazolone is consistently at lower field than the corresponding bridgehead proton adjacent to the triazolone *N*-phenyl, allowing assignment of the minor signal at δ 3.22 to H_4 in isomer **12**. A NOESY experiment confirmed this, showing an interaction between H_4 and the aryl ring in the case of **13** but not **12**. The isomeric triazolones **12** and **13** were not separated and photolysis of the mixture gave **14** as a single stereoisomer. Clearly, **14** can be converted into a 6-azabicyclo[4.1.0]hexane derivative corresponding to **8** using established hydrolysis or reduction procedures.

We wanted to explore the feasibility of addition to the 2-azabicyclo[2.2.2]oct-5-ene-3-one ring system as a potential source of the corresponding 7-azabicyclo[4.1.0]heptane homologues and we chose the readily available benzo-derivative **4**.

Equimolar amounts of phenyl azide and the lactam **4** were heated in toluene solution at 85 °C for 17 hours. The product was shown by NMR and TLC analysis to consist of a mixture of four cycloadducts (Scheme 4) and the triazolines were investigated in some detail.



Scheme 4

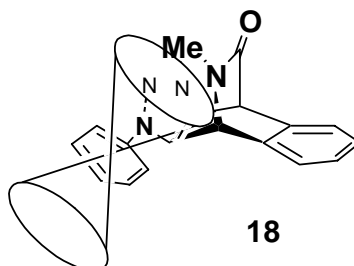
A small quantity of each of the triazolines **18** - **21** was separated by chromatography on silica (60% recovery, together with *ca.* 10% of unchanged **4**). Additional mixed fractions were eluted containing [**18** & **19**] and [**20** & **21**]. Analysis of the ¹H NMR spectra of all of the isolated fractions gave the percentages indicated in Scheme 4. The mixed fractions were photolysed separately; each pair of compounds gave a single aziridine showing that in one pair the aziridine was *exo*- to the benzo- group and in the other pair, it was *endo*-.¹⁴ The structural assignments shown in Scheme 4 were made on the basis of this information and a detailed analysis of the ¹H NMR data (Table 1).

Table 1 ¹H NMR data for compounds **18** - **23**

	18		19		22		20		21		23	
	δ	J	δ	J	δ	J	δ	J	δ	J	δ	J
	(Hz)		(Hz)		(Hz)		(Hz)		(Hz)		(Hz)	
H ₁	4.93	d	5.13	d	4.75	d	4.88	d	5.09	d	4.78	d
H ₄	4.58	d	4.43	d	4.28	d	4.58	d	4.44	d	4.25	d
H ₅	5.19	dd	4.42	dd	2.82	dd	5.46	dd	4.70	dd	2.94	dd
H ₆	4.34	dd	5.13	ddd	2.83	dd	4.82	dd	5.56	dd	3.21	dd
NMe	2.64	s	2.94	s	2.96	s	3.00	s	3.06	s	2.93	s
J _{1,6}	2.2		2.5		3.0		3.6		4.1		4.6	
J _{4,5}	3.6		3.0		3.9		3.7		3.3		4.3	
J _{5,6}	11.2		ca. 12 *		6.4		11.1		11.2		6.8	
aryl	6.85 - 7.45	m	7.05 - 7.45	m	6.7 - 7.35	m	6.75 - 7.35	m	6.75 - 7.35	m	6.75 - 7.25	m

* 2nd-order spectrum; estimated J value

NOESY experiments on the triazolines were of limited value. However, J values established full connectivity between the protons H₁, H₆, H₅, and H₄, and the relative chemical shifts are in accord with those for the triazolines discussed earlier. The relatively larger values for J_{1,6} and J_{4,5} in **20** and **21** compared with **18** and **19** fit with predictions based on calculated dihedral angles and with relative values from adducts of **4** with cyclic dienes (for which X-ray data are available).⁷



The dramatic upfield shift of the *N*-Me signal for **18** relative to the other three isomers (*ca.* 0.3 ppm) is consistent with the unique placement of the methyl group within the shielding zone of the triazoline *N*-phenyl group in this stereoisomer and provides a crucial point of reference. The relative J values measured for the aziridines **22** and **23** (Table 1) reflect similar differences in dihedral angle; homonuclear spin-decoupling experiments confirmed the assignments. These aziridines were produced efficiently (*ca.* 80% yield) as single stereoisomers by photolysis of mixed samples of [**18** and **19**] and [**20** and **21**] respectively, in acetone solvent.

Summary

We have shown that cycloaddition of phenyl azide to selected bicyclic amines and secondary and tertiary lactams based on the 2-azabicyclo[2.2.1]hept-5-ene and 2-azabicyclo[2.2.2]hex-5-ene ring systems occurs at modest temperatures without the need for high pressure. Modest regioselectivity is observed in attack on the double bond with a very slight preference for the adducts having the *N*-phenyl group further from the amino- or amido- nitrogen.^{12b} Only *exo*-products are formed in attack on the bicyclo[2.2.1]hept-5-ene examples but there is no significant facial discrimination as far as the bicyclo[2.2.2]oct-6-ene system is concerned, allowing isolation and characterisation of all four possible stereoisomers. The yields of aziridines from photolysis of the triazolines in acetone solvent in the present work were significantly higher than those reported for photolyses carried out in acetonitrile.¹¹ The established hydrolysis and reductive cleavage of the amide bond in bicyclic lactams^{9,10,11} opens the way to a wider range of

nucleoside variants and, with this in mind, we are currently looking at simpler 2-azabicyclo[2.2.2]oct-6-ene examples which should allow formation of both aziridine stereoisomers in the higher homologues of **8** based on the 7-azabicyclo[4.1.0]heptane ring system.

Experimental Section

General Procedures. NMR spectra were recorded on Varian EM 390 (90 MHz), Bruker ARX 250, AM 300, or DPX 300 spectrometers. Spectra were measured in CDCl₃ with tetramethylsilane (TMS) as internal reference unless indicated otherwise. Signal characteristics are described using standard abbreviations: s (singlet), d (doublet), dd (doublet of doublets), m (multiplet), br (broad). Selective spin-decoupling experiments were performed on the series of compounds **18** – **23** in order to allow measurement of J values and to confirm the assignment of the methine protons. Selected NOESY experiments were performed as described in the discussion section. In the ¹³C spectra, (s), (d), (t), (q), are used to indicate quaternary, methine, methylene and methyl carbons respectively, as shown by DEPT experiments.

IR spectra were recorded on a Perkin-Elmer 298 spectrometer as solutions in CH₂Cl₂ unless indicated otherwise. Mass spectra were measured routinely on VG Micromass 14 (EI) [an asterisk is used to indicate the base peak in EI spectra] or Micromass Quattro LC (ES) spectrometers. Accurate mass measurements were obtained using a Kratos Concept mass spectrometer (FAB); they were measured to 5 decimal places but are quoted to 4. Melting point measurements were made using a Kofler hot stage apparatus and are uncorrected. Petroleum ether refers to the fraction b.p. 40 – 60°C.

Addition of phenyl azide to amine (5). The amine **5**¹⁵ (0.33 g; 1.78 mmol) and phenyl azide¹⁶ (0.212 g; 1.78 mmol) in dichloromethane (5 mL) were stirred at room temperature and monitored by IR spectroscopy until the azide peak at ca. 2120 cm⁻¹ had disappeared (5 days). The sample was concentrated under vacuum and passed through a short column of silica to give a quantitative yield of the triazolines **9** and **10** as a yellow viscous oil after evaporation of solvent. ¹H NMR (CDCl₃, 300 MHz) δ 0.95-1.10 (m, 1H, H_{7a}), 1.5 – 1.65 (m, 1H, H_{7s}), 2.25 – 4.0 (complex, 6H: H₁, H₄, H_{3x}, H_{3n}, CH₂Ph, & total 1H: H_{6endo(9)}, H_{5endo(10)}), 4.65 & 4.91 (2 x d, J_{5,6} = 9.5 Hz, ratio 60:40, total 1H: H_{6endo(10)}, H_{5endo(9)}), 6.9 - 7.4 (complex, 10H); M.S. (EI) ^{m/z} 304 (M⁺), 276*.¹⁷ The triazolines **9** and **10** were not separated or further characterised but were photolysed directly.

Photolysis of triazolines **9** and **10** to give *exo*- aziridine **11**

A sample of **9** and **10** (0.29 g) was dissolved in acetone (55 mL) and irradiated for 4 h in a quartz tube using a medium pressure mercury lamp. The solvent was evaporated and the product

chromatographed on silica using 2:1 diethyl ether:petroleum ether to give the aziridine **11** as a pale yellow viscous oil (0.23 g; 90%). ^1H NMR (CDCl_3 , 300 MHz) δ 1.31 (brd, $J_{7,7} = 9.9$ Hz, 1H, H_{7a}), 1.72 (brd, $J_{7,7} = 9.9$ Hz, 1H, H_{7s}), 2.44 (dd, $J_{3\text{endo},3\text{exo}} = 9.4$ Hz, $J_{3\text{endo},4} = 1.1$ Hz, 1H, $\text{H}_{3\text{endo}}$), 2.46 (brd, $J_{5,6} = 5.5$ Hz, 1H, H_6), 2.58 (dd, $J_{3\text{endo},3\text{exo}} = 9.4$ Hz, $J_{3\text{exo},4} = 3.4$ Hz, 1H, $\text{H}_{3\text{exo}}$), 2.64 (brd, $J_{5,6} = 5.5$ Hz, $J_{4,5} < 1$ Hz, 1H, H_5), 2.72 (brs, 1H, H_4) 3.50 (bs, 1H, H_1), 3.73 (s, 2H, benzylic), 6.85 - 7.40 (m, 10H, aryl); ^{13}C NMR (CDCl_3 , 75 MHz) δ 26.1 (CH_2), 38.6, 39.8, 39.9 (CH), 55.7, 59.1 (CH_2), 60.6, 120.8, 121.6, 126.8, 128.2, 128.4 (CH), 139.8 (C), 152.4 (CO); ν_{max} (CH_2Cl_2) 3028, 2964, 2930, 2856, 1602, 1494, 1369, 1314 cm^{-1} ; M.S. (EI) m/z 276 (M^+), 156, 91^{*}, 77; HRMS (FAB) calc. for $\text{C}_{19}\text{H}_{21}\text{N}_2$ (MH^+) 277.1705; found: 277.1705.

Addition of phenyl azide to lactam **6**

A solution of lactam **6**⁸ (0.2 g; 1.83 mmol) and phenyl azide (0.22 g; 1.85 mmol) in dichloromethane (2 mL) was heated at 90 °C in a sealed tube for 16 h with magnetic stirring. After removal of the solvent under vacuum, the crude product was washed with cold diethyl ether to give a mixture of two triazolines **12** and **13** (0.33 g; 79%) which could not be separated. ^1H NMR (CDCl_3 , 250 MHz) δ 1.34 (brd, $J_{7,7} = 10.5$ Hz, 1H, H_{7a}), 1.93 (brd, $J_{7,7} = 10.5$ Hz, 1H, H_{7s}), 3.12 & 3.22 (brs, H_4 , ratio 60:40 total 1H), 4.26 and 4.38 (2 x s, 1H, $\text{H}_{1\text{maj}}$ & $\text{H}_{1\text{min}}$), 4.35 and 4.40 (2 x d, $J_{5,6} \approx 9$ Hz, 1H, $\text{H}_{6\text{min}}$ & $\text{H}_{5\text{maj}}$), 5.18 - 5.22 (2 x d, $J_{5,6} \approx 9$ Hz, 1H, $\text{H}_{6\text{maj}}$ & $\text{H}_{5\text{min}}$), 6.9 (NH), 7.0 - 7.5 (m, 5H, aryl); ^{13}C NMR (CDCl_3 , 62.9 MHz): **12** (*minor isomer*) δ 35.5 (CH_2), 50.5, 58.2, 62.5, 83.1, 114.5, 119.4, 123.5, 125.3, 130.2 (CH), 139.8 (C), 178.8 (CO); **13** (*major isomer*) δ 35.5 (CH_2), 50.0, 57.9, 59.5, 88.8, 114.7, 119.4, 123.6, 125.3, 130.1 (CH), 139.6 (C), 178.4 (CO); ν_{max} (CH_2Cl_2) 3440, 3030, 1720, 1600, 1490; M.S. (FAB) m/z 229 (MH^+).

Photolysis of triazolines **12** and **13** to give *exo*- aziridine **14**

A sample of **12** and **13** (0.15 g; 0.657 mmole) was irradiated in acetone (50 mL) in a quartz tube for 4.5 h using a medium pressure mercury lamp. The solvent was evaporated and the product chromatographed on silica using 2:1 diethyl ether:petroleum ether to give the aziridine **14** as a crystalline solid (0.125 g; 95%) which was recrystallised from ethyl acetate/diethyl ether to give colourless crystals, m.p. 140 - 142 °C. ^1H NMR (CDCl_3 , 250 MHz) δ 1.53 (brd, $J_{7,7} = 9.6$ Hz, 1H, H_{7a}), 1.98 (brd, $J_{7,7} = 9.6$ Hz, 1H, H_{7s}), 2.65 (d, $J_{5,6} = 5.5$ Hz, 1H, H_5), 2.83 (d, $J_{5,6} = 5.5$ Hz, 1H, H_6), 2.92 (s, 1H, H_4), 3.88 (s, 1H, H_1), 6.8 - 7.2 (m, 6H, aryl & NH); ^{13}C NMR (CDCl_3 , 62.9 MHz) δ 33.1 (CH_2), 40.0, 45.9, 46.9, 55.7 (CH), 120.8, 122.9, 129.5 (CH), 151.7 (C), 181.9 (CO); ν_{max} (CH_2Cl_2) 3440, 3030, 1720, 1600, 1490, 1380, 1350 cm^{-1} ; M.S (FAB) m/z 201 (MH^+), 156; HRMS calc. for $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}$ (MH^+) 201.1028; found: 201.1028.

Addition of phenyl azide to lactam **4**

A solution of lactam **4**¹⁸ (0.31 g; 1.68 mmol) and phenyl azide (0.2 g; 1.68 mmol) in toluene (2 mL) was heated at 85 °C for 17 h. After cooling, the toluene was removed with a pipette and the yellow solid which remained was then washed with petroleum ether (yield 0.375 g; 75%).

TLC revealed the presence of four compounds. The product was chromatographed on silica using 1:1 diethyl ether:ethyl acetate as eluant to give samples of the four triazolines as pure fractions, together with mixed fractions (total 60%) and a small quantity of unchanged **4** (ca. 10%). **19** (30 mg) Rf 0.55, m.p. 195 – 197°C; ν_{\max} (CH₂Cl₂) 1675 cm⁻¹; M.S. (FAB) 277 (MH⁺ - 28);¹⁷ **18** + **19** (125 mg); **18** (10 mg) Rf 0.48; ν_{\max} (CH₂Cl₂) 1675 cm⁻¹; HRMS calc. for C₁₈H₁₇N₄O (MH⁺): 305.1402, found: 305.1403; **20** (15 mg) Rf 0.24; ν_{\max} (CH₂Cl₂) 1675 cm⁻¹; HRMS calc. for C₁₈H₁₇N₄O (MH⁺): 305.1402, found: 305.1402; **20** + **21** (55 mg); **21** (70 mg) Rf 0.15; ν_{\max} (CH₂Cl₂) 1675 cm⁻¹; M.S. (FAB) 277 (MH⁺ - 28);¹⁷

Analysis of the ¹H NMR spectra gave the following overall yields: **18** (19%); **19** (33%); **20** (13%); **21** (32%). ¹H NMR data for all four compounds are shown in Table 1.

Photolysis of triazolines **18** and **19**; formation of *exo*-aziridine **22**

A mixture of **18** and **19** (96 mg) in acetone (52 mL) was irradiated in a quartz tube for 2.5 h using a Hanovia medium pressure lamp. The solvent was removed under vacuum and chromatographed on silica using 70:30 diethyl ether:petroleum ether to give **22** as white crystals (71 mg; 81%), m.p. 184 – 186 °C. ¹H NMR (CDCl₃, 300 MHz) see Table 1; ¹³C NMR (CDCl₃, 75 MHz) δ 33.0 (CH₃), 42.1, 42.4, 50.5, 59.8, 120.1, 122.6, 123.3, 125.6, 126.6, 127.7, 129.0 (CH), 138.2, 139.8, 151.4 (C), 171.2 (CO); ν_{\max} (CH₂Cl₂) 1675 cm⁻¹; M.S. m/z 276 (M⁺), 235, 218, 161, 77, 28*; HRMS (FAB) calc. for C₁₈H₁₇N₂O (MH⁺): 277.1341; found: 277.1341.

Photolysis of triazolines **20** and **21**; formation of *endo*-aziridine **23**

A mixture of **20** and **21** (58 mg) in acetone (30 mL) was irradiated for 2.5 h and was chromatographed as described above to give **23** as a white waxy solid (42 mg; 80%). ¹H NMR (CDCl₃, 300 MHz) see Table 1; ¹³C NMR (CDCl₃, 75 MHz) δ 32.8 (CH₃), 35.7, 42.3, 51.1, 62.4, 120.0, 122.37, 122.43, 124.9, 126.8, 127.8, 128.8 (CH), 134.9, 137.0, 151.4 (C), 173.5 (CO); ν_{\max} (CH₂Cl₂) 1675 cm⁻¹; M.S. m/z 276 (M⁺), 235, 184, 161, 128, 116, 77, 42, 32, 28*; HRMS (FAB) calc. for C₁₈H₁₇N₂O (MH⁺): 277.1341; found: 277.1341.

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12. (a) A claim has been made that homoallylic interactions between the nitrogen and the double bond in derivatives of **6** (X = NCO₂R) induce total regioselectivity in Pd-catalysed reductive Heck reactions [Kasyan, A; Wagner, C.; Maier, M.E. *Tetrahedron* **1998**, *54*, 8047]. Our own results disagree with this [Cox, C.D.; Malpass, J.R. *Tetrahedron Lett.* **1999**, *40*, 1419; *Tetrahedron* **1999**, *55*, 11879], showing little discrimination. (b) Azide addition to 2-phenylsulphonyl-2-azabicyclo[3.2.1]octa-3,6-diene gives an unequal ratio (87:13) of regioisomeric (*exo*) triazolines with a preference for addition of the negative end of the 1,3-dipole to the alkene carbon furthest from nitrogen: Taniguchi, H.; Ikeda, T.; Imoto, E. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1859.
13. (a) compounds **2a** & **6** in Belkacemi, D.; Malpass, J.R. *Tetrahedron* **1993**, *49*, 9105. (b) compounds **9** & **16** in ref. 7.
14. Clearly, the *N*-containing bridge in (**18**) - (**23**) should take priority in defining the terms *exo*- and *endo*- with respect to the facial attack on (**4**) but this unfortunately reverses the terminology with respect to the norbornyl and hetero-norbornyl adducts in Scheme 1. In this paper, we prefer to use the benzo- group as the point of reference in line with previous usage (ref. 13a and references therein).

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