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Synthesis of Hindered Spiro-Oxindoles by Photolysis of 1-(1-Alkenyl)benzotriazoles

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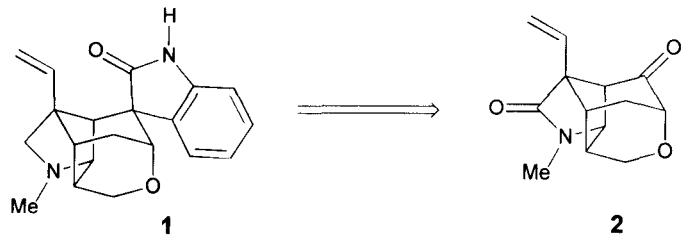
Abstract: Photolysis of 1-(1-alkoxy-1-alkenyl)benzotriazoles gives moderate yields of 2-alkoxy-indolenines, which can be hydrolysed to oxindoles. A side reaction leads to the formation of imino-oxetanes. The formation of the 2-alkoxy-indolenines is quite insensitive to steric hindrance at the reacting centres. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Keywords: Benzotriazoles; Silicon and compounds; Spiro compounds; Radicals and radical reactions.

INTRODUCTION

A key step in our total synthesis[1,2] of the oxindole gelsemine **1** involved the conversion of the ketone functionality in **2** into a spiro-oxindole (Scheme 1).



Scheme 1

Extensive investigations in our laboratory and elsewhere[3-6] have shown that the conversion of a sterically hindered ketone, such as adamantanone into an oxindole is not an easy process, and furthermore, that many of the methods which are successful with the model do not work in the real series. After the expenditure of considerable effort, we became convinced that the steric congestion at the reaction site was severe enough to prevent the application of most conventional methods for creation of a quaternary centre at this site, and that any successful method would need to be unusually insensitive to steric hindrance. In this context, a process involving C-C bond formation by combination of two radical centres was attractive because of the very low activation energy associated with these reactions.[7] A possible route to the required diradical is shown in Scheme 2.

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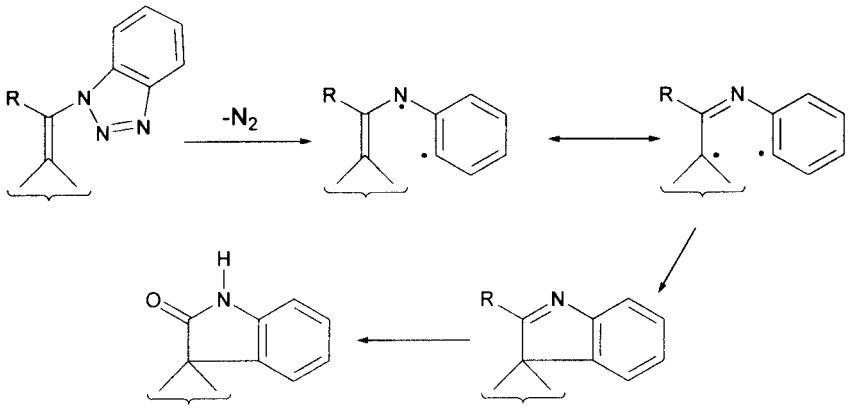


Scheme 2

The generation of such diradicals from 1-(1-alkenyl)benzotriazoles followed by C-C bond formation, has ample precedent,[8-12] including the photochemical synthesis of indoles developed by Wender and co-workers.[13] In order to test the route shown in Scheme 2, we first developed an efficient general route to 1-(1-alkenyl)benzotriazoles.[14] We now report in detail the reactions which these compounds undergo on irradiation and on the subsequent use of some of the photo-products in the synthesis of spiro-oxindoles.

RESULTS AND DISCUSSION

The first substrate to be examined was **3a** which was prepared by a base-induced aldol condensation between adamantanone and 1-(1-cyanomethyl)-1*H*-benzotriazole. As shown in Scheme 3, irradiation of **3a** in acetonitrile, followed by acid work up, gave a mixture of the desired cyclisation product **4a** (18%), and its hydrolysis product **5** (12%). The major product was the amide **6a** (53%), formed by the hydrolysis of the ketenimine intermediate obtained as a result of the migration of the cyano group onto the benzene ring (Scheme 3). A plausible mechanism for the transfer of the nitrile group involves initial attack of the aryl radical on the nitrile triple bond. At this stage, it was thought that this undesirable side reaction might be avoided by replacing the nitrile group by moieties which lack π-bonds, such as alkoxy groups.

A number of 1-(1-alkoxy-1-alkenyl)benzotriazoles were prepared by the procedure described in the preceding paper.[14] Photolysis of these substrates gave the results depicted in Scheme 4 and summarised in the Table.

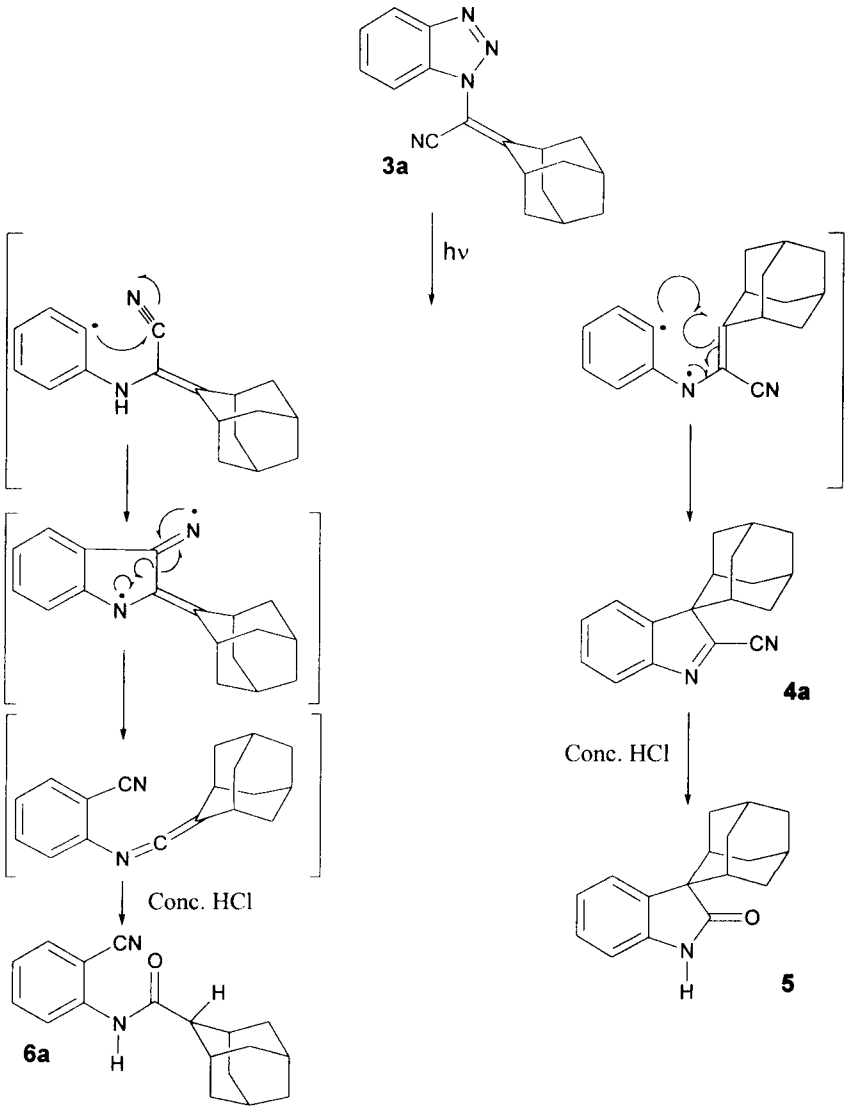
Photolysis of 1-(1-methoxy-1-alkenyl)benzotriazole **3b** (Scheme 5) gave the desired cyclisation product **4b** in a yield of 40%. However, an equal amount of the oxetane **7b** ((R^2 =R^3 = H) was formed, presumably *via* the hydrogen transfer/cyclisation mechanism outlined in Scheme 5.

Photolysis of the corresponding 1-ethoxy derivative **3c** gave a similar result. The corresponding iminoether **4c** was obtained in a yield of 43% along with the oxetane side-product **7c** (27%). Similarly, in the case of the 1-(2-propyloxy) substrate **3d**, the desired compound **4d** was isolated (41%).

Interestingly, the hydrogen transfer pathway led to a ketenimine intermediate by elimination of a molecule of acetone, and gave amide **6d** (40%) upon subsequent hydrolysis (Scheme 6).

In all the cases described, unwanted side reactions are triggered by hydrogen transfer. A number of strategies to reduce or alleviate this pathway were developed. For example, the 1-(1-aryloxy-1-

alkenyl)benzotriazoles **3e** and **3f** lack hydrogen atoms at the carbon α to the ether carbon atom, and so cannot undergo the hydrogen transfer process. However, the photolysis of both substrates did not give any of the desired cyclisation product **4** but led to the formation of the oxindoles **8e** and **8f** respectively, presumably as a result of the aryl transfer process depicted in Scheme 7.

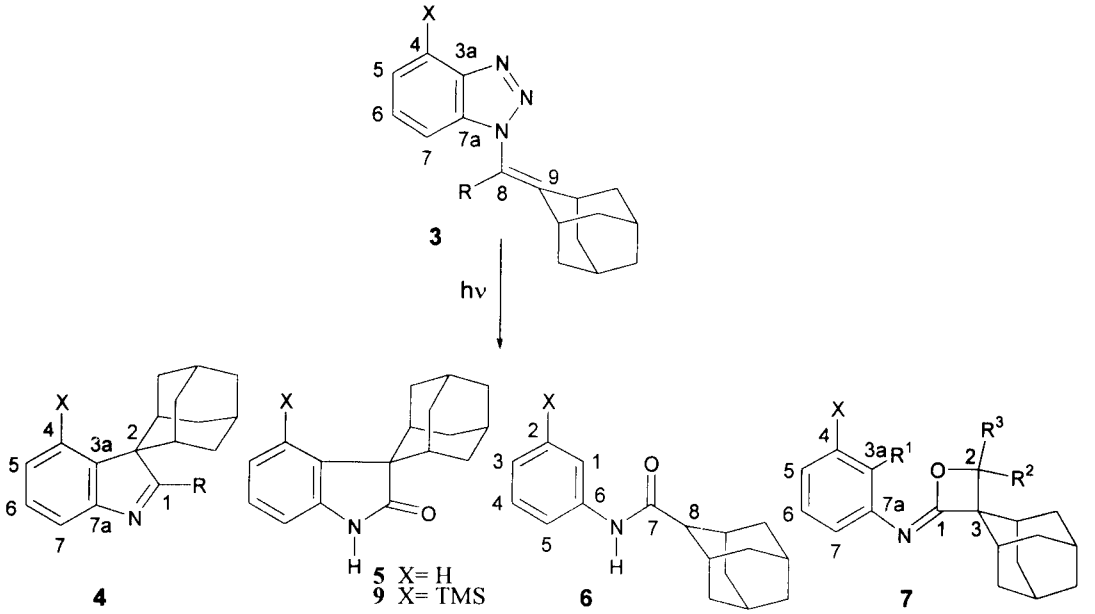


Scheme 3

The *para* substitution of the starting material **3f** is retained in **8f**, which is consistent with the suggested mechanism of formation.

One other attractive alternative was the introduction of a *tert*-butoxy group because of its lack of both hydrogen atoms at the α position and a π-bond to which a radical might add. As detailed in the preceding

paper,[14] the substrate **3g** could not be prepared by the Peterson condensation and was obtained by a different method.[15]

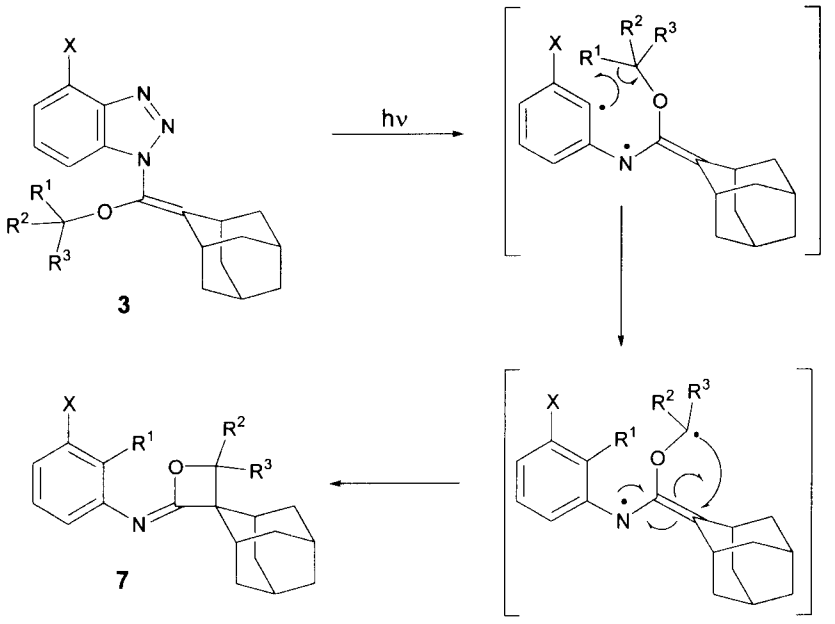


Scheme 4

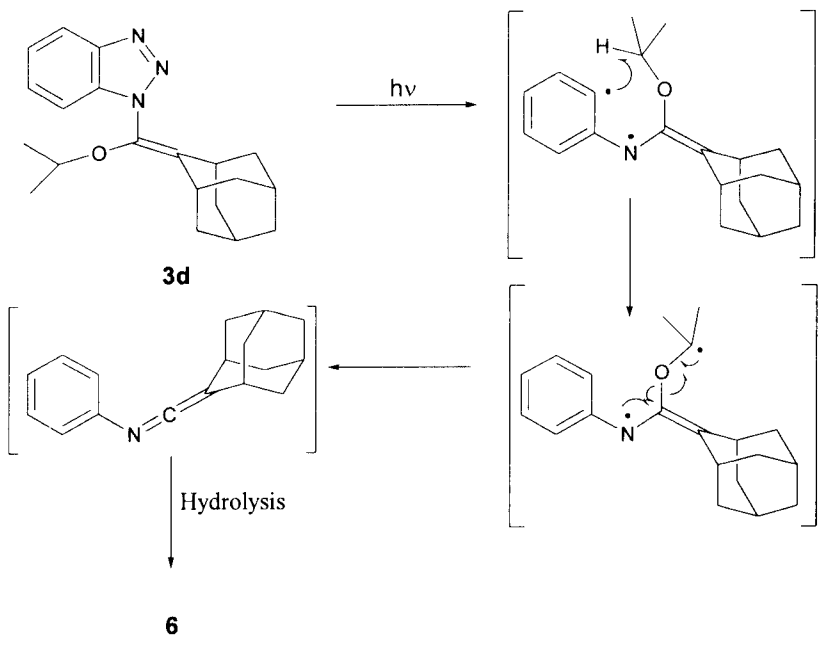
Table
Photolysis experiments.

Entry	R	X	**4** (%)	**5** (%)	**6** (%)	**7** (%)	**8** (%)
3a	CN	H	18	12	53	--	--
3b	OCH_3	H	40	--	--	40	--
3c	OC_2H_5	H	43	--	--	27	--
3d	O^iPr	H	41	--	40	--	--
3e	OPh	H	--	--	--	--	52
3f	OAr[a]	H	--	--	--	--	45
3g	O^tBu	H	--	35	--	--	--
3h	OCD_3	H	44	--	--	34	--
3i	OC_2D_5	H	36	--	--	27	--
3j	OCH_3	TMS	35	--	--	35	--
3k	OCD_3	TMS	41	--	--	36	--
3l	OPh	TMS	31	--	--	--	--

[a] Ar = 4-$MeOC_6H_4$



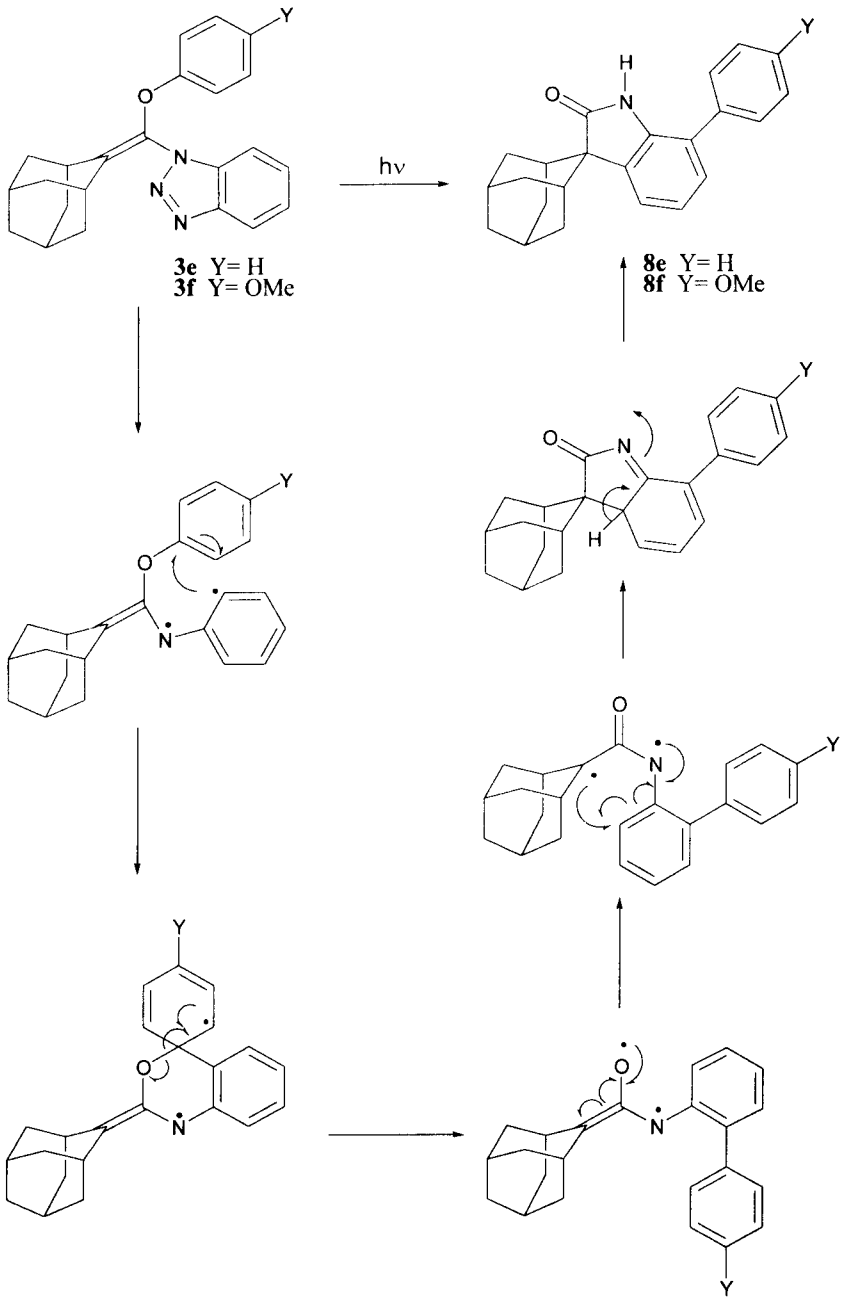
Scheme 5



Scheme 6

Its photolysis did lead to compound **5** as the sole isolatable product, in a disappointing yield of 35%. The steric hindrance existing in the presumed iminoether intermediate **4g** could provide the driving force for the

spontaneous conversion to **5** either by elimination of 2-methyl-propene or by hydrolysis brought about by traces of water.



Scheme 7

The *para* substitution of the starting material **3f** is retained in **8f**, which is consistent with the suggested

mechanism of formation.

One other attractive alternative was the introduction of a *tert*-butoxy group because of its lack of both hydrogen atoms at the α position and a π-bond to which a radical might add. As detailed in the preceding paper,[14] the substrate **3g** could not be prepared by the Peterson condensation and was obtained by a different method.[15] Its photolysis did lead to compound **5** as the sole isolatable product, in a disappointing yield of 35%. The steric hindrance existing in the presumed iminoether intermediate **4g** could provide the driving force for the spontaneous conversion to **5** either by elimination of 2-methyl-propene or by hydrolysis brought about by traces of water.

Another approach was the replacement of the hydrogen atoms of the alkoxy group by deuterium atoms. The C-D bond is known to be stronger than the C-H bond[16] and therefore the deuterium transfer process may take place to a lesser extent. In the event, photolysis of **3h** gave a slightly improved yield of **4h** (44%) and a slightly reduced yield (34%) of **7h** (R^2=R^3=D) for a ratio of **4h**:**7h** of 1.3:1. The photolysis of **3i** gave a similar ratio of **4i**:**7i** in a lower overall yield of 63%.

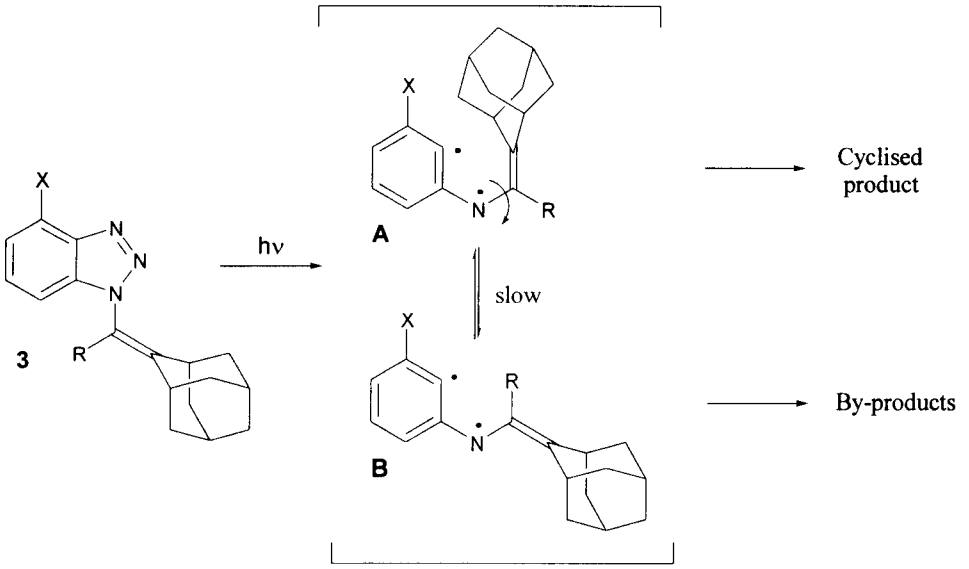
The availability of 4-trimethylsilyl substituted benzotriazoles, **3j**, **3k**, and **3l**, provided an opportunity to test the effect of substitution at the 4-position on both the desired and the unwanted photo-induced pathways. The presence of such a large substituent on the carbon atom adjacent to the reacting centre might be expected to significantly reduce the C-C bond and to a lesser extent the C-H bond formation at this centre. Thus a reduction in the formation of products **4j** and **4k** might be anticipated, particularly since non-bonded interactions between the trimethylsilyl group and adamantane nucleus are likely to cause very severe steric strain. As shown in the table, the presence of a trimethylsilyl group at the 4-position had no significant effect on the course of the photolysis of **3j** and **3k**. As in the photolysis of **3b** and **3h**, the same distribution of photo-products was observed. On the other hand, the photolysis of **3l** gave the compound **4l** as the only product isolated albeit in the low yield of 31%. These results indicate that the 4-trimethylsilyl substituent completely blocks the transfer of an aryl group, but has very little effect on either hydrogen/deuterium transfer or cyclisation to the iminoether structure of type **4** (X = TMS). An X-ray structure of the cyclised product **4j** provided confirmation of the extraordinary strain imposed on the molecule by the steric clash of the TMS group and the adamantyl moiety.[17]

In the light of these results, it can be concluded that the desired cyclisation process occurs to the extent to 30 to 45% alongside competitive side reactions. However, somewhat surprisingly, the cyclisation pathway does not benefit significantly when the side reactions are prevented (as in the compounds **3e**, **3g**, **3j** and **3l**). This implies that, as depicted in Scheme 8, the conformation of the diradical intermediate required for transfer of hydrogen (or aryl or nitrile) may not interconvert sufficiently rapidly with the conformation required for the desired cyclisation. Similar situations have been reported in the literature[18-20] in which 1,5-hydrogen transfer reactions of radicals in amide systems led to different products. These observations were explained on the basis that the amide rotamers interconvert with a lifetime of 10^{-1}s to 10^{-3}s whereas the radical lifetimes do not exceed 10^{-5}s. In other words, the conformation of the amide is fixed during the lifetime of the radical. A similar analysis can be applied to our systems. The photo-induced extrusion of N_2 generates a diradical intermediate which can exist in two different reactive conformations A and B (Scheme 7). A and B do not interconvert because of the possible high energy barrier to rotation and the very short lifetime of the diradical species and lead to their respective products. This hypothesis provides an explanation for the fact that even when the hydrogen abstraction pathway is rendered impossible, the cyclisation process does not take place to any greater extent.

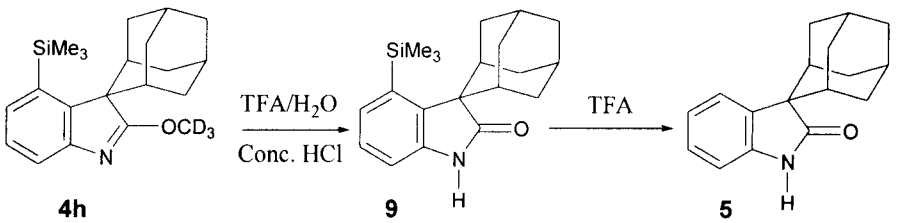
Finally, the hydrolysis and desilylation of compound **4h** yielded the spiro-oxindole **5** in two steps, in an overall yield of 85% (Scheme 9).

The presence of the TMS group in compound **9** makes it an attractive intermediate for further chemical

manipulations such as *ipso* substitution.[21] Barrett and co-workers[22] have shown that 4-TMS substituted indoles are potential intermediates in the synthesis of natural products such as ergot alkaloids.



Scheme 8



Scheme 9

CONCLUSION

We have shown that 1-(1-alkenyl)benzotriazoles are useful intermediates for the synthesis of spiro-oxindoles. The method described herein involves the formation of a C-C bond by combination of two radical centres and the subsequent hydrolysis of the iminoether intermediate for the construction of highly sterically hindered spiro-oxindoles. The photolysis of a series of compounds carefully designed, showed that this method permits the formation of a C-C bond in remarkably sterically congested environments.

EXPERIMENTAL

The preamble described in the experimental section of the preceding paper[14] applies herein but for the following details. The structures **3**, **4**, **6** and **7** (Scheme 4) carry the numbering system referred to in ^1H and ^{13}C data. The ^{13}C signals for C-3a and C-2 in compounds 7h and 7k are not reported. Due to the dramatic diminution of the ^{13}C signals resulting from deuteration, the expected triplet and quintet could be assigned unambiguously. Photolysis experiments were carried out in a Rayonet photochemical reactor, fitted with a high pressure mercury lamp, with the cooling fan on, unless otherwise indicated. Acetonitrile was distilled from calcium hydride

***1-(Adamantylidene-cyano-methyl)-1H-benzotriazole* (3a).** Dry diisopropylamine (0.36 ml, 2.55 mmol) was dissolved in dry THF (15 ml) under a dry nitrogen atmosphere and cooled to -78°C. *n*-BuLi (1.7 ml of a 1.45 M solution in hexanes, 2.47 mmol) was added dropwise with stirring and the mixture was stirred at -78°C for 15 min, before 1-cyanomethyl-1*H*-benzotriazole (366 mg, 2.32 mmol) was added dropwise. The resulting mixture was stirred for 1 h and adamantanone (338 mg, 2.25 mmol) was added dropwise. The reaction mixture was stirred at -78°C for 15 min and was then allowed to warm to room temperature over 1 hour and stirred at room temperature for 16 hours. Ether (30 ml) and a saturated NH_4Cl solution (20 ml) were added. The organic layer was successively washed with a saturated aqueous solution of NH_4Cl(3x20 ml), dried with $MgSO_4$ and filtered. Removal of the solvent gave an oil. Purification by column chromatography, using Kieselgel G and elution with 40/60 ether/light petroleum gave **3a** (494 mg, 76%); microcrystals; mp 114.8 - 116.5°C; ^1H NMR (90 MHz; $CDCl_3$) 8.05 (1H, d, J = 8 Hz, H-4), 7.6-7.3 (3H, m, H-5, H-6, H-7), 3.4 (1H, br.s), 2.4 (1H, br.s) and 2.2-1.7 (12H, br.m) (adamantyl); ^{13}C NMR (22.5 MHz, $CDCl_3$) 175.19 (C-9), 145.20 (C-3a), 132.96 (C-7a), 128.71 (C-6), 124.57, (C-5), 120.12 (C-4), 111.3 (CN), 109.10 (C-7), 97.8 (C-8), 39.46, 39.19 and 35.80 (CH_2 adamantyl), 37.16, 33.93 and 27.21 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 2230 (CN); λ_{max} (EtOH)/nm 216, 230, 247, 281; Anal. Calcd. for $C_{18}H_{18}N_4$: C, 74.5; H, 6.2; N, 19.3. Found: C, 74.3; H, 6.2; N, 19.1.

***Photolysis of* 3a.** Compound **3a** (49 mg, 0.17 mmol) was dissolved in dry acetonitrile (10 ml), under a dry argon atmosphere and the solution was subsequently subjected to ultrasound for 20 min under a positive pressure of dry argon and photolysed for 3h. Water (2ml) was the added and the mixture was stirred for 14 h, before conc. HCl (3 drops) was added and the stirring was prolonged for one more hour. A saturated aqueous solution of $NaHCO_3$ (5 ml) and ether (25 ml) were added. The organic layer was successively washed with water (10 ml), brine (10 ml), dried with $MgSO_4$ and filtered. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography using flash silica and elution with 20/80 ether/light petroleum gave three products **4a**, **5** and **6a**. **4a** (8 mg, 18%); microcrystals; mp 123 - 127°C; ^1H NMR (300 MHz; $CDCl_3$) 7.84 (1H, d, J = 8 Hz) and 7.78 (1H, d, J = 8 Hz) (H-4, H-7), 7.56-7.38 (2H, m, H-5, H-6), 3.03

(2H, d, J = 16 Hz), 2.62 (2H, d, J = 16 Hz), 2.22 (2H, d, J = 16 Hz) and 2.1-1.6 (8H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 159.09 (C-1), 152.76 (C-7a), 142.88 (C-3a), 128.50, 128.06, 127.24, 123.64 (C-4, C-5, C-6, C-7), 118.13 (CN), 67.29 (C-2), 39.16, 34.53 and 33.21 (CH_2 adamantyl), 33.45, 26.68 and 26.59 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 2220 (CN), 1510, 1455, 1200, 1090; HRMS Calcd. for $C_{18}H_{20}N_2O$: 280.1576 (M^+). Found: 280.1576.

***Compound* 6a.** (25 mg, 53%); Oil; ^{1}H NMR (90 MHz; $CDCl_3$) 8.45 (1H, d, J = 7 Hz, H-5), 7.95 (1H, br.s, NH), 7.7-7.45 (2H, m, H-2, H-4), 7.15 (1H, t, J = 7 Hz, H-3), 2.70 (1H, br.s), 2.45 (2H, br.s) and 2.3-1.5 (12H, m) (adamantyl); ^{13}C NMR (22.5 MHz, $CDCl_3$) 172.92 (C-7), 140.71 (C-6), 134.10 (C-4), 132.01 (C-2), 123.75 (C-3), 121.13 (C-5), 116.41 (C-1), 101.67 (CN), 51.10 (C-8), 38.10, 33.15 and 37.05 (CH_2 adamantyl), 30.09 and 27.21 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 3405 (NH), 2215 (CN), 1700 (C=O), 1600, 1580, 1515, 1450, 1300, 1200, 1170, 1105, 1070, 1050; HRMS Calcd. for $C_{18}H_{20}N_2O$: 280.1576 (M^+). Found: 280.1576.

***Photolysis of* 3b.** Compound **3b** (67 mg, 0.23 mmol) was dissolved in dry acetonitrile (10 ml), under a dry argon atmosphere and the solution was subsequently subjected to ultrasound for 20 min under a positive pressure of dry argon and photolysed for 1.5 h. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography using flash silica and elution with 10/90 ether/light petroleum gave two products **4b** and **7b**. **4b** (24 mg, 40%); microcrystals; mp 135-137°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.76 (1H, d, J = 8 Hz, H-4), 7.37 (1H, d, J = 8 Hz, H-7), 7.27 (1H, t, J = 8 Hz) and 7.05 (1H, t, J = 8 Hz) (H-5, H-6), 4.13 (3H, s, OMe), 2.78 (2H, d, J = 12 Hz), 2.64 (2H, d, J = 12 Hz) and 2.16-1.61 (10H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 184.57 (C-1), 152.19 (C-7a), 141.18 (C-3a), 127.59, 126.99, 122.02, 118.36 (C-4, C-5, C-6, C-7), 58.74 (C-2), 56.05 (OMe), 39.77, 33.59 and 32.81 (CH_2 adamantyl), 33.16, 27.16 and 26.94 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 1750, 1680, 1585, 1475, 1350, 1330, 1110, 1020; Anal. Calcd. for $C_{18}H_{21}NO$: C, 80.9; H, 7.9; N, 5.2. Found: C, 80.95; H, 8.0; N, 5.25.

***Compound* 7b.** (24 mg, 40%); microcrystals; mp 70 - 73°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.51-7.04 (5H, m, H-3a, H-4, H-5, H-6, H-7a), 4.37 (2H, s, H-2), 2.62 (2H, br. d, J = 12 Hz), 2.32 (2H, br.s) and 2.2-1.6 (10H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 164.72 (C-1), 144.31 (C-7a), 128.61, 123.24 (C-3a, C-7, C-4, C-6), 123.90 (C-5), 76.62 (C-2), 58.55 (C-3), 36.78, 34.59 and 33.00 (CH_2 adamantyl), 33.55, 26.55 and 26.47 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 1725, 1620, 1495, 1390, 1225, 1160, 1100w, 1080, 1000, 935, 920; Anal. Calcd. for $C_{18}H_{21}NO$: C, 80.9; H, 7.9; N, 5.2. Found: C, 81.20; H, 8.10; N, 5.05.

***Photolysis of* 3c.** Same procedure as the one described for **3b** using **3c** (98 mg, 0.32 mmol) in dry acetonitrile (10 ml) and irradiating for 1.5 h. Removal of the solvent under reduced pressure gave an oil. Purification by

column chromatography using flash silica and elution with 10/90 ether/light petroleum gave two products **4c** and **7c**. **4c** (38 mg, 43%); microcrystals; mp 122-124°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.85 (1H, d, J = 8 Hz, H-4), 7.44 (1H, d, J = 8 Hz, H-7), 7.37 (1H, t, J = 8 Hz) and 7.17 (1H, t, J = 8 Hz) (H-5, H-6), 4.61 (2H, q, J = 6 Hz, OEt), 2.95 (2H, br.d, J = 12 Hz), 2.78 (2H, br.d, J = 12 Hz), 2.24-1.72 (10H, m) (adamantyl), 1.58 (3H, t, J = 6 Hz, OEt); ^{13}C NMR (75 MHz, $CDCl_3$) 183.81 (C-1), 152.48 (C-7a), 140.97 (C-3a), 127.54, 126.96, 121.85, 118.24 (C-4, C-5, C-6, C-7), 65.10 ($O\underline{C}H_2CH_3$), 58.60 (C-2), 39.84, 33.66 and 32.79 (CH_2 adamantyl), 33.22, 27.21 and 27.20 (CH adamantyl), 14.53 ($OCH_2\underline{C}H_3$); ν_{max} (dichloromethane)/cm^{-1} 1560, 1455, 1310; Anal. Calcd. for $C_{19}H_{23}NO$: C, 81.1; H, 8.2; N, 5.0. Found: C, 81.45; H, 8.25; N, 4.55.

***Compound* 7c.** (24 mg, 27%); Oil; ^{1}H NMR (300 MHz; $CDCl_3$) 7.26 (2H, t, J = 8 Hz) and 7.11 (2H, d, J = 8 Hz) (H-3a, H-7, H-4, H-6), 7.05 (1H, t, J = 8 Hz, H-5), 4.55 (1H, q, J = 6 Hz, H-2), 2.64 (2H, br.d, J = 12 Hz), 2.36 (1H, br.s), 2.20 (1H, br.s) and 1.96-1.57 (10H, m, adamantyl), 1.54 (3H, d, J = 6 Hz, Me); ^{13}C NMR (75 MHz, $CDCl_3$) 164.29 (C-1), 144.74 (C-7a), 128.59, 123.19 (C-3a, C-7, C-4, C-6), 123.68 (C-5), 83.67 (C-2), 58.66 (C-2), 36.92, 34.24, 33.96, 33.11 and 33.00 (CH_2 adamantyl), 35.77, 29.12, 27.05, 26.04 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 1715, 1590, 1025; Anal. Calcd. for $C_{19}H_{23}NO$: C, 81.1; H, 8.2; N, 5.0. Found: C, 81.4; H, 8.1; N, 4.9.

***Photolysis of* 3d**. Same procedure as the one described for **3b** using **3d** (41 mg, 0.13 mmol) in dry acetonitrile (10 ml) and irradiating for 1.5 h. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography using Kieselgel and elution with 15/8 ether/light petroleum gave two products **4d** and **6d**. **4d** (15 mg, 41%); microcrystals; mp 112-115°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.67 (1H, d, J = 7 Hz, H-4), 7.32-7.18 (2H, m) and 6.98 (1H, t, J = 7 Hz) (H-5, H-6, H-7), 5.34 (1H, m, O^{i}Pr), 2.81 (2H, br.d, J = 12 Hz), 2.62 (2H, br.d, J = 12 Hz) and 2.10-1.43 (10H, m) (adamantyl), 1.37 (6H, d, J = 6, O^{i}Pr); ^{13}C NMR (75 MHz, $CDCl_3$) 184.39 (C-1), 153.29 (C-7a), 141.87 (C-3a), 127.68, 126.99, 122.13, 118.26 (C-4, C-5, C-6, C-7), 72.49 ($O\underline{C}H(CH_3)_2$), 58.81 (C-2), 40.06, 34.12 and 32.83 (CH_2 adamantyl), 33.61, 27.17 and 26.94 (CH adamantyl), 21.97 (CH_3, isopropyl); ν_{max} (dichloromethane)/cm^{-1} 1600, 1560, 1450, 1360m, 1300, 1100, 905; Anal. Calcd. for $C_{20}H_{25}NO$: C, 81.35; H, 8.5; N, 4.75. Found: C, 81.65; H, 8.35; N, 4.4.

***Compound* 6d**. (13 mg, 40%); microcrystals; mp 164.5-166.5°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.48 (2H, d, J = 8 Hz) and 7.27 (2H, t, J = 8 Hz) (H-1, H-5, H-2, H-4), 7.03 (1H, t, J = 8 Hz, H-3), 2.58 (1H, br.s, H-8), 2.31 (2H, br.s) and 2.03-1.60 (12H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 72.56 (C-7), 138.11(C-6), 128.92, 119.80 (C-1, C-5, C-2, C-4), 123.98 (C-3), 50.85 (C-8), 38.34, 33.30 and 37.27 (CH_2 adamantyl), 30.22, 27.42 and 27.37 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 3420 (NH), 1675 (C=O), 1590, 1500, 1425, 1300; Anal. Calcd. for $C_{17}H_{21}NO$: C, 80.3; H, 7.9; N, 5.5. Found: C, 79.95; H, 8.1; N, 5.7.

***Photolysis of* 3e.** Same procedure as the one described for **3b** using **3e** (88 mg, 0.25 mmol) in dry acetonitrile (20 ml) and irradiating for 2.5 h. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography, using Kieselgel and elution with 20/20/60 ether/dichloromethane/light petroleum gave product **8e** (42 mg, 52%); microcrystals; mp 255-257°C(sublimation); ^{1}H NMR (300 MHz; $CDCl_3$) 7.94 (1H, br.s, NH), 7.78 (1H, d, J = 6 Hz, H-4), 7.55-7.35 (5H, m, aromatic H), 7.23 (1H, d, J = 6 Hz, H-6), 7.08 (1H, t, J = 6 Hz, H-5), 3.0 (2H, br.d, J = 12 Hz), 2.64 (2H, br.d, J = 12 Hz) and 2.12-1.53 (10H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 180.70 (C-1), 137.99, 137.80, 134.65, 123.58 (*ipso*-C, C-3a, C-7, C-7a), 129.11, 128.22 (*o*-, *m*-C), 127.66, 127.65, 127.41, 121.16 (*p*-C, C-4, C-5, C-6), 53.95 (C-2), 39.67, 33.09 and 31.61 (CH_2 adamantyl), 33.54, 27.21 and 26.92 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 3450 (NH), 1710 (C=O), 1520, 1255; Anal. Calcd. for $C_{23}H_{23}NO$: C, 83.9; H, 7.0; N, 4.25. Found: C, 83.7; H, 7.15; N, 4.15.

***Photolysis of* 3f.** Same procedure as the one described for **3b** using **3f** (31 mg, 0.08 mmol) in dry acetonitrile (15 ml) and irradiating for 3 h. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography, using Kieselgel and elution with 5/35/60 ether/dichloromethane/light petroleum gave product **8f** (13 mg, 45%); microcrystals; mp 273-274°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.86 (1H, br.s, NH), 7.75 (1H, d, J = 8 Hz, H-4), 7.35 (2H, d, J = 7 Hz), 6.99 (2H, d, J = 7 Hz) (*o*-, *m*-H), 7.20 (1H, d, J = 8 Hz, H-6), 7.06 (1H, t, J = 8 Hz, H-5), 3.85 (3H, s, OMe), 3.01 (2H, br.d, J = 12 Hz), 2.63 (2H, br.d, J = 12, Hz) and 2.11-1.53 (10H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 180.70 (C-1), 159.15 (*p*-C), 137.94, 134.59, 130.10, 123.30 (*ipso*-C, C-3a, C-7, C-7a), 129.33 (*o*-C), 127.95, 127.06, 121.14 (C-4, C-5, C-6), 114.54 (*m*-C), 53.34 (OMe), 54.00 (C-2), 39.67, 33.08 and 31.64 (CH_2 adamantyl), 33.53, 27.20 and 26.89 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 3420 (NH), 1680 (C=O), 1505, 1240; Anal. Calcd. for $C_{24}H_{25}NO_2$: C, 80.2; H, 7.0; N, 3.9. Found: C, 80.0; H, 6.95; N, 3.75.

***Photolysis of* 3h.** Same procedure as the one described for **3b** using **3h** (55 mg, 0.18 mmol) in dry acetonitrile (10 ml) and irradiating for 1.5 h. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography using flash silica and elution with 10/90 ether/light petroleum gave two products **4h** and **7h**. **4h** (22 mg, 44%); microcrystals; mp 129-132°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.73 (1H, d, J = 8 Hz, H-4), 7.35 (1H, d, J = 8 Hz, H-7), 7.27 (1H, t, J = 8 Hz) and (1H, t, J = 8 Hz) (H-5, H-6), 2.76 (2H, d, J = 15 Hz), 2.66 (2H, d, J = 15 Hz) and 2.13-1.61 (10H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 184.58 (C-1), 152.21 (C-7a), 141.18 (C-3a), 127.59, 126.98, 122.02, 118.37 (C-4, C-5, C-6, C-7), 58.75 (C-2), 39.78, 33.62 and 32.84 (CH_2 adamantyl), 33.20, 27.18 and 26.97 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 1600, 1570, 1460, 1365, 1345, 1315, 1260-1240, 1130, 980; Anal. Calcd. for $C_{18}H_{18}D_3NO$: C, 80.0; H/D, 7.95; N, 5.2. Found: C, 79.9; H/D, 9.15; N, 5.3.

***Compound* 7h.** (17 mg, 34%); microcrystals; mp 59.0-64.5°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.4-7.24 (2H, m),

7.19-7.03 (2H, m) (H-4, H-5, H-6, H-7), 2.55 (2H, d, J = 12 Hz), 2.28 (1H, s) and 2.02-1.59 (11H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 164.75 (C-1), 144.26 (C-7a), 128.60, 128.49, 123.90, 123.28 (C-4, C-7, C-5, C-6), 58.36 (C-3), 36.79, 34.31 and 33.01 (CH_2 adamantyl), 33.52, 26.57 and 26.49 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 2230 (C-D), 1710, 1575, 1455, 1435, 1210, 1185, 1090, 1070, 945, 900; Anal. Calcd. for $C_{18}H_{18}D_3NO$: C, 80.0; H/D, 7.95; N, 5.2. Found: C, 80.15; H/D, 9.05; N, 5.1.

***Photolysis of* 3i.** Same procedure as the one described for **3b** using **3i** (34 mg, 0.11 mmol) in dry acetonitrile (10 ml) and irradiating for 3 h. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography using Kieselgel and elution with 10/90 ether/light petroleum gave two products **4i** and **7i**. **4i** (12 mg, 36%); microcrystals; mp 118-120°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.8 (1H, d, J = 8 Hz, H-4), 7.47-7.25 (2H, m) and 7.09 (1H, t, J = 8 Hz) (H-5, H-6, H-7), 2.87 (2H, br.d, J = 12 Hz), 2.69 (2H, br.d, J = 12 Hz) and 2.2-1.6 (10H, m) (adamantyl); ^{13}C NMR (75 MHz, $CDCl_3$) 183.90 (C-1), 152.53 (C-7a), 141.03 (C-3a), 127.57, 127.00, 121.88, 118.28 (C-4, C-5, C-6, C-7), 58.67 (C-2), 39.90, 33.72 and 32.85 (CH_2 adamantyl), 33.29, 27.26 and 27.07 (CH adamantyl); ν_{max} (dichloromethane)/cm^{-1} 1560, 1450, 1360, 1340, 1190, 1090, 1050; Anal. Calcd. for $C_{19}H_{18}D_5NO$: C, 79.7; H/D, 8.3; N, 4.9. Found: C, 79.95; H/D 8.65; N, 5.15.

***Photolysis of* 3j.** Same procedure as the one described for **3b** using **3j** (101 mg, 0.28 mmol) in dry acetonitrile (15 ml) and irradiating for 2 h (fan off). Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography, using flash silica and elution with 10/90 ether/light petroleum gave two products **4j** and **7j**. **4j** (33 mg, 35%); microcrystals; mp 114.1-116.6°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.45 (1H, d, J = 8 Hz, H-7), 7.30 (1H, d, J = 8 Hz) and 7.17 (1H, t, J = 8 Hz) (H-5, H-6), 4.05 (3H, s, OMe), 2.80 (2H, br.d, J = 15 Hz), 2.45 (2H, br.d, J = 15 Hz) and 1.60-2.05 (10H, m) (adamantyl), 0.35 (9H, s, aryl TMS); ^{13}C NMR (75 MHz, $CDCl_3$) 185.59 (C-1), 151.71, 150.10 (C-3a, C-7a), 136.11 (C-4), 131.20 (C-6), 125.95 (C-5), 120.29 (C-7), 64.51 (C-2), 55.12 (Me), 38.57, 36.00 and 33.64 (CH_2 adamantyl), 36.07, 27.36 and 26.92 (CH adamantyl), 3.73 (aryl TMS); ν_{max} (dichloromethane)/cm^{-1} 3060, 2990, 2900, 2300, 1600, 1415, 1250, 890, 750; Anal. Calcd. for $C_{21}H_{29}NOSi$: C, 74.28; H, 8.61; N, 4.13. Found: C, 74.00; H, 8.85; N, 4.05.

***Compound* 7j.** (33 mg, 35%); microcrystals; mp 72.4-74.6°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.35-7.15 (4H, m, H-3a, H-5, H-6, H-7), 4.32 (2H, s, H-2), 2.60 (2H, br.d, J = 15 Hz), 2.32 (2H, br.s) and 2.00-1.60 (10H, m) (adamantyl), 0.25 (9H, s, aryl TMS); ^{13}C NMR (75 MHz, $CDCl_3$) 164.59 (C-1), 143.63 (C-7a), 140.91 (C-4), 128.88, 128.23, 127.93, 123.63 (C-3a, C-5, C-6, C-7), 76.55 (C-2), 58.61 (C-3), 36.83, 34.63 and 33.05 (CH_2 adamantyl), 33.60, 26.60 and 26.53 (CH adamantyl), -1.12 (aryl TMS); ν_{max} (dichloromethane)/cm^{-1} 2900, 2850, 1720, 1570, 1450, 1070, 930; Anal. Calcd. for $C_{21}H_{29}NOSi$: C, 74.28; H, 8.61; N, 4.13. Found: C, 74.15; H, 8.80; N, 4.05.

***Photolysis of* 3k.** Same procedure as the one described for **3b** using **3k** (102 mg, 0.28 mmol) in dry acetonitrile (15 ml) and irradiating for 2.25 h (fan off). Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography using flash silica and elution with 5/95 ether/light petroleum gave two products **4k** and **7k**. **4k** (38 mg, 41%); microcrystals; mp 104.9-106.9°C; ^{1}H NMR (300 MHz; $CDCl_3$) 7.45 (1H, d, J = 8 Hz, H-7), 7.30 (1H, t, J = 8 Hz) and 7.17 (1H, t, J = 8 Hz) (H-5, H-6), 2.80 (2H, br.d, J = 15 Hz), 2.45 (2H, br.d, J = 15 Hz) and 1.60-2.10 (10H, m) (adamantyl), 0.40 (9H, s, aryl TMS); ^{13}C NMR (75 MHz, $CDCl_3$) 185.63 (C-1), 151.88, 150.32 (C-3a, C-7a), 136.12 (C-4), 131.20 (C-6), 125.95 (C-5), 120.30 (C-7), 64.52 (C-2), 38.59, 36.09 and 33.66 (CH_2 adamantyl), 36.02, 27.38 and 26.62 (CH adamantyl), 3.73 (aryl TMS); ν_{max} (dichloromethane)/cm^{-1} 2920, 2860, 2270 (C-D), 1600, 1580, 1375, 1080, 835; Anal. Calcd. for $C_{21}H_{26}D_3NOSi$: C, 73.63; H/D, 8.56; N, 4.09. Found: C, 73.45; H/D, 8.85; N, 4.00.

***Compound* 7k.** (33 mg, 36%); microcrystals; mp 48.9-49.5°C; ^{1}H NMR (400 MHz; $CDCl_3$) 7.35-7.15 (3H, m, H-5, H-6, H-7), 2.55 (2H, br.d, J = 15 Hz), 2.30 (2H, br.s) and 1.95-1.60 (10H, m) (adamantyl), 0.25 (9H, s, aryl TMS); ^{13}C NMR (100 MHz, $CDCl_3$) 164.71 (C-1), 143.60 (C-7a), 140.85 (C-4), 128.93, 127.99, 123.69 (C-5, C-6, C-7), 58.44 (C-3), 36.87, 34.68 and 33.10 (CH_2 adamantyl), 33.59, 26.65 and 26.58 (CH adamantyl), -1.06 (aryl TMS); ν_{max} (dichloromethane)/cm^{-1} 3040, 2990, 2840, 2235 (C-D), 1710, 1440, 1240, 830, 730; HRMS Calcd. for $C_{21}H_{26}D_3NOSi$: 342.2206 (M^+). Found: 342.2210.

***Photolysis of* 3l.** Same procedure as the one described for **3b** using **3l** (80 mg, 0.19 mmol) in dry acetonitrile (30 ml) and irradiating for 1.5h (fan off). Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography, using flash silica and elution with 10/90 ether/light petroleum gave product **4l** (23 mg, 31%); Oil; ^{1}H NMR (400 MHz; $CDCl_3$) 7.45 (3H, m, H-5, H-6, H-7), 7.25 (4H, m, *o*- and *m*-H), 7.15 (1H, m, *p*-H), 3.10 (2H, br.d, J = 15 Hz), 2.55 (2H, br.d, J = 15 Hz), 1.65-2.15 (10H, m) (adamantyl), 0.45 (9H, s, aryl TMS); ^{13}C NMR (100 MHz, $CDCl_3$) 184.19 (C-1), 153.06, 151.29, 149.94, 136.24 (*ipso* C, C-3a, C-4, C-7a), 131.80, 125.95, 125.43, 121.24 (C-5, C-6, C-7, *p*-C), 129.57, 121.40 (*o*- and *m*-C), 64.54 (C-2), 38.66, 36.15 and 33.83 (CH_2 adamantyl), 36.20 , 27.42 and 26.68 (CH adamantyl), 3.83 (aryl TMS); ν_{max} (dichloromethane)/cm^{-1} 3040, 2900, 1460, 730; HRMS Calcd. for $C_{26}H_{31}NOSi$: 401.2174 (M^+). Found: 401.2184.

***Desilylation of* 4h.** Compound **4h** (42 mg, 0.12 mmol) was dissolved in TFA / H_2O (2:1, 6 ml) and the reaction mixture stirred at room temperature for 30 min before conc. HCl (1 ml) was added. It was then stirred for a further 6 h and water (30 ml) was added. The reaction was extracted with ether (3x15 ml) and the combined ethereal extracts were successively washed with a saturated $NaHCO_3$ solution (until the washings remained basic), water (2x15 ml), brine (20 ml), dried with $MgSO_4$. Removal of the solvent under reduced

pressure gave an oil. Purification by column chromatography, using Kieselgel and elution with 10/90 ethyl acetate/light petroleum gave **9** (28 mg, 85%); microcrystals; mp 225.3-226.6°C; ^{1}H NMR (300 MHz; $CDCl_3$) 8.10 (1H, br.s, NH), 7.30 (1H, t, J = 8 Hz, H-7), 7.10 (1H, t, J = 18 Hz) and 6.85 (1H, d, J = 8 Hz) (H-5, H-6), 3.05 (2H, br.d, J = 15 Hz), 2.35 (2H, br.d, J = 15 Hz) and 1.55-2.05 (10H, m) (adamantyl), 0.40 (9H, s, aryl TMS); ^{13}C NMR (75 MHz, $CDCl_3$) 183.97 (C-1), 142.65, 140.15, 137.81 (C-3a, C-4, C-7a), 129.92 (C-6), 125.52 (C-5), 110.93 (C-7), 60.32 (C-2), 38.11, 35.59 and 33.09 (CH_2 adamantyl), 36.02, 27.37 and 26.57 (CH adamantyl), 3.58 (aryl TMS); ν_{max} (dichloromethane)/cm^{-1} 3030, 2960, 2880, 1590, 1250, 840, 730; HRMS Calcd. for $C_{20}H_{27}NOSi$: 325.1861 (M^+). Found: 325.1858.

Compound **9** (23 mg, 0.08 mmol) was dissolved in TFA (2 ml) and the reaction mixture stirred at room temperature for 6 h. It was then diluted with water (30 ml) and extracted with ether (3x15ml). The combined ethereal extracts were successively washed with a saturated $NaHCO_3$ solution (until the washings remained basic), water (2x15 ml), brine (20 ml), dried with $MgSO_4$. Removal of the solvent under reduced pressure gave an oil. Purification by column chromatography, using Kieselgel and elution with 35/65 ethyl acetate/light petroleum gave **5** (17 mg, 99%).

REFERENCES

1. Sheikh, Z.; Steel, R.; Tasker, A. S.; Johnson, A. P. *J. Chem. Soc., Chem. Comm.* **1994**, 763-764.

2. Dutton, J. K.; Steel, R.W.; Tasker, A. S.; Popsavin, V.; Johnson, A. P. *J. Chem. Soc., Chem. Comm.* **1994**, 765-766.

3. Dutton, J. K. PhD Thesis, University of Leeds, **1991**.

4. Zaracostas C Unpublished work, University of Leeds.

5. Fleming I.; Moses R. C.; Tercel M.; Ziv J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 617-626 and references therein.

6. Fleming I; Loreto M. A.; Wallace I. H. M.; Michael J. P. *J. Chem. Soc., Perkin Trans. 1* **1986**, 349-359.

7. Giese B. Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds, Baldwin J. E., editor, Pergamon Press, 1986; p.2.

8. Burgess, E. M.; Carithers, R.; McCullagh, L. *J. Am. Chem. Soc.* **1968**, *90*, 1923-1924.

9. Märky, M.; Schmid, H.; Hansen, H.-J. *Helv. Chim. Acta* **1979**, *62*, 2129-2153.

10. Mehta L. K.; Parrick J.; Payne F. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1261-1267.

11. Parrick J.; Yahya A. *J. Chem. Research (S)* **1990**, 1 or *J. Chem. Research (M)* **1990**, 201-214.

12. Edstrom, E. D.; Yuan, W. *Tetrahedron Lett.* **1991**, *32*, 323-326 and references therein.

13. Wender, P. A.; Cooper, C. B. *Tetrahedron* **1986**, *42*, 2985-2991.

14. Pleynet D. P. M.; Dutton J. K.; Johnson A. P. *Tetrahedron*, preceding paper.

15. Johnson, A. P.; Dutton, J. K.; Pleynet, D. P. M. *Heterocycles* **1994**, *37*, 1913-1932.

16. Brunton G.; Griller D.; Barclay L. R.; Ingold K. U. *J. Am. Chem. Soc.* **1976**, *98*, 6803-6811.

17. Pleynet, D. P. M.; Dutton, J. K.; Thornton-Pett, M.; Johnson, A. P. *Tetrahedron Lett.* **1995**, 6321-6324.

18. Bowman W. R.; Heaney H.; Jordan B. M. *Tetrahedron Lett.* **1988**, *29*, 6657-6660.

19. Snieckus V.; Cuevas J.-C.; Sloan C. P.; Liu H.; Curran D. P. *J. Am. Chem. Soc.* **1990**,*112*, 896-898.

20. Curran D. P.; Abraham A. C.; Liu H. *J. Org. Chem.* **1991**, *56*, 4335-4337.

21. Colvin, E. W. Silicon in Organic Synthesis, Krieger publishing company, Florida reprint edition, 1985 and references therein.

22. Barrett, A. G. M.; Dauzonne, D.; O'Neil, I. A.; Renaud, A. *J. Org. Chem.* **1984**, *49*, 4409-4415.