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Palladium-mediated fragmentation of *meta* photocycloadducts using carbon based electrophiles. Part 1

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Abstract—Substituted benzene derived *meta* photocycloadducts have been shown to undergo a fragmentation/arylation reaction under Heck reaction conditions to give bridged bicyclo[3.2.1] compounds in a highly atom-efficient manner. When an anisole derived *meta* photocycloadduct is used, a bridgehead ketone is generated. However, if an alkylbenzene derived *meta* photocycloadduct is used, a bridgehead alkene is formed. This strategy has been used to create novel enol ether and transient allyl silane compounds.

1. Introduction

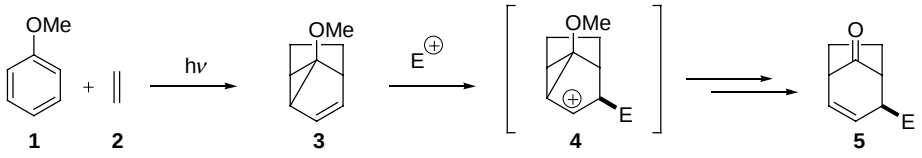
The remarkable *meta* photocycloaddition reaction[1] between an alkene and an arene has inspired considerable interest for the formation of complex polycyclic molecules.[2] Although generally stable under ambient conditions, *meta* photocycloadducts are highly strained chemical entities and hence are inclined to undergo relief of ring strain in the presence of certain reagents. Wender and co-workers[1d–f] have been the greatest exponent of this reaction's synthetic potential and they have used a variety of strategies to cleave the strained three-membered ring. Radical based methods involving dissolving metal conditions[3] and thiophenol[4] have been used to prepare the angular and linear fused triquinanes silphinene and coriolin, respectively. More commonly electrophiles have been employed in conjunction with anisole derived *meta* photocycloadducts, which add to the electron rich olefin portion of the oxygen-substituted photocycloadduct and the resulting cationic intermediate fragments to give a [3.2.1] bridged bicyclic ketone (Scheme 1).

In this context an acid[5] has acted as a source of H^+, bromine[6] or *N*-bromosuccinimide[7] as a source of Br^+ and *m*CPBA[7] as a source of OH^+ (via an epoxide), however, the synthetic potential of this reaction would be significantly enhanced if a carbocation-mediated equivalent could be developed. We reasoned that an aryl halide would behave as a carbon based electrophile in the presence of a palladium catalyst to cause an analogous fragmentation[8] and we now describe the Heck reaction of *meta* photocycloadducts.

2. Results and discussion

2.1. Arylation of anisole derived photoadducts

The palladium-mediated Heck reaction[9] has become one of the most versatile carbon–carbon bond forming methods



Scheme 1.

Keywords: Photoaddition; Palladium; Heck reaction; Tandem reaction; Atom efficiency; Allylsilane formation.
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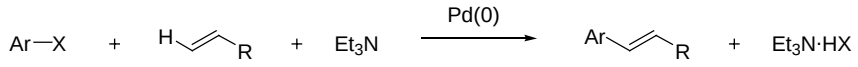


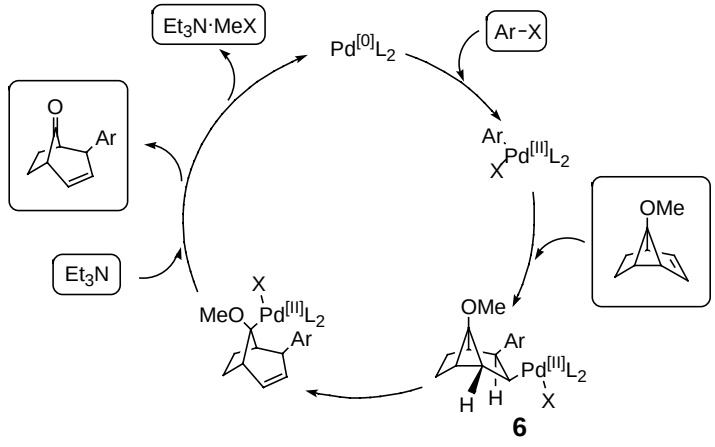
Scheme 2.

known to synthetic chemists. During this process an aryl halide is commonly coupled to an alkene in the presence of a palladium catalyst and a base to yield an arylated olefin along with a salt bi-product (Scheme 2).

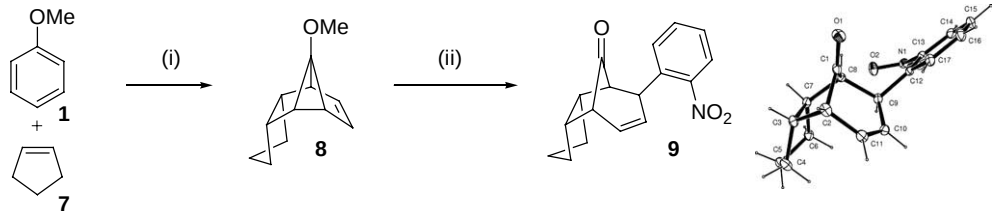
A modified version of the generally accepted catalytic cycle can be proposed for the reaction of an anisole derived *meta* photoadduct with an aryl halide in the presence of a palladium(0) catalyst (Scheme 3). The initial steps involving oxidative addition of the aryl halide with the palladium(0) catalyst and *syn* carbopalladation of the alkene portion are common to the classic mechanism, however, the rigid structure of **6** does not allow the carbon–palladium σ-bond to align *syn* with a β hydrogen atom. This prevents β-hydride elimination from taking place and cyclopropane ring fragmentation occurs as a consequence. The final stages of the catalytic cycle involve the formation of an arylated bicyclic ketone product and the regeneration of the palladium(0) catalyst with the assistance of the base.

To verify this proposed mechanism we carried out some preliminary studies using the simple anisole/cyclopentene sourced *meta* photocycloadduct **8**.[5] This was prepared predominantly as the *endo* isomer by irradiating a solution of anisole and cyclopentene in cyclohexane using 254 nm UV light, with the powerful electron donating properties of anisole's methoxy group directing the addition of the olefin between the 2- and 6- positions of the aromatic ring. This photoadduct **8** was separated from the crude photolysis mixture by distillation under reduced pressure and used without any further purification during the modified Heck reaction. Our initial attempt at a palladium-mediated arylation reaction involved heating a solution of the photoadduct **8** and 1-iodo-2-nitrobenzene in DMF with palladium(II) acetate and dppe ligand as the catalyst and triethylamine as the base.[10] The reaction mixture was heated at 80 °C until the starting material was no longer observed by TLC analysis and we were delighted to find that our predictions about the reactivity of the *meta* photocycloadduct proved correct for the formation of the desired fragmentation/arylation product **9** (Scheme 6). This compound was obtained in 20% yield as a yellow crystalline solid[8] and as expected the aryl group had been introduced onto the *exo*-face of the bridged bicyclic ketone **9** (Scheme 4).

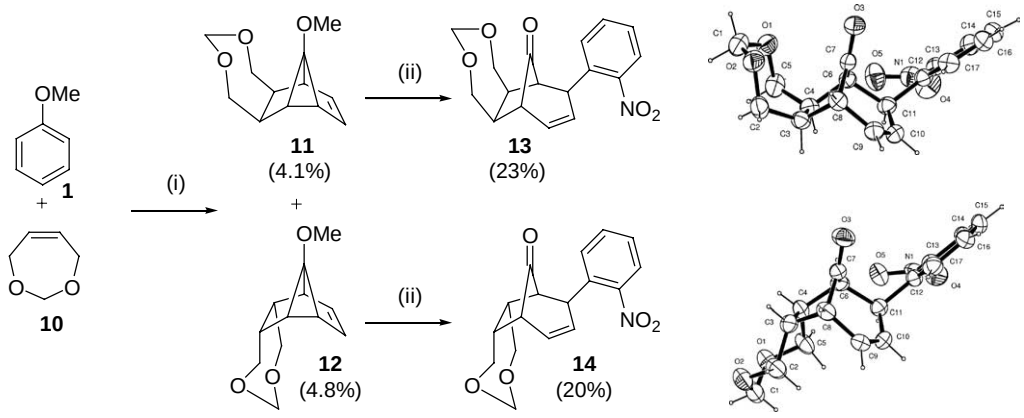
A second series of compounds was prepared from the photoadducts derived from anisole and *cis*-4,7-dihydro-1,3-dioxepin **10**. A solution of anisole and the alkene in cyclohexane was irradiated using 254 nm UV light and both *exo* and *endo* photoadducts (**11** and **12**) were isolated separately. These were then subjected to the same Heck reaction conditions using 1-iodo-2-nitrobenzene to afford the arylation/fragmentation products **13** and **14**, whose structures were again confirmed by X-ray crystallography[11a,b] (Scheme 5).



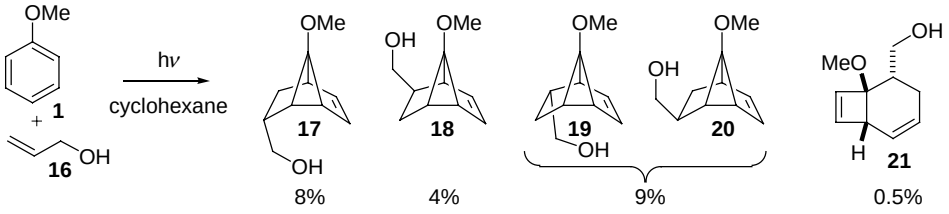
Scheme 3.



Scheme 4. Reagents and conditions: (i) hν, cyclohexane, 19%; (ii) 1-iodo-2-nitrobenzene, $Pd(OAc)_2$ (5 mol%), dppe (5 mol%), NEt_3, DMF, 80 °C, 32 h, 20%.



Scheme 5. Reagents and conditions: (i) hν, cyclohexane; (ii) 1-iodo-2-nitrobenzene, $Pd(OAc)_2$ (5 mol%), dppe (5 mol%), NEt_3, DMF, 80 °C, 32 h.



Scheme 6.

2.2. A gelsemine model

One of the initial aims of this research was to establish a rapid method of assembling the core structure of the alkaloid gelsemine **15**.[7,12] Gelsemine provides a unique challenge to the synthetic organic chemist, as six rings (one spirofused with another) and seven chiral centres (two of which are quaternary) are contained within its compact structure. The level of interest shown towards this alkaloid is probably more a reflection of its complex molecular architecture than any intrinsic biological activity and the varied strategies used for its assembly have been the focus of a recent review by Danishefsky and Lin.[13]

The basic carbon framework of gelsemine lends itself to being assembled by the fragmentation of an appropriate *meta* photocycloadduct. Preliminary studies were aimed at the formation of its core structure and were focused on the use of *meta* photocycloadducts derived from anisole and allyl alcohol. These were prepared by the irradiation of a solution of anisole and allyl alcohol in cyclohexane using 254 nm UV light. The electron donating properties of anisole's methoxy group directed the addition of the olefin between the 2- and 6- positions of the aromatic ring during the photochemical reaction and four *meta* photocycloadduct isomers were formed (Scheme 6). The 7-*endo* and the 6-*exo* isomers **17** and **18** could be obtained as single compounds, but the 6-*endo* and the 7-*exo* isomers **19** and **20** co-eluted as a mixture. In addition to these compounds a small amount of the *ortho* photoadduct **21** was also obtained. Although the percentage yields of products for this process tended to be low, multigram quantities of the desired photoadducts could be easily separated from the simple starting materials and it is difficult to conceive of a more straight-forward synthetic route to these complex products.

In our approach to gelsemine a nitrogen-substituted aryl group needed to be introduced onto the alkene of an appropriate *meta* photoadduct at what would become the C7 position of gelsemine (see Fig. 1). Fortunately the more plentiful 7-*endo* photocycloadduct **17** was also the isomer most closely related to the structure of gelsemine. When the same arylation conditions as before were used (heating a solution of the photoadduct **17**, 1-iodo-2-nitrobenzene, palladium(II) acetate, dppe and triethylamine in DMF at 80 °C), the familiar arylation/fragmentation reaction occured to provide compound **22**[8] in 21% yield (Scheme 7). It was interesting to note that an unprotected hydroxyl group in the substrate did not appear to significantly hinder the palladium(0) catalysed process.

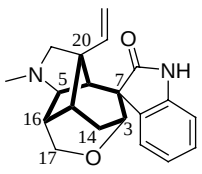
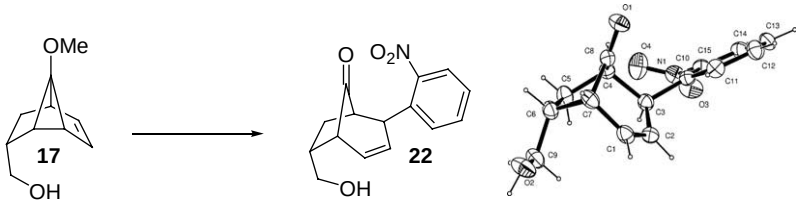


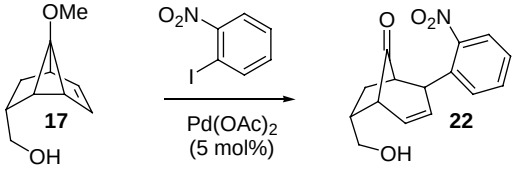
Figure 1. The alkaloid gelsemine **15** with its numbering system shown.

Various experiments were then undertaken with a view to improving the yield of **22** from **17** by altering the ligand, base, solvent, temperature and time of the reaction with the results being summarised in Table 1. Initially reactions were carried out at 80 °C and doubling the reaction time from 32 to 64 h had a detrimental effect on the yield of **22**. Silver salts are known to improve the reactivity of electron rich



Scheme 7. Reagents and conditions: 1-iodo-2-nitrobenzene, $Pd(OAc)_2$ (5 mol%), dppe (5 mol%), NEt_3, DMF, 80 °C, 32 h, 21%.

Table 1. Optimisation studies for the conversion of **17** to **22**



Variables: ligand, base, solvent, temperature, time, solvent.

Entry	Ligand	Base	Solvent	Temperature (°C)	Time (h)	Yield of **22** (%)
1	Dppe	NEt_3	DMF	80	32	21
2	Dppe	NEt_3	DMF	80	68	8
3	Dppe	$AgCO_3$	DMF	80	32	11
4	PPh_3	NEt_3	DMF	80	32	28
5	P(*o*-Tol)$_3$	NEt_3	DMF	80	32	36
6	P(*o*-Tol)$_3$	NEt_3	DMF	120	32	17
7	P(*o*-Tol)$_3$	NEt_3	DMF	120	24	24
8	P(*o*-Tol)$_3$	NEt_3	DMF	120	12	42
9	P(*o*-Tol)$_3$	NEt_3	DMF	120	8	37
10	P(*o*-Tol)$_3$	NEt_3	DMF	120	4	37
11	P(*o*-Tol)$_3$	NEt_3	DMF	120	2	35
12	P(*o*-Tol)$_3$	NEt_3	DMF	120	0.5	28
13	P(*o*-Tol)$_3$	NEt_3	DMSO	120	12	35
14	P(*o*-Tol)$_3$	NEt_3	Dioxane	120	12	0
15	P(*o*-Tol)$_3$	NEt_3	Acetonitrile	120	12	<5%

alkenes during Heck reactions,[14] but the use of silver carbonate as a base led to less **22** being obtained. Using the monodentate ligand triphenylphosphine instead of the bidentate dppe ligand brought about an improvement in yield indicating that cyclopropane fragmentation required a vacant coordination site, as the bidentate ligand appeared to slow down the rate of catalysis. The yield of **22** was further improved by the use of tri-*ortho*-tolylphosphine, which was advantageous as this ligand was known to exhibit good thermal stability at elevated temperatures.[9c] After raising the reaction temperature to 120 °C it was found that the highest yield of **22** was obtained after 12 h. Other solvents were used, but DMF remained the solvent of choice.

It was interesting to note that at the higher temperature of 120 °C another isomeric compound **23** (Fig. 2) was obtained and in the case of entry 8 (Table 1) **23** was obtained in 9% yield.

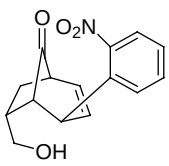


Figure 2. The minor isomeric compound **23**.

The presence of **23** in the product mixture indicates that the proposed mechanism in Scheme 4 is either flawed or another mechanism is operating, which may involve the formation of a π-allyl palladium species **24**[15] (Fig. 3). It may also be that this alternative reaction pathway only becomes significant at higher reaction temperatures.

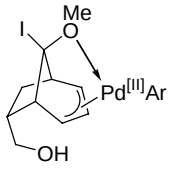
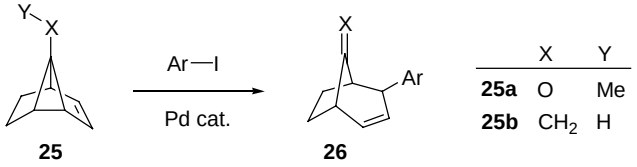


Figure 3. The proposed π-allyl palladium species **24**.

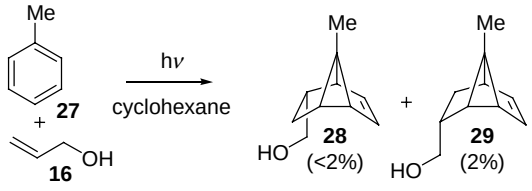
2.3. Formation of a bridgehead alkene using an alkylbenzene derived photoadduct

So far we had shown that *meta* photocycloadducts obtained from oxygen-substituted benzene derivatives would undergo a palladium-catalysed arylation/fragmentation process in the presence of an aryl halide. This transformation can be summarised as the conversion of **25a** to **26a** (Scheme 8) with X_a as oxygen and Y_a as methyl.



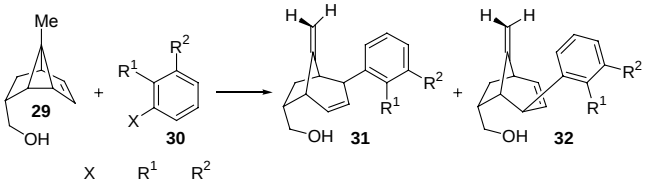
Scheme 8.

We wondered if X_b could be CH_2 and Y_b could be H and then employ palladium's versatile reactivity to initiate a similar arylation/fragmentation process of an alkyl substituted *meta* photoadduct **25b** to generate an alkenyl bridgehead compound **26b** (Scheme 9). To test this hypothesis a simple alkyl substituted *meta* photoadduct system was prepared by irradiating a solution of toluene and allyl alcohol in cyclohexane using 254 nm UV light. The electron donating methyl group directed *meta* addition of the alkene across the 2,6 positions of toluene during the photoreaction, however, only the 6 and 7-*endo* photoadducts **28** and **29** were obtained on this occasion (Scheme 9) and the 6-*endo* isomer **28** proved inseparable from a co-eluting impurity.



Scheme 9.

The 7-*endo* photoadduct **29** was reacted with a variety of aryl halides **30** using the best yielding conditions from the anisole variant **17** (Table 1, entry 8) and as predicted a range of [3.2.1] bicyclic dienes were formed that exhibited a methylene group at the bridgehead position instead of a ketone (Scheme 10). Again a major isomer **31** and a minor isomer **32** were formed in a similar fashion to the anisole variants **22** and **23** and we found the reaction to be equally tolerant of electron rich bromides as to electron-poor iodides, but the less reactive chlorobenzene failed to afford any arylation products. The spectroscopic details of the minor 1-bromo-3-methylbenzene derivative **32b** are not quoted in the Section 4 as it could not be obtained free of co-eluting impurities.



	X	R^1	R^2				
30a	I	NO_2	H	**31a**	29%	**32a**	13%
30b	Br	H	Me	**31b**	30%	**32b**	<10%
30c	Cl	H	H	**31c**	0%	**32c**	0%

Scheme 10. Reagents and conditions: $Pd(OAc)_2$ (5 mol%), P(*o*-Tol)$_3$, (10 mol%), NEt_3, DMF, 120 °C, 12 h.

2.4. Tandem formation of an allylsilane and an enol ether

Inspired by Fleming's allylsilane approach[16] to create the key quaternary centre at the C20 position of gelsemine (Fig. 1), we contemplated a novel strategy for preparing a similar bridgehead allylsilane using a version of the chemistry described above. We have shown that the arylation/fragmentation of a simple methylbenzene-derived photoadduct would give rise to a [3.2.1] bicycle with an alkene at the bridgehead position and conceived that a similar alkene could also form part of an allylsilane unit (see compound **33**, Fig. 4).

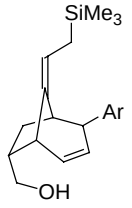
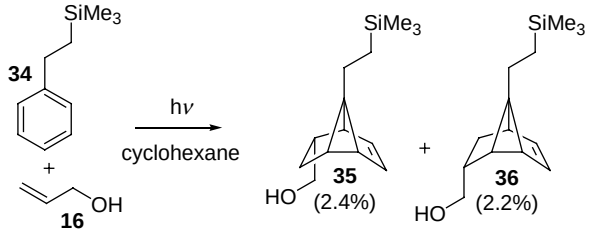


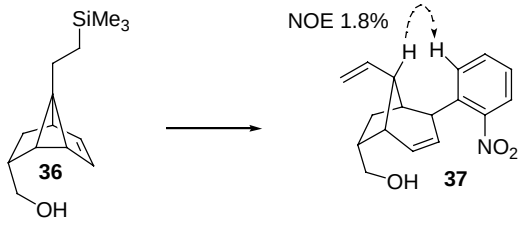
Figure 4. Compound **33** with a bridgehead allylsilane unit.

An appropriate photoadduct to attempt this arylation/fragmentation reaction was prepared by the irradiation of a solution of trimethyl phenethyl silane **34**[17] and allyl-alcohol in cyclohexane using 254 nm UV light. Two *meta* photoadducts were isolated from the crude reaction mixture after chromatographic separation and their structures were identified as the 6 and 7-*endo* isomers **35** and **36** using NMR techniques (Scheme 11).



Scheme 11.

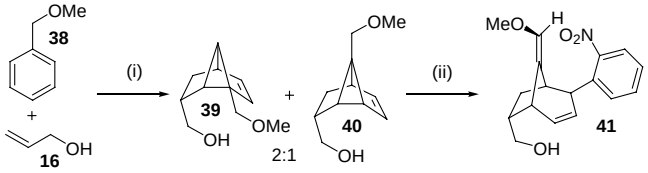
After subjecting the 7-*endo* isomer (**36**) to the arylation/fragmentation process, compound **37** was obtained after chromatographic separation from the crude reaction mixture (Scheme 12). It would appear that a bridgehead allylsilane similar to compound (Fig. 4) had formed, but underwent



Scheme 12. Reagents and conditions: 1-iodo-2-nitrobenzene, $Pd(OAc)_2$ (5 mol%), P(*o*-Tol)$_3$, (10 mol%), NEt_3, DMF, 120 °C, 12 h, 15%.

proto-desilylation to give the vinyl group under the reaction conditions. It is interesting to note that the hydrogen atom at the bridgehead position had been introduced on to what was the more sterically encumbered face of the allylsilane next to the aryl group during the proto-desilylation stage. This reaction was repeated in the presence of Eschenmoser's salt in the hope of trapping the in situ formed allylsilane **33** with an iminium ion, but the same proto-desilylated compound **37** was obtained again. In an attempt to form a more stable allylsilane variant during the arylation/fragmentation stage, triisopropyl phenethyl silane was prepared using the same procedure as for compound **34** and irradiated in the presence of allylalcohol, however, no evidence could be found of *meta* photocycloaddition between the two.

During the course of studying enantioselective intramolecular versions of the Heck reaction, Overman and Shibasaki showed how silyl enol ethers could be prepared in high yield from silyl protected allylic alcohols.[18] The apparent stability of these functional groups under Heck reaction conditions led us to contemplate the formation of an enol ether at the bridgehead position after initiating an arylation/fragmentation procedure on an appropriate *meta* photocycloadduct. Various benzyl silyl ethers were prepared and irradiated in the presence of allyl alcohol, but no evidence of *meta* photocycloaddition could be detected. However, benzyl methyl ether did undergo *meta* photocycloaddition with allyl alcohol, although the 2,6 *meta* photoadduct isomer of interest (**40**) co-eluted with what was tentatively assigned as the 2,4 *meta* photoadduct isomer **39**. This mixture was subjected to the arylation/fragmentation process and afforded the bridgehead methyl enol ether compound **41** (Scheme 13).



Scheme 13. Reagents and conditions: (i) hν, cyclohexane, 6.8%; (ii) 1-iodo-2-nitrobenzene, $Pd(OAc)_2$ (5 mol%), P(*o*-Tol)$_3$ (10 mol%), NEt_3, DMF, 120 °C, 12 h, 15%.

3. Conclusion

A unique fragmentation/carbon–carbon bond forming process has been shown to occur when a Heck reaction is performed with various *meta* photocycloadducts for the formation of complex polycyclic compounds. The degree of added molecular complexity after only two synthetic operations is remarkable and, depending on the nature of the substituted benzene used during the photoaddition stage, [3.2.1] bicycles can be prepared with either a ketone or an alkene at the bridgehead position. This methodology has been shown to be tolerant of unprotected hydroxyl groups and its versatility has been demonstrated for the formation of bridgehead ketones, alkenes, enol ethers and in situ generated allylsilanes.

4. Experimental

4.1. General

^{1}H NMR spectra were recorded on Bruker DPX300, Varian unityINOVA-400 or Bruker AMX500 Fourier transform spectrometers at 300, 400 or 500 MHz, respectively. Chemical shifts (δ) are quoted in ppm using tetramethylsilane or residual chloroform as internal reference (δ= 0.00 ppm), and coupling constants (J) are quoted in Hz. ^{13}C NMR spectra were recorded using the same instruments, and chemical shifts (δ) are quoted in ppm using $CDCl_3$ as internal reference (δ=77.0 ppm).

IR spectra were recorded on Perkin-Elmer Spectrum One Fourier transform instruments and frequencies (ν_{max}) are quoted in wavenumbers (cm^{-1}).

Low- and high-resolution electron impact (EI) and chemical impact (CI) mass spectra were recorded using a Fisons Autospec instrument. High-resolution electrospray ionisation (ESI) mass spectra were recorded using a Bruker Daltonics APEXIII instrument.

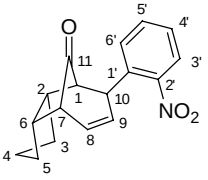
The starting materials for the synthesis of the compounds were obtained from the usual suppliers (Sigma–Aldrich–Fluka, Lancaster, Fisher etc.) unless otherwise stated. The anhydrous solvents were obtained from Aldrich Chemicals in Sure/Seal™ bottles and were used without further purification. Petrol refers to petroleum ether with a boiling range of 40–60 °C. Flash column chromatography was performed using Fisher Matrex 60 (35–70 μm) silica. Analytical thin-layer chromatography (TLC) was performed using Whatman K6F silica gel plates (60 Å porosity) developed with UV light or an alkaline solution of potassium permanganate followed by heating to give yellow spots.

Irradiations were carried out in quartz immersion-well reactors fitted with 6 or 16 W low-pressure mercury vapour lamps or 125 or 400 W medium-pressure mercury vapour lamps as supplied by Photochemical Reactors Ltd, Reading, UK. Oxygen free solvent for the irradiation experiments was simply obtained by passing a vigorous stream of nitrogen gas through a sintered glass tube into the solvent for 15 min at rt. Experiments were conducted with gentle stirring of the reaction solution under an atmosphere of nitrogen and with cold-water cooling of the lamp and vessel contents throughout.

4.1.1. *rac*-(1*R*,2*S*,6*R*,7*R*,10*S*)-10-(2′-Nitrophenyl)tricyclo[5.3.1.0^{2,6}]undec-8-en-11-one 9. A solution of anisole (34.5 g, 320 mmol) and cyclopentene (21.8 g, 320 mmol) in cyclohexane (270 ml) was added to a quartz immersion-well photoreactor and degassed by passing a stream of nitrogen through it for 10 min. This solution was then irradiated with short wavelength UV light for 35 h using a 400 W medium-pressure mercury vapour lamp. The solvent and unreacted starting materials were removed in vacuo and the residue was distilled under reduced pressure using an oil rotary pump to yield the photoadduct as a colourless oil (10.7 g, 19%). This photoadduct was primarily the 2,6 *endo* adduct

and was used without further purification during the arylation reaction.

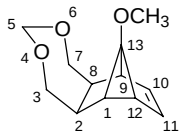
A mixture of the *endo meta* photoadduct (4.00 g, 23.4 mmol), 2-iodo-1-nitrobenzene (5.80 g, 23.4 mmol), triethylamine (89 mg, 0.88 mmol), palladium (II) acetate (260 mg, 1.16 mmol) and 1,2-bis(diphenylphosphine) ethane (466 mg, 1.17 mmol) and dry DMF (70 ml) was heated at 80 °C for 32 h. The reaction was poured into 2 M hydrochloric acid (150 ml) and the aqueous portion was washed with ethyl acetate (3×150 ml). The combined organics were washed with brine (150 ml), water (150 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography to afford the product **9** (1.32 g, 20%) as a yellow crystalline solid (for crystallographic details see Ref. 8) mp 147–149 °C.



^{1}H NMR (300 MHz, $CDCl_3$) δ 1.3–1.9 (6H, m, H-3, H-4, H-5), 2.4–2.6 (4H, m, H-1, H-2, H-6, H-7), 4.60 (1H, m, H-10), 5.51 (1H, ddd, J=1.2, 3.4, 9.2 Hz, H-9), 5.94 (1H, dd, J=6.2, 9.2 Hz, H-8), 7.23–7.32 (2H, m, H-4′, H-6′), 7.44 (1H, t, J=7.6 Hz, H-5′), 7.83 (1H, d, J=8.1 Hz, H-3′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.6, 27.7, 28.0, 40.3, 43.7, 47.2, 48.2, 52.0, 124.9, 127.9, 129.1, 130.6, 133.2, 133.5, 136.1, 148.2, 214.8; IR 1605, 1740, 2923 cm^{-1}; HRMS (ESI) *m/z* calcd $C_{17}H_{17}NNaO_3$ $[M+Na]^+$ 306.1101, found 306.1083.

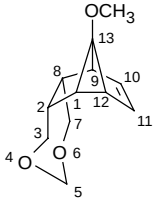
4.1.2. *rac*-(1*S*,2*S*,8*R*,9*S*,13*R*)-13-Methoxy-4,6-dioxatetracyclo[7.3.1.0.^{2,8}0^{12,13}]tridec-10-ene (*exo* isomer) 11 and *rac*-(1*S*,2*R*,8*S*,9*S*,13*R*)-13-methoxy-4,6-dioxatetracyclo-[73.1.0.^{2,8}0^{12,13}]tridec-10-ene (*endo* isomer) 12. A solution of anisole (1.35 g, 12 mmol) and *cis*-4,7-dihydro-1,3-dioxepin (1.29 g, 12 mmol) in cyclohexane (175 ml) was added to a quartz immersion-well photoreactor and degassed by passing a stream of nitrogen through it for 10 min. This solution was then irradiated with 254 nm UV light for 16½ h using a 6 W low-pressure mercury vapour lamp. The solvent was removed in vacuo and the residue subjected to column chromatography (silica, petrol/ether 3:1) to obtain the *exo* isomer **11** (0.105 g, 4.1%) and *endo* isomer **12** (0.113 g, 4.5%) as light green oils.

Compound **11**



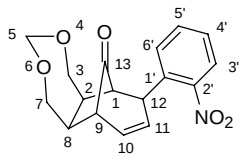
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.92 (1H, m, H-2a), 2.09 (1H, dd, J=1.6, 8.4 Hz, H-1), 2.21 (1H, m, H-8a), 2.22 (1H, ddd, J=1.4, 2.4, 8.4 Hz, H-12), 2.79 (1H, d, J=2.7 Hz, H-9), 3.30 (3H, s, OCH_3), 3.72 (1H, ddd, J=0.9, 4.5, 12.0 Hz, H-7a), 3.90 (1H, dd, J=3.4, 12.4 Hz, H-3b), 3.97 (1H, dd, J=2.7, 12.4 Hz, H-3a), 4.04 (1H, t, J=11.7 Hz, H-7b), 4.77 (1H, d, J=4.5 Hz, H-5b), 4.78 (1H, d, J=4.6 Hz, H-5a), 5.58 (1H, ddd, J=1.4, 2.7, 5.7 Hz, H-10), 5.64 (1H, dd, J=2.4, 5.7 Hz, H-11); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.5, 37.4, 40.7, 52.7, 56.0, 56.4, 66.6, 67.6, 89.9, 95.5, 127.5, 131.9; IR 1645, 2935, 3053 cm^{-1}; HRMS (ESI) *m/z* calcd $C_{12}H_{16}NaO_3$ $[M+Na]^+$ 231.0992, found 231.0989.

Compound **12**



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.71 (1H, ddd, J=1.2, 2.4, 8.4 Hz, H-12), 1.77 (1H, dd, J=6.3, 8.4 Hz, H-1), 2.07 (1H, ddd, J=1.6, 2.6, 5.7 Hz, H-9), 2.89 (1H, m, H-8b), 2.94 (1H, m, H-2b), 3.07 (3H, s, OCH_3), 3.20 (1H, dd, J=9.1, 12.5 Hz, H-7a), 3.51 (1H, ddd, J=0.4, 3.8, 12.0 Hz, H-3b), 3.58 (1H, dd, J=10.6, 12.0 Hz, H-3a), 3.65 (1H, dd, J=5.5, 12.5 Hz, H-7b), 4.22 (1H, d, J=6.3 Hz, H-5a), 4.93 (1H, d, J=6.3 Hz, H-5b), 5.42 (1H, ddd, J=0.4, 2.4, 5.8 Hz, H-11), 5.48 (1H, ddd, J=1.2, 2.6, 5.8 Hz, H-10); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.3, 37.7, 47.6, 53.1, 54.1, 56.5, 70.3, 71.4, 92.0, 99.8, 131.0, 134.3; IR 1644, 2930, 3051 cm^{-1}; HRMS (EI) *m/z* calcd $C_{12}H_{17}O_3$ $[M+H]^+$ 209.1178, found 209.1170.

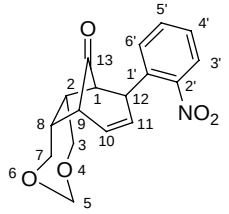
4.1.3. *rac*-(1*S*,2*R*,8*S*,9*R*,12*S*)-12-(2′-Nitrophenyl)-4,6-dioxatricyclo[7.3.1.0^{2,8}]tridec-10-en-13-one 13. A mixture of the *exo meta* photoadduct **11** (171 mg, 0.822 mmol), 2-iodo-1-nitrobenzene (222 mg, 0.891 mmol), triethylamine (89 mg, 0.88 mmol), palladium (II) acetate (7 mg, 0.03 mmol) and 1,2-bis(diphenylphosphine) ethane (57 mg, 0.14 mmol) and dry DMF (3.5 ml) was added to a re-sealable reaction tube. The tube was flushed with a stream of dry nitrogen, sealed and the mixture heated at 80 °C for 32 h. The reaction was poured into water (50 ml) and acidified with 2 M HCl. The aqueous portion was washed with ethyl acetate (5×10 ml) and the combined organics washed with brine (50 ml), water (50 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica, eluting with petrol/ethyl acetate 3:1) to afford the product **13** (60 mg, 23%) as an off-white crystalline solid (for crystallographic details see Ref. 11a) mp 190.6–191.3 °C.



^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (1H, m, H-1), 2.45 (1H, dd, J=2.0, 7.2 Hz, H-9), 2.87 (2H, m, H-2a, H-8a), 3.81 (1H, ddm, J=6.6, 13.0 Hz, H-3), 3.86 (1H, ddm, J=3.8, 13.0 Hz, H-3), 4.01 (1H, ddm, J=5.7, 12.9 Hz, H-7), 4.06 (1H, ddm, J=3.1, 12.8 Hz, H-7), 4.64 (1H, d, J=6.7 Hz,

H-5b), 4.70 (1H, m, H-12a), 4.74 (1H, d, J=6.7 Hz, H-5a), 5.60 (1H, ddd, J=1.3, 3.5, 9.1 Hz, H-11), 6.27 (1H, ddd, J=1.3, 7.2, 8.9 Hz, H-10), 7.33 (1H, dd, J=1.4, 7.8 Hz, H-6′), 7.41 (1H, ddd, J=1.4, 7.4, 8.1 Hz, H-4′), 7.54 (1H, ddt, J=0.4, 1.4, 7.4 Hz, H-5′) 7.94 (1H, dd, J=1.4, 8.1 Hz, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 45.6, 48.2, 51.4, 53.3, 55.0, 72.0, 73.4, 99.2, 125.0, 127.2, 128.3, 130.1, 133.3, 134.5, 135.0, 148.3, 213.5; IR 1599, 1630, 1744, 2855, 2922 cm^{-1}; HRMS (ESI) m/z calcd $C_{17}H_{18}NO_5$ $[M+H]^+$ 316.1185, found 316.1196.

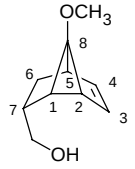
4.1.4. *rac*-(1*S*,2*S*,8*R*,9*R*,12*S*)-12-(2′-Nitrophenyl)-4,6-dioxatricyclo[7.3.1.0^{2,8}]tridec-10-en-13-one 14. A mixture of the *endo meta* photoadduct **12** (474 mg, 2.28 mmol), 2-iodo-1-nitrobenzene (615 mg, 2.46 mmol), triethylamine (474 mg, 2.43 mmol), palladium (II) acetate (19 mg, 0.084 mmol) and 1,2-bis(diphenylphosphine) ethane (157 mg, 0.394 mmol) and dry DMF (9 ml) was added to a re-sealable reaction tube. The tube was flushed with a stream of dry nitrogen, sealed and the mixture heated at 80 °C for 32 h. The reaction was poured into water (100 ml) and acidified with 2 M HCl. The aqueous portion was washed with ethyl acetate (5×25 ml) and the combined organics washed with brine (100 ml), water (100 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica, eluting with petrol/ether 1:1) to afford the product **14** (143 mg, 20%) as a white crystalline solid (for crystallographic details see Ref. 11b) mp 198.0–198.4 °C.



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.69 (1H, dd, J=5.6, 6.4 Hz, H-9), 2.75 (1H, d, J=7.6 Hz, H-1), 2.87 (1H, m, H-8a), 3.00 (1H, m, H-2a), 4.05 (2H, t, J=12.0 Hz, H-7b, H-3b), 4.27 (1H, dd, J=4.8, 12.8 Hz, H-7a), 4.53 (1H, d, J=7.2 Hz, H-5b), 4.59 (1H, dd, J=3.6, 12.0 Hz, H-3a), 4.75 (1H, m, H-12a), 5.18 (1H, d, J=7.2 Hz, H-5a), 5.69 (1H, dd, J=2.4, 8.8 Hz, H-11), 6.12 (1H, dd, J=7.2, 8.8 Hz, H-10), 7.27 (1H, d, J=8.2 Hz, H-6′), 7.43 (1H, dt, J=1.2, 7.8 Hz, H-4′), 7.56 (1H, dt, J=1.2, 7.6 Hz, H-5′) 7.99 (1H, d, J=8.4 Hz, H-3′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.1, 43.6, 46.6, 47.9, 52.5, 71.1, 72.0, 100.0, 125.3, 128.4, 129.2, 130.4, 132.5, 133.3, 134.9, 148.1, 211.1; IR 1602, 1641, 1753, 2876, 2956 cm^{-1}; HRMS (ESI) m/z calcd $C_{17}H_{17}NNaO_5$ $[M+Na]^+$ 338.1004, found 338.1000.

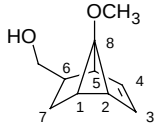
4.1.5. *rac*-(1*S*,2*R*,5*R*,7*R*,8*S*)-7-Hydroxymethyl-8-methoxytricyclo[3.2.1.0^{2,8}]oct-3-ene 17 and *rac*-(1*S*,2*R*,5*S*,6*R*,8*R*)-6-hydroxymethyl-8-methoxytricyclo[32.1.0^{2,8}]oct-3-ene 18 and *rac*-(1*S*,2*R*,6*R*)-1-methoxy-2-hydroxymethylbicyclo[42.0]octa-4,7-diene 21. A solution of anisole (43.2 g, 400 mmol) and allyl alcohol (46.4 g, 800 mmol) in cyclohexane (302 ml) was added to a quartz immersion-well photoreactor and degassed by passing a stream of nitrogen through it for 20 min. This solution was then irradiated with 254 nm UV light for 120 h using a 16 W low-pressure mercury vapour lamp. The unreacted starting materials and solvent were removed in vacuo and the residue subjected to column chromatography to obtain the *ortho* photoadduct **21** (350 mg, 0.5%), the 6-*exo* isomer **18** (2.65 g, 4%), a mixture of the 6-*endo* and 7-*exo* isomers **19** and **20** (6.0 g, 9%) and the 7-*endo* isomer **17** (5.3 g, 8%).

Compound **17**



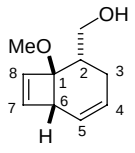
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (1H, dd, J=1.3, 12.9 Hz, H-6a), 2.05 (1H, br s, –OH), 2.09 (1H, ddd, J=0.6, 2.2, 8.5 Hz, H-2), 2.15 (1H, dd, J=6.2, 8.5 Hz, H-1), 2.43 (1H, ddd, J=6.6, 11.4, 12.9 Hz, H-6b), 2.75 (1H, m, H-7b), 3.18 (1H, ddd, J=1.3, 2.7, 6.8 Hz, H-5), 3.37 (3H, s, OCH_3), 3.51 (1H, dd, J=7.2, 10.3 Hz, –C*H*HO–), 3.59 (1H, dd, J=8.4, 10.3 Hz, –CH*H*O–), 5.57 (1H, dddd, J=0.6, 1.3, 2.7, 5.6 Hz, H-4), 5.65 (1H, dd, J=2.2, 5.6 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.7, 38.9, 40.0, 44.9, 51.2, 56.2, 65.7, 91.4, 129.1, 136.5; IR 1645, 2933, 3403 cm^{-1}; HRMS (EI) m/z calcd $C_{10}H_{14}O_2$ $[M]^+$ 166.0994, found 166.0996.

Compound **18**



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (1H, ddd, J=1.4, 6.3, 13.9 Hz, H-7a), 1.68 (1H, dddd, J=0.5, 1.7, 6.7, 13.9 Hz, H-7b), 2.05 (1H, ddd, J=1.4, 6.3, 8.4 Hz, H-1), 2.06 (1H, dddd, J=0.5, 6.3, 7.0, 7.9 Hz, H-5), 2.10 (1H, br s, –OH), 2.18 (1H, dddd, J=0.6, 1.4, 2.4, 8.4 Hz, H-2), 3.12 (1H, dd, J=1.7, 2.7 Hz, H-5), 3.32 (3H, s, OCH_3), 3.58 (1H, dd, J=7.0, 10.6 Hz, –C*H*HO–), 3.69 (1H, dd, J=7.9, 10.6 Hz, –CH*H*O–), 5.55 (1H, ddd, J=1.4, 2.7, 5.7 Hz, H-4), 5.60 (1H, dd, J=2.4, 5.7 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.0, 34.5, 36.6, 52.3, 53.1, 56.4, 63.6, 89.8, 126.8, 132.2; IR 1645, 2931, 3409 cm^{-1}; HRMS (ESI) m/z calcd $C_{10}H_{14}NaO_2$ $[M+Na]^+$ 189.0891, found 189.0885.

Compound **21**

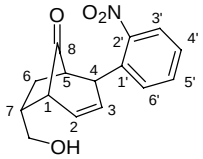


^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20 (1H, br s, –OH), 1.60–1.69 (1H, m, H-3), 1.94–2.06 (1H, m, H-2b, H-3), 3.35 (3H, s, –OCH_3), 3.36 (1H, dd, J=0.9, 5.7 Hz, H-6b), 3.54 (1H, dd, J=4.5, 10.6 Hz, –C*H*HO–), 3.71 (1H, dd, J=8.5, 10.6 Hz, –CH*H*O–), 5.70 (1H, dddd, J=0.5, 3.3, 5.9,

9.7 Hz, H-5), 5.87 (1H, ddd, J=2.1, 6.8, 9.6 Hz, H-4), 6.11 (1H, dd, J=0.9, 2.9 Hz, H-7), 6.15 (1H, d, J=2.9 Hz, H-8); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.7, 42.3, 46.4, 50.9, 64.8, 88.1, 126.1, 129.4, 134.2, 139.6; IR 1644, 3419 cm^{-1}; HRMS (ESI) m/z calcd $C_{10}H_{14}NaO_2$ $[M+Na]^+$ 189.0891, found 189.0889.

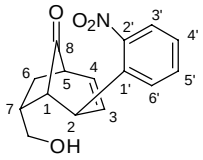
4.1.6. *rac*-(1*R*,4*S*,5*R*,7*R*)-4-(2′-Nitrophenyl)-7-hydroxymethylbicyclo[3.2.1]oct-2-en-8-one 22 and *rac*-(1*R*,2*R*,5*R*,7*R*)-2-(2′-nitrophenyl)-7-hydroxymethylbicyclo[3.2.1]oct-3-en-8-one 23. A mixture of the 7-*endo* allyl alcohol/anisole derived *meta* photoadduct **17** (330 mg, 1.21 mmol), 2-iodo-1-nitrobenzene (303 mg, 1.22 mmol), triethylamine (123 mg, 1.22 mmol), palladium (II) acetate (13 mg, 0.060 mmol) and tri-*ortho*-tolylphosphine (37 mg, 0.12 mmol) and dry DMF (4 ml) was added to a re-sealable reaction tube. The tube was flushed with a stream of dry nitrogen, sealed and the mixture heated at 120 °C for 12 h. The reaction was poured into 2 M hydrochloric acid (50 ml) and the aqueous portion was washed with ethyl acetate (5× 40 ml) and the combined organic portions were washed with brine (100 ml), water (100 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica, eluting with petrol/EtOAc 1:1) to afford **22** (139 mg, 42%) as a yellow oil that became crystalline upon standing (for crystallographic details see Ref. 8) (mp 118.5–119.4 °C) and **23** (33 mg, 10%) as a pale yellow oil.

Compound **22**



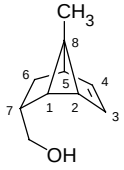
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (1H, ddd, J=1.5, 7.7, 13.5 Hz, H-6a), 1.67 (1H, br s, –OH), 2.44 (1H, ddd, J=8.4, 9.8, 13.5 Hz, H-6b), 2.54 (1H, dm, J=8.4 Hz, H-5), 2.59 (1H, m, H-7b), 2.83 (1H, ddd, J=1.5, 5.3, 6.8 Hz, H-1), 3.79–3.83 (2H, m, –CH_2O–), 4.56 (1H, ddm, J=1.1, 3.6 Hz, H-4a), 5.72 (1H, ddd, J=1.3, 3.6, 9.2 Hz, H-3), 6.14 (1H, ddd, J=1.1, 6.8, 9.1 Hz, H-2), 7.32 (1H, dd, J=1.4, 7.8 Hz, H-6′), 7.42 (1H, dt, J=1.4, 8.2 Hz, H-4′), 7.55 (1H, dt, J=1.3, 7.6 Hz, H-5′), 7.94 (1H, dd, J=1.4, 8.1 Hz, H-3′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 43.1, 47.4, 48.7, 55.0, 63.3, 124.8, 128.2, 129.1, 130.0, 131.0, 133.0, 134.9, 148.4, 214.5; IR 1606, 1632, 1751, 2871, 2931, 3415 cm^{-1}; HRMS (ESI) m/z calcd $C_{15}H_{15}NNaO_4$ $[M+Na]^+$ 296.0899, found 296.0901.

Compound **23**



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.68 (1H, dd, J=4.7, 12.8 Hz, H-6a), 2.19 (1H, ddd, J=6.4, 10.6, 12.7 Hz, H-6b), 2.43 (1H, s, –OH), 2.6–2.7 (3H, m, H-1, H-5, H-7b), 3.81 (1H, dd, J=6.4, 10.9 Hz, –C*H*HO–), 4.09 (1H, dd, J=8.2, 10.9 Hz, –C*H*HO–), 4.79 (1H, dm, J=3.5 Hz, H-2a), 5.55 (1H, ddd, J=1.2, 3.6, 9.1 Hz, H-3), 6.27 (1H, ddd, J=1.1, 7.0, 9.1 Hz, H-4), 7.33 (1H, dd, J=1.4, 7.9 Hz, H-6′), 7.40 (1H, dt, J=1.4, 7.8 Hz, H-4′), 7.54 (1H, dt, J=1.4, 7.7 Hz, H-5′), 7.90 (1H, dd, J=1.4, 8.1 Hz, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.5, 36.7, 44.8, 46.1, 50.9, 64.1, 124.9, 127.6, 128.2, 130.6, 133.1, 135.1, 136.4, 148.3, 214.2; IR 1606, 1635, 1748, 2874, 2936, 3406 cm^{-1}; HRMS (ESI) m/z calcd $C_{15}H_{15}NNaO_4$ $[M+Na]^+$ 296.0899, found 296.0885.

4.1.7. *rac*-(1*R*,2*R*,5*R*,7*R*,8*R*)-7-Hydroxymethyl-8-methyltricyclo[3.2.1.0^{2,8}]oct-3-ene 29. A solution of total volume (400 ml) containing toluene (36.8 g, 400 mmol), allyl alcohol (46.4 g, 800 mmol) and cyclohexane was added to a quartz immersion-well photoreactor and degassed by passing a stream of nitrogen through it for 20 min. This solution was then irradiated with 254 nm UV light for 120 h using a 16 W low-pressure mercury vapour lamp. The unreacted starting materials and solvent were removed in vacuo and the residue subjected to column chromatography to obtain the 7-*endo* isomer **29** as a pale yellow oil (1.23 g, 2%).

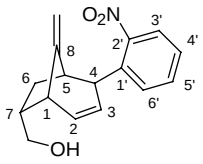


^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (3H, s, –CH_3), 1.48 (1H, br s, –OH), 1.48 (1H, d, J=12.8 Hz, H-6a), 1.53 (1H, dd, J=6.3, 7.1 Hz, H-1), 1.56 (1H, dm, J=7.2 Hz, H-2), 2.36 (1H, ddd, J=6.2, 11.3, 12.8 Hz, H-6b), 2.72–2.78 (1H, m, H-7b), 2.78 (1H, dm, J=6.0 Hz, H-5), 3.64 (1H, dd, J=7.3, 10.3 Hz, –C*H*HO–), 3.74 (1H, dd, J=8.4, 10.2 Hz, –CH*H*O–), 5.45 (1H, dddd, J=0.8, 0.8, 2.4, 5.3 Hz, H-4), 5.66 (1H, dd, J=2.0, 5.3 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.5, 37.6, 37.9, 41.3, 45.6, 46.4, 54.6, 66.4, 129.8, 136.7; IR 1596, 2923, 3308 cm^{-1}; HRMS (EI) m/z calcd $C_{10}H_{14}O$ $[M]^+$ 150.1045, found 150.1045.

4.1.8. *rac*-(1*R*,4*S*,5*R*,7*R*)-4-(2′-Nitrophenyl)-7-hydroxymethyl-8-methylenebicyclo[3.2.1]oct-2-ene 31a and *rac*-(1*R*,2*R*,5*R*,7*R*)-2-(2′-nitrophenyl)-7-hydroxymethyl-8-methylenebicyclo[3.2.1]oct-3-ene 32a. A mixture of the 7-*endo* allyl alcohol/toluene-derived *meta* photoadduct **29** (150 mg, 1.00 mmol), 2-iodo-1-nitrobenzene (299 mg, 1.20 mmol), triethylamine (121 mg, 1.20 mmol), palladium (II) acetate (11 mg, 0.050 mmol) and tri-*ortho*-tolylphosphine (30 mg, 0.10 mmol) and dry DMF (3 ml) was added to a re-sealable reaction tube. The tube was flushed with a stream of dry nitrogen, sealed and the mixture heated at 120 °C for 12 h. The reaction was poured into 2 M hydrochloric acid (50 ml) and the aqueous portion was washed with ethyl acetate (5×40 ml) and the combined organic portions were washed with brine (100 ml), water (100 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica, eluting with petrol/Et_2O

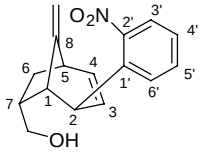
3:2) to afford **31a** (78 mg, 29%) as a yellow oil and **32a** (35 mg, 13%) as a yellow oil.

Compound **31a**



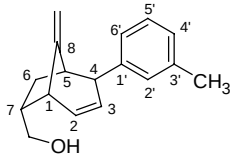
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (1H, ddd, J=1.2, 7.2, 13.4 Hz, H-6a), 1.65 (1H, br s, –OH), 2.29 (1H, ddd, J=7.8, 10.0, 13.3 Hz, H-6b), 2.42–2.49 (1H, m, H-7b), 2.66 (1H, dm, J=7.9 Hz, H-5), 2.96 (1H, ddd, J=1.1, 5.2, 6.4 Hz, H-1), 3.69 (1H, dd, J=9.2, 10.4 Hz, –C*H*HO–), 3.74 (1H, dd, J=6.1, 10.4 Hz, –CH*H*O–), 3.98 (1H, m, H-4a), 4.17 (1H, d, J=1.1 Hz, =C*H*H), 4.74 (1H, d, J=0.7 Hz, =CH*H*), 5.49 (1H, ddd, J=1.6, 3.6, 9.4 Hz, H-3), 6.13 (1H, ddd, J=1.7, 6.4, 9.3 Hz, H-2), 7.34–7.37 (2H, m, H-4′, H-6′), 7.50 (1H, ddd, J=1.4, 7.1, 8.4 Hz, H-5′), 7.87 (1H, ddd, J=0.7, 1.4, 7.8 Hz, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.1, 44.0, 46.4, 49.1, 50.3, 64.4, 102.9, 124.1, 127.2, 127.7, 131.7, 132.0, 132.5, 136.3, 148.8, 150.3; IR 1606, 1634, 2866, 2926, 3469 cm^{-1}; HRMS (ESI) *m*/*z* calcd $C_{16}H_{17}NNaO_3$ $[M+Na]^+$ 294.1106, found 294.1101.

Compound **32a**



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (1H, dd, J=4.7, 12.2 Hz, H-6a), 1.60 (1H, br s, –OH), 2.06 (1H, dddd, J=0.8, 6.4, 11.3, 12.2 Hz, H-6b), 2.57–2.64 (1H, m, H-7b), 2.76 (1H, ddm, J=1.4, 6.9 Hz, H-1), 2.81 (1H, ddd, J=1.2, 5.8, 6.6 Hz, H-5), 3.75 (1H, dd, J=6.3, 11.1 Hz, –C*H*HO–), 3.97 (1H, dd, J=9.0, 11.1 Hz, –CH*H*O–), 4.22 (1H, m, H-2a), 4.23 (1H, d, J=1.1 Hz, =C*H*H), 4.74 (1H, m, =CH*H*), 5.34 (1H, ddd, J=1.5, 3.7, 9.2 Hz, H-3), 6.27 (1H, ddd, J=1.4, 6.6, 9.2 Hz, H-4), 7.37 (1H, ddd, J=1.5, 7.3, 8.1 Hz, H-4′), 7.41 (1H, dd, J=1.5, 7.9 Hz, H-6′), 7.52 (1H, ddd, J=1.4, 7.5, 7.5 Hz, H-5′), 7.88 (1H, ddd, J=0.3, 1.4, 8.1 Hz, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.3, 41.5, 41.7, 42.7, 48.5, 64.8, 103.2, 124.3, 125.6, 127.3, 132.1, 132.5, 136.5, 137.8, 148.5, 150.6; IR 1640, 2955, 3422 cm^{-1}; HRMS (ESI) *m*/*z* calcd $C_{16}H_{17}NNaO_3$ $[M+Na]^+$ 294.1106, found 294.1102.

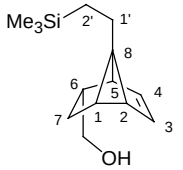
4.1.9. *rac*-(1*R*,4*S*,5*R*,7*R*)-4-(3′-Methylphenyl)-7-hydroxymethyl-8-methylenebicyclo[3.2.1]oct-2-ene 31b. A mixture of the 7-*endo* allyl alcohol/toluene-derived *meta* photoadduct **29** (150 mg, 1.00 mmol), 3-bromotoluene (205 mg, 1.20 mmol), triethylamine (121 mg, 1.20 mmol), palladium (II) acetate (11 mg, 0.050 mmol) and tri-*ortho*-tolylphosphine (30 mg, 0.10 mmol) and dry DMF (3 ml) was added to a re-sealable reaction tube. The tube was flushed with a stream of dry nitrogen, sealed and the mixture heated at 120 °C for 12 h. The reaction was poured into 2 M hydrochloric acid (50 ml) and the aqueous portion was washed with ethyl acetate (5×40 ml) and the combined organic portions were washed with brine (100 ml), water (100 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica, eluting with petrol/Et_2O 2:1) to afford **31b** (71 mg, 30%) as a yellow oil. The minor isomer **32b** (24 mg, <10%) was also obtained but could not be separated from some co-eluting impurites.



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (1H, ddd, J=1.0, 7.1, 13.0 Hz, H-6a), 1.60 (1H, br s, –OH), 2.23 (1H, ddd, J=7.8, 10.1, 13.0 Hz, H-6b), 2.33 (3H, s, –CH_3), 2.39–2.46 (1H, m, H-7b), 2.51 (1H, dm, J=8.0 Hz, H-5), 2.89 (1H, ddd, J=1.0, 5.1, 6.4 Hz, H-1), 3.43 (1H, m, H-4a), 3.73–3.75 (2H, m, –CH_2O–), 4.20 (1H, d, J=1.4 Hz, =C*H*H), 4.71 (1H, d, J=0.8 Hz, =CH*H*), 5.59 (1H, ddd, J=1.5, 3.6, 9.4 Hz, H-3), 6.02 (1H, ddd, J=1.6, 6.4, 9.6 Hz, H-2), 6.98 (3H, m, H-2′, H-4′, H-6′), 7.17 (1H, t, J=7.5 Hz, H-5′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4, 33.4, 43.9, 47.5, 49.3, 56.3, 64.7, 102.0, 125.4, 127.0, 127.7, 129.0, 129.1, 130.8, 137.3, 142.7, 150.8; IR 1637, 2924, 3433 cm^{-1}; HRMS (ESI) *m*/*z* calcd $C_{17}H_{20}NaO$ $[M+Na]^+$ 263.1412, found 263.1414.

4.1.10. *rac*-(1*S*,2*R*,5*S*,6*S*,8*S*)-6-Hydroxymethyl-8-(2′-trimethylsilanylethyl)tricyclo[3.2.1.0^{2,8}]oct-3-ene 35 and *rac*-(1*R*,2*R*,5*R*,7*R*,8*R*)-7-hydroxymethyl-8-(2′-trimethylsilanylethyl)tricyclo[32.1.0^{2,8}]oct-3-ene 36. A solution of total volume (400 ml) containing phenethyltrimethyl silane[16] (14.2 g, 80 mmol), allyl alcohol (14 g, 240 mmol) and cyclohexane was added to a quartz immersion-well photoreactor and degassed by passing a stream of nitrogen through it for 20 min. This solution was then irradiated with UV light for 13 h using a 400 W medium-pressure mercury vapour lamp. The solvent and unreacted allyl alcohol were removed in vacuo and the residue subjected to column chromatography to obtain the 6-*endo* isomer **35** (453 mg, 2.4%) and the 7-*endo* isomer **36** (415 mg, 2.2%).

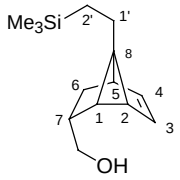
Compound **35**



^{1}H NMR (500 MHz, $CDCl_3$) δ −0.03 (9H, s, –Si(CH_3)$_3$), 0.47 (1H, ddd, J=5.0, 12.5, 14.2 Hz, Si–C*H*H–), 0.53 (1H, ddd, J=5.0, 12.5, 14.2 Hz, Si–CH*H*–), 1.22 (1H, ddd, J=1.5, 10.7, 13.0 Hz, H-7a), 1.44 (1H, ddd, J=1.5, 7.0, 7.0 Hz, H-1), 1.55 (1H, ddd, J=5.0, 12.6, 14.1 Hz, C(8)–CH*H*–), 1.61 (1H, m, H-2), 1.63 (1H, ddd, J=5.0, 12.6, 14.1 Hz, C(8)–C*H*H–), 1.78 (1H, br s, –OH), 1.89 (1H, dddd, J=1.4, 6.6, 7.9, 12.9 Hz, H-7b), 2.53–2.68 (1H, m,

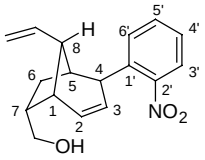
H-6b), 2.87 (1H, ddd, J=1.3, 2.4, 5.1 Hz, H-5), 3.42 (2H, d, J=7.5 Hz, –CH_2O–), 5.47 (1H, dd, J=2.4, 5.5 Hz, H-4), 5.69 (1H, dd, J=2.3, 5.5 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ −1.8, 13.5, 26.2, 26.8, 30.2, 35.7, 53.1, 53.2, 57.1, 63.2, 129.8, 130.1; IR 2952, 3429 cm^{-1}; HRMS (EI) m/z calcd $C_{14}H_{24}OSi$ $[M]^+$ 236.1608, found 236.1596.

Compound **36**



^{1}H NMR (500 MHz, $CDCl_3$) δ −0.02 (9H, s, –Si(CH_3)$_3$), 0.52 (1H, ddd, J=5.0, 12.6, 14.2 Hz, Si–CHH–), 0.57 (1H, ddd, J=4.9, 12.6, 14.2 Hz, Si–CHH–), 1.48 (1H, dd, J=1.2, 12.8 Hz, H-6a), 1.58 (2H, m, H-1, C(8)–CHH–), 1.63 (1H, ddd, J=5.1, 12.6, 14.1 Hz, C(8)–CHH–), 1.69 (1H, br s, –OH), 1.72 (1H, ddd, J=5.2, 12.6, 14.2 Hz, C(8)–CHH–), 2.31 (1H, ddd, J=6.2, 11.3, 12.8 Hz, H-6b), 2.69–2.76 (1H, m, H-7b), 2.85 (1H, ddd, J=1.3, 2.5, 6.0 Hz, H-5), 3.64 (1H, dd, J=7.3, 10.3 Hz, –CHHO–), 3.74 (1H, dd, J=8.4, 10.2 Hz, –CHHO–), 5.47 (1H, dddd, J=0.8, 0.8, 2.4, 5.3 Hz, H-4), 5.66 (1H, dd, J=1.9, 5.3 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ −1.8, 13.4, 26.7, 36.0, 36.2, 41.6, 45.6, 52.7, 53.7, 66.4, 130.0, 136.9; IR 1597, 1637, 2922, 3350 cm^{-1}; HRMS (ESI) m/z calcd $C_{14}H_{24}NaOSi$ $[M+Na]^+$ 259.1494, found 259.1489.

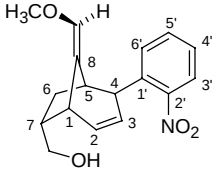
4.1.11. *rac*-(1*R*,4*R*,5*S*,7*R*,8*R*)-4-(2′-Nitrophenyl)-7-hydroxymethyl-8-vinylbicyclo[3.2.1]oct-2-ene 37. A mixture of the 7 *endo* phenethyltrimethyl silane derived *meta* photoadduct **36** (300 mg, 1.27 mmol), 2-iodo-1-nitrobenzene (380 mg, 1.53 mmol), triethylamine (154 mg, 1.53 mmol), palladium (II) acetate (14 mg, 0.060 mmol) and tri-*ortho*-tolylphosphine (39 mg, 0.13 mmol) and dry DMF (8 ml) was added to a re-sealable reaction tube. The tube was flushed with a stream of dry nitrogen, sealed and the mixture heated at 80 °C for 12 h. The reaction was poured into 2 M hydrochloric acid (75 ml) and the aqueous portion was washed with ethyl acetate (5×50 ml) and the combined organic portions were washed with brine (100 ml), water (100 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica, eluting with petrol/EtOAc 5:1) to afford **37** (54 mg, 15%) as a yellow oil.



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (1H, dd, J=6.3, 13.8 Hz, H-6a), 1.58 (1H, br s, –OH), 2.27 (1H, ddd, J=7.7, 10.0, 13.9 Hz, H-6b), 2.37 (1H, dm, J=7.7 Hz, H-5), 2.51 (1H, dm, J=5.8 Hz, H-8), 2.53–2.59 (2H, m, H-1, H-7b), 3.69 (1H, dd, J=8.5, 10.3 Hz, –CHHO–), 3.74 (1H, dd, J=6.1, 10.3 Hz, –CHHO–), 3.91 (1H, ddd, J=1.8, 1.8, 3.6 Hz, H-4a), 4.94 (1H, dd, J=1.7, 17.2 Hz, =CHH), 4.96 (1H, dd, J=1.6, 10.7 Hz, =CHH), 5.56 (1H, ddd, J=1.7, 3.6, 9.5 Hz, H-3), 5.73 (1H, ddd, J=5.8, 10.7, 17.2 Hz, C(8)–CH=), 6.26 (1H, ddd, J=2.0, 6.8, 9.5 Hz, H-2), 7.39 (1H, ddd, J=1.5, 7.3, 8.1 Hz, H-4′), 7.45 (1H, dd, J=1.5, 7.8 Hz, H-6′), 7.56 (1H, ddd, J=1.4, 7.7, 7.7 Hz, H-5′), 7.92 (1H, dd, J=1.3, 8.1 Hz, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.9, 42.1, 43.9, 44.3, 47.6, 48.1, 64.8, 114.4, 124.9, 126.9, 127.3, 131.2, 132.6, 134.6, 138.3, 139.7, 149.0; IR 1606, 1637, 2929, 3365 cm^{-1}; HRMS (ESI) m/z calcd $C_{17}H_{19}NNaO_3$ $[M+Na]^+$ 308.1263, found 308.1260.

4.1.12. *rac*-(1*R*,4*S*,5*R*,7*R*)-4-(2′-Nitrophenyl)-7-hydroxymethyl-8(*Z*)-methoxymethylenebicyclo[3.2.1]oct-2-ene 41. A solution of total volume (400 ml) containing benzylmethylether (4.89 g, 40 mmol), allyl alcohol (6.96 g, 120 mmol) and cyclohexane was added to a quartz immersion-well photoreactor and degassed by passing a stream of nitrogen through it for 20 min. This solution was then irradiated with 254 nm UV light for 87 h using a 16 W medium-pressure mercury vapour lamp. The solvent and unreacted starting materials were removed in vacuo and the residue subjected to column chromatography to obtain a 2:1 mixture of the 2,4 *meta* photoadduct **39** and the 2,6 *meta* photoadduct **40** (487 mg, 6.8%) as a pale green oil.

This inseparable mixture of photoadducts **39** and **40** (487 mg, 2.70 mmol) was added to a re-sealable reaction tube along with 2-iodo-1-nitrobenzene (674 mg, 2.70 mmol), triethylamine (328 mg, 3.25 mmol), palladium (II) acetate (30 mg, 0.135 mmol) and tri-*ortho*-tolylphosphine (82 mg, 0.27 mmol) and dry DMF (10 ml). The tube was flushed with a stream of dry nitrogen, sealed and the mixture heated at 120 °C for 2 h. The reaction was poured into 2 M hydrochloric acid (75 ml) and the aqueous portion was washed with ethyl acetate (5×50 ml) and the combined organic portions were washed with brine (100 ml), water (100 ml) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica, eluting with petrol/EtOAc 2:1) to afford **41** (54 mg, 15% with respect to the mixture of photoadducts **39** and **40**) as an orange oil.



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (1H, ddm, J=6.7, 13.2 Hz, H-6a), 1.65 (1H, br s, –OH), 2.26 (1H, ddd, J=7.8, 10.1, 13.2 Hz, H-6b), 2.38–2.46 (1H, m, H-7b), 2.59 (1H, tm, J=7.9 Hz, H-5), 3.44 (1H, tm, J=5.7 Hz, H-1), 3.47 (3H, s, –OCH_3), 3.68 (1H, dd, J=9.2, 10.5 Hz, –CHHO–), 3.74 (1H, dd, J=6.2, 10.5 Hz, –CHHO–), 3.88 (1H, m, H-4a), 5.19 (1H, s, =CHO–), 5.47 (1H, ddd, J=1.6, 3.7, 9.4 Hz, H-3), 6.15 (1H, ddd, J=1.7, 6.4, 9.3 Hz, H-2), 7.34–7.37 (2H, m, H-4′, H-6′), 7.52 (1H, ddd, J=1.4, 7.6, 7.6 Hz, H-5′), 7.86 (1H, dd, J=1.3, 8.0 Hz, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.7, 36.7, 43.2, 49.6, 49.9, 59.6, 64.5, 119.4, 124.1, 127.1, 127.9, 131.9, 132.1, 132.3, 135.1,

136.5, 148.8; IR 1636, 2930, 3417 cm^{-1}; HRMS (ESI) *m/z* calcd $C_{17}H_{19}NNaO_4$ $[M+Na]^+$ 324.1212, found 324.1204.

Acknowledgements

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References and notes

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10. We thank Mark Charles, DPhil thesis, University of Sussex, 2003 for suggesting these initial reaction conditions.
11. (a) The crystallographic data for compound **13** have been deposited with Cambridge Crystallographic Data Centre as supplementary publication number CCDC 283162. Formula: $C_{17}H_{17}N_1O_5$ Unit cell parameters: *a* 7.1064(12) *b* 9.7290(16) *c* 11.6227(16) Å alpha 110.028(8) beta 106.858(8) gamma 91.824(6)° space group $P\bar{1}$. (b) The crystallographic data for compound **14** have been deposited with Cambridge Crystallographic Data Centre as supplementary publication number CCDC 283163. Formula: $C_{17}H_{17}N_1O_5$ Unit cell parameters: *a* 9.1079(17) *b* 12.352(2) *c* 13.656(2) Å beta 107.32° space group *P*21/*n*.
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