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Investigating the Arenyl-Diene Double [3 + 2] Photocycloaddition Reaction

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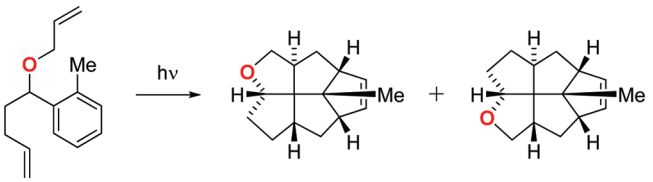

The double [3 + 2] photocycloaddition reaction involving arenyl−dienes has been used to assemble seven separate [5.5.5.5] fenestrane structures that include ether and aza variants. The primary photolysis step was a *meta* photocycloaddition reaction, while a secondary photocycloaddition step formed the fenestrane structure. Investigations involving the insertion of an additional methylene group into the basic arenyl−diene skeleton failed to afford the desired [5.5.5.6] fenestrane structure. The presence of an oxime moiety in the aromatic photosubstrate allowed the primary photolysis step to take place; however, an attempted secondary photocycloaddition reaction involving the oxime did not provide the intended polyheterocyclic fenestrane. An alternative strategy to form various "criss-cross" double *meta* photocycloadducts was investigated and led to the discovery of a Paterno−Büchi cycloaddition reaction between acetone and an angular *meta* photocycloadduct. Other novel thermally and photochemically mediated skeletal rearrangement reactions were also recorded.

Introduction

The generation of structurally complex molecules in a concise step-efficient manner is one of the primary challenges facing organic synthesis. Our previously reported double [3 + 2] photocycloaddition reaction[1] is a remarkable chemical process that addresses this issue by converting simple arenyl−diene substrates into products with architecturally complex three-dimensional structures in two photochemical steps (Scheme 1). During the course of such a process four new carbon−carbon bonds, five new rings, and up to nine new stereocenters are created.

As previously highlighted by Wender, Dore, and deLong,[2] fenestranes compare favorably to the steroid class of compounds in that they are "conformationally rigid and chemically robust". A lack of wider interest in the usage of fenestranes as materials and in medicinal research has been largely due to their unavailability. However, the recent total synthesis of the dioxafenestrane Penifulvin A,[3] which shows efficacy as an insecticide toward the fall armyworm, provides an indication that the potentially useful properties of compounds containing fenestrane scaffolds may have been overlooked.

Consequently, a route toward fenestranes that is simple to perform and permits the attachment of different functional groups could provide libraries of novel compounds for the management of disease and infection. Our initial communication[1] revealing the double [3 + 2] photocycloaddition reaction focused on the conversion of the acetal substrate **1** into the fenestrane[4] product **2** via the linear *meta* photocycloadduct **3**. This article will display the reaction's wider application particularly with respect to the formation of ether and amino analogues.

Results and Discussion

Acetal Fenestranes. The conversion of arenyl−diene acetal **1** into fenestrane **2** was found to be a two-stage process. The

(1) Penkett, C. S.; Woolford, J. A.; Day, I. J.; Coles, M. P. *J. Am. Chem. Soc.* **2010**, *132*, 4.
(2) Wender, P. A.; Dore, T. M.; deLong, M. A. *Tetrahedron Lett.* **1996**, *37*, 7687.
(3) Gaich, T.; Mulzer, J. *J. Am. Chem. Soc.* **2009**, *131*, 452.
(4) (a) Mani, J.; Keese, R. *Tetrahedron* **1985**, *41*, 5697. (b) Mani, J.; Schüttel, S.; Zhang, C.; Bigler, P.; Müller, C.; Keese, R. *Helv. Chim. Acta* **1989**, *72*, 487. (c) Thommen, M.; Keese, R. *Synlett* **1997**, 231. (d) Denmark, S. E.; Kramps, L. A.; Montgomery, J. I. *Angew. Chem., Int. Ed.* **2002**, *41*, 4122. (e) Keese, R. *Chem. Rev.* **2006**, *106*, 4787.

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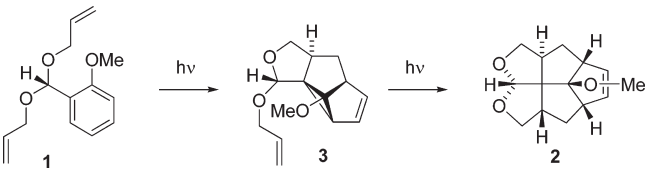
SCHEME 1. The Double [3 + 2] Photocycloaddition Reaction



SCHEME 2. Intramolecular *meta* Photocycloaddition of Arenyl-Diene 1 Involving Exciplex 1*

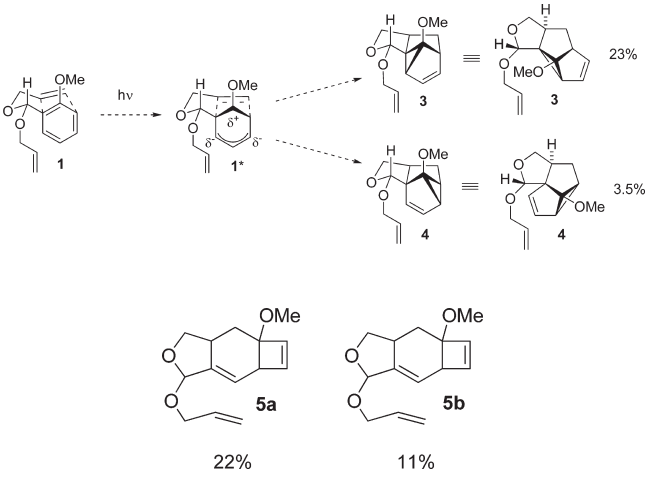


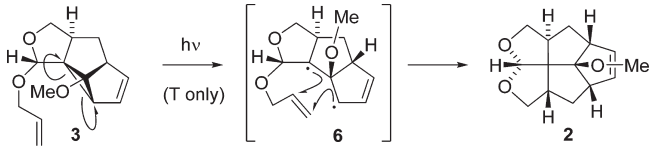
FIGURE 1. The *ortho*-derived photocycloadducts **5a** and **5b** generated from the arenyl diene photosubstrate **1**.

first step involved the familiar intramolecular *meta* photocycloaddition reaction.[5] The generally accepted mechanism[5] for this transformation begins with the absorption of a photon of 254 nm UV light by the aromatic ring of **1** and formation of its first singlet excited state. Interaction with one of the alkenes would afford exciplex **1*** and subsequent cyclopropane ring-closure would then lead to the formation of the linear and angular *meta* photoadducts **3** and **4** (Scheme 2).[1]

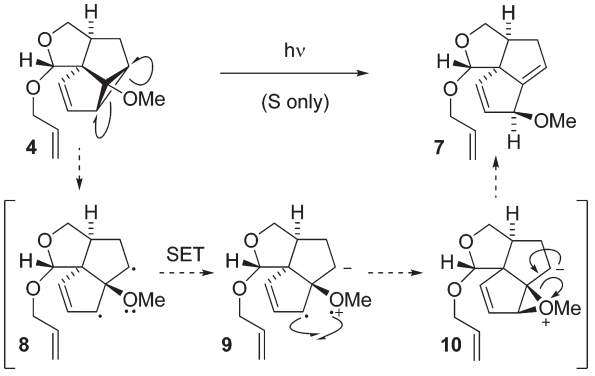
In addition to the *meta* adducts, this methoxy-substituted arenyl−diene **1** also generated *ortho*-derived photocycloadducts[6] **5a** and **5b** (Figure 1).

The linear form **3** was found to be the major isomer, although interconversion between it and the angular form **4** occurred during irradiations and resulted in variable

SCHEME 3. Proposed Mechanism to Account for the Conversion of Linear *meta* Photoadduct 3 into Fenestrane 2



SCHEME 4. Proposed Mechanism to Account for the Conversion of Angular *meta* Photoadduct 4 into Compound 7



relative proportions of **3** and **4** being observed. This meant that either the linear or the angular *meta* photocycloadducts (**3** or **4**) would undergo conversion to fenestrane **2** during a second irradiation step. The efficiency of fenestrane formation from either *meta* photocycloadduct was dramatically improved by the addition of a triplet sensitizer. It was also found that the amount of observed decomposition was reduced, if the second stage photolysis reaction was performed in acetonitrile instead of cyclohexane. Under these circumstances fenestrane **2** was prepared from the linear photoadduct **3** in 50% yield after irradiation for 3.75 h in the presence of acetophenone using a 6 W low pressure mercury vapor lamp in a quartz immersion-well photoreactor. It was discovered that fenestrane formation was inhibited if either of the linear or angular forms were irradiated in the presence of a triplet quencher, which indicated that fenestrane formation was occurring through the triplet manifold. We accounted for the formation of fenestrane **2** by proposing the reaction mechanism presented in Scheme 3.[1] Diradical **6** was generated by the homolytic fission of the external cyclopropane bond of the linear *meta* photocycloadduct **3**, which then cyclized onto the tethered vinyl group to form fenestrane **2**.

As well as forming fenestrane **2** during the irradiation of the linear or angular *meta* adducts (**3** or **4**), a novel photoinduced 1,2-methoxy migration reaction was discovered that resulted in the formation of angular tricycle **7**. This type of triquinane is a common structural motif found in a range of natural products; a noteworthy example being the crinipellin series of antibiotics.[7]

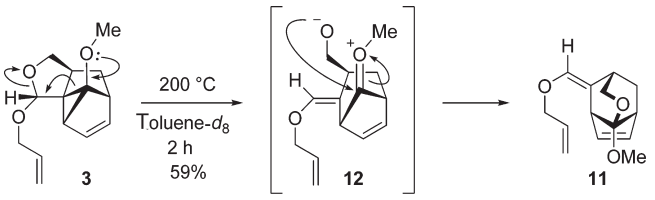
The extent of compound **7** formation appeared to be dependent on the age and condition of the lamp used, while the presence of a triplet sensitizer in the reaction mixture

(5) (a) Wilzbach, K. E.; Kaplan, L. *J. Am. Chem. Soc.* **1966**, *88*, 2066. (b) Bryce-Smith, D.; Gilbert, A.; Orger, B. H. *J. Chem. Soc., Chem. Commun.* **1966**, 512. (c) Cornelisse, J. *Chem. Rev.* **1993**, *93*, 615. (d) Wender, P. A.; Siggel, L.; Nuss, J. M. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel-Dekker: New York, 1989; Vol 10, Chapter 4, p 357. (e) Wender, P. A.; Siggel, L.; Nuss, J. M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, UK, 1991; Vol. 5, p 645. (f) Wender, P. A.; Ternansky, R.; deLong, M.; Singh, S.; Olivero, A.; Rice, K. *Pure Appl. Chem.* **1990**, *62*, 1597. (g) Hoffmann, N. *Synthesis* **2004**, 481. (h) Chappell, D.; Russell, A. T. *Org. Biomol. Chem.* **2006**, *4*, 4409. (i) Mattay, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 663. (j) Streit, U.; Bochet, C. G. *Chimia* **2008**, *62*, 962.

(6) (a) Ayer, D. E.; Büchi, G. U.S. Patent 2,805,252, 1957. (b) Atkinson, J. E.; Ayer, D. E.; Büchi, G.; Robb, E. W. *J. Am. Chem. Soc.* **1963**, *85*, 2257. (c) Al-Qaradawi, S. Y.; Cosstick, K. B.; Gilbert, A. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1145. (d) Hoffmann, N.; Pete, J.-P. *J. Org. Chem.* **1997**, *62*, 6952. (e) Avent, A. G.; Byrne, P. W.; Penkett, C. S. *Org. Lett.* **1999**, *1*, 2073. (f) Vízvárdi, K.; Toppet, S.; Hoornaert, G. J.; De Keukeleire, D.; Bakó, P.; van der Eycken, E. *J. Photochem. Photobiol. A: Chem.* **2000**, *133*, 135. (g) Hoffmann, N.; Pete, J.-P.; Inoue, Y.; Mori, T. *J. Org. Chem.* **2002**, *67*, 2315. (h) Wagner, P. J.; Lee, J.-I. *Tetrahedron Lett.* **2002**, *43*, 3569.

(7) (a) Kupka, J.; Anke, T.; Oberwinkler, F.; Schramm, G.; Steglich, W. *J. Antibiot.* **1979**, *32*, 130. (b) Wender, P. A.; Dore, T. M. *Tetrahedron Lett.* **1998**, *39*, 8589.

SCHEME 5. Thermolytic Conversion of Linear *meta* Photoadduct 3 into Tricyclic Acetal 11



during this secondary photolysis step prevented its formation. This indicated that the 1,2-methoxy migration reaction to form **7** was occurring through the singlet manifold. We accounted for the formation **7** by proposing the reaction mechanism presented in Scheme 4.[1] Diradical **8** was generated by the homolytic fission of the external cyclopropane bond of the angular *meta* photocycloadduct **4**, which then underwent single electron transfer (SET) from the methoxy lone pair to create the radical cation moiety of species **9**. Radical−radical recombination resulted in the formation of the zwitterion **10**, which ring-opened to afford **7**.

Although not reported in the original communication, the thermolysis properties of the *meta* adduct **3** were also investigated. The linear form **3** was found to undergo a fragmentive elimination−addition reaction to afford the tricyclic acetal **11** when heated for 2 h at 200 °C in deuterated toluene (Scheme 5). The formation of **11** can be explained by invoking zwitterion **12** as an intermediate, which would form following the fragmentation of the strained three-membered ring with the assistance of the methoxy group's oxygen lone pair of electrons. The alkoxy anion moiety of **12** would then ring-close onto the oxonium ion to afford **11**. Related events have been observed by us on previous occasions.[8] It should be pointed out that the structural characteristics of the angular form **4** do not lend themselves to undergoing a similar transformation and unsurprisingly **4** was found, to be thermally stable at 230 °C for many hours.

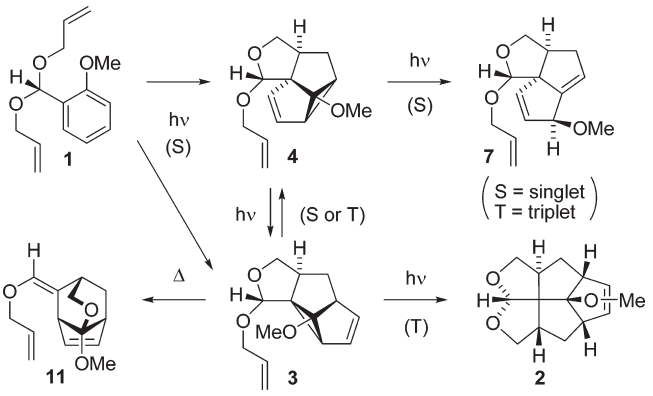
The photochemical and thermochemical transformations involving the arenyl−diene **1** are summarized in Scheme 6.

Wender et al.[2] showed that irradiation of the *o*-tolualdehyde-derived acetal **13**[2] resulted in the formation of linear and angular *meta* adducts **14** and **15**, the former of which was converted into a [5.5.5.5] fenestrane using a radical-based method.[2] By comparison; our own photochemical method furnished the alternative fenestrane **16** from **14**. Our initial attempt of directly irradiating **14** for a week using a 6 W low pressure mercury vapor lamp and cyclohexane as the solvent gave less than 10% yield of **16**.[1] Repetition of this transformation using acetophenone as a triplet sensitizer and acetonitrile as the solvent afforded the fenestrane **16** free of other impurities in 31% yield after 4.5 h (Scheme 7).

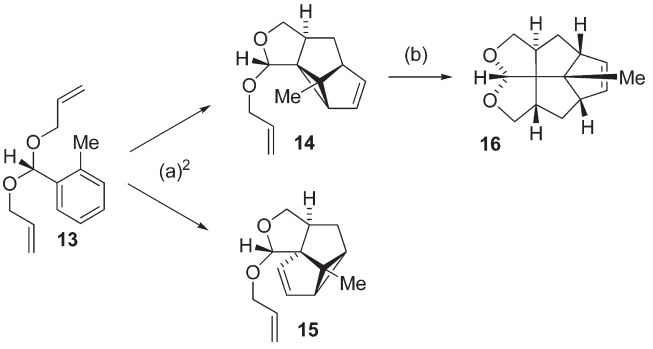
It was noteworthy that no equivalent 1,2-methyl migration product (c.f. compound **7**) was formed following prolonged direct irradiation and no thermal rearrangement of the linear *meta* adduct **14** occurred even when heated above 230 °C for many hours. This revealed that an alkoxy group on the aromatic ring of the arenyl−diene photosubstrate had quite a profound influence on the subsequent chemical pathways available to it.

(8) (a) Penkett, C. S.; Byrne, P. W.; Teobald, B. J.; Rola, B.; Ozanne, A.; Hitchcock, P. B. *Tetrahedron* **2004**, *60*, 2771. (b) Prantz, K.; Mulzer, J. *Chem. Rev.* **2010**, *110*, 3741.

SCHEME 6. Summary of Photochemical and Thermochemical Transformations Involving the Arenyl-Diene 1



SCHEME 7. Photoconversion of *o*-Tolualdehyde-Derived *meta* Photoadduct 14[2] into Fenestrane 16[a]



[a]Conditions: (a) hv, 254 nm, cyclohexane;[2] (b) hv, 254 nm, MeCN, acetophenone, 4.5 h, 31%.

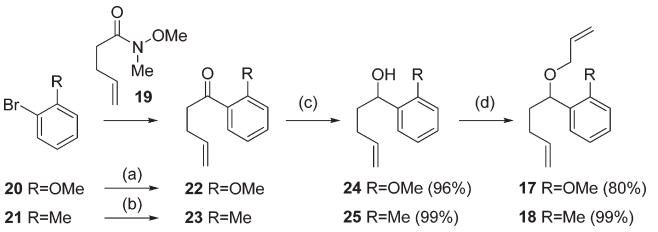
Ether Fenestrane Formation. To investigate the generality of this fenestrane-forming process the two ether photosubstrates **17** and **18** were prepared with either a methoxy or a methyl substituent on the aromatic ring. A simple yet flexible route to preparing the photosubstrates was chosen that involved attaching the alkenyl chain to the aromatic core using the Weinreb amide **19**.[9] The ketones **22** and **23** were reduced with sodium borohydride and the resulting secondary alcohols **24**[10] and **25** were allylated under phase transfer conditions to afford the methoxy and methyl substituted ether photosubstrates **17** and **18**, respectively (Scheme 8).

During the initial photolysis stage the methoxy arenyl−diene **17** was directly irradiated with 254 nm light until it had been completely consumed. As was expected for ether **17** compared with acetal **1**, a more complex mixture of isomeric products was created. This was due to one alkene of **17** being tethered through an all-carbon chain, while the other was tethered through an ether chain. We were able to isolate four of the photoadducts free of contamination, however several different isomeric products coeluted, which hindered their structural determination. In addition to the creation of various *meta* photoadducts the methoxy substituent on the

(9) Fournial, A.; Ranaivondrambola, T.; Mathé-Allainmat, M.; Robins, R. J.; Lebreton, J. *Eur. J. Org. Chem.* **2010**, 152.

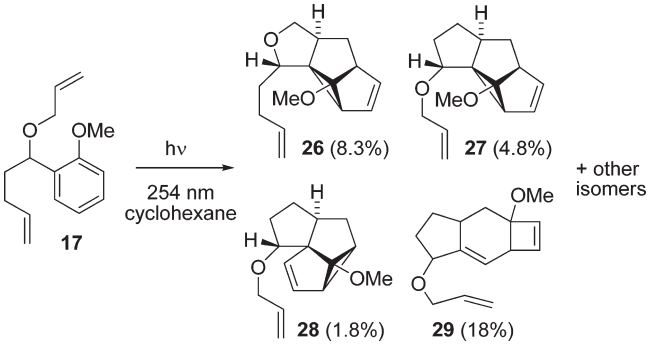
(10) Timmermans, J. L.; Wamelink, M. P.; Lodder, G.; Cornelisse, J. *Eur. J. Org. Chem.* **1999**, 463.

SCHEME 8. Formation of Arenyl−Diene Photosubstrates 17 and 18[a]



[a]Conditions: (a) *n*-BuLi then **19**, −78 °C, THF, 62%; (b) Li then **19**, 0 °C, Et_2O, 50%; (c) $NaBH_4$, 0 °C, MeOH, (d) Bu_4NHSO_4, $NaOH_{(aq)}$, CH_2Cl_2, allyl bromide.

SCHEME 9. Collection of Photoadducts Formed during Primary Photolysis Stage Involving Arenyl−Diene Photosubstrate 17

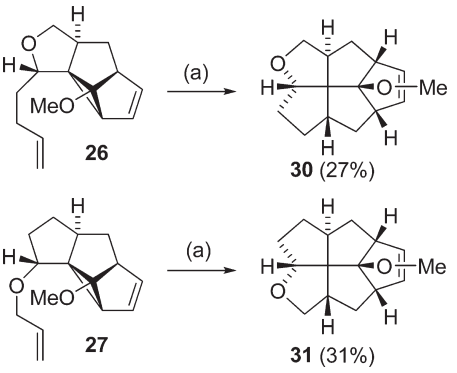


aromatic ring also caused the formation of *ortho*-derived photoadducts. The four isolated isomers were the linear *meta* photoadduct with the ether in the core structure **26**, the linear *meta* photoadduct with the ether outside the core structure **27**, the angular *meta* photoadduct with the ether outside the core structure **28**, and an *ortho*-derived photoadduct with the ether outside the core structure **29** (Scheme 9). It was interesting that the ether-tethered alkene showed no significant preference for undergoing photocycloaddition compared to the all-carbon tethered equivalent.

Gratifyingly both linear *meta* photoadducts **26** and **27** were available from the primary photolysis step involving arenyl−diene **17**. *meta* Photoadduct **26** had an all-carbon tethered vinyl group that was available to undergo secondary photolysis to form fenestrane **30**, while *meta* photoadduct **27** had an ether tethered vinyl group that was available to undergo secondary photolysis to form fenestrane **31**. These two secondary photolysis reactions were performed in cyclohexane using acetophenone as the triplet sensitizer to afford fenestranes **30** and **31** in 27% and 31% yields, respectively (Scheme 10). It should be noted that, when these reactions were performed, acetonitrile was unavailable due to a worldwide shortage of the solvent.

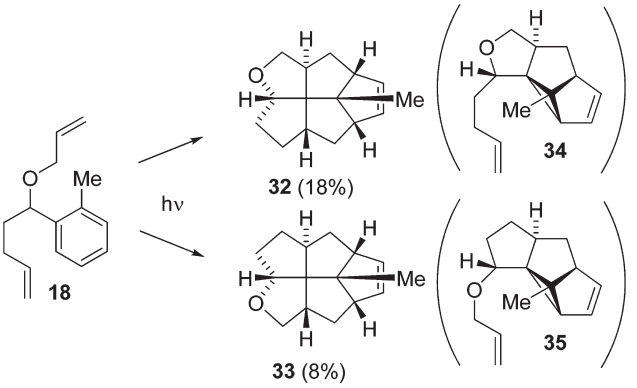
The photochemical transformation of the methyl analogue **18** deviated from the normally observed two-step behavior in cyclohexane, with fenestrane formation occurring prior to the complete consumption of the arenyl−diene photosubstrate. Direct irradiation of **18** for an initial 8 h in cyclohexane using 254 nm UV light revealed a complex mixture of products that still included the arenyl−diene **18**,

SCHEME 10. The Conversion of Linear *meta* Photoadducts 26 and 27 into Fenestranes 30 and 31[a]



[a]Conditions: (a) hv 254 nm, acetophenone 150 mol %, cyclohexane.

SCHEME 11. The Conversion of Arenyl−Diene 18 into Fenestranes 32 and 33[a]



[a]Conditions: (a) hv 254 nm, acetophenone 150 mol %, cyclohexane.

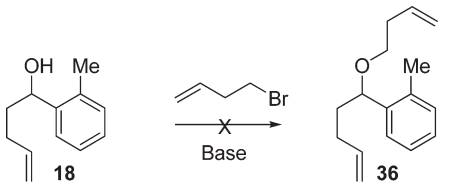
in addition to the fenestranes **32** and **33** and the intermediary linear *meta* photocycloadducts **34** and **35**. A further 8 h of irradiation of this reaction mixture afforded the fenestranes **32** and **33** in 18% and 8% yields, respectively (Scheme 11).

If acetonitrile was used as the solvent for the primary photolysis step of the arenyl−diene **18**, the linear *meta* photocycloadducts **34** and **35** were formed without any noticeable conversion to their respective fenestranes. Unfortunately the complexity of this process meant that it was not possible to obtain either linear *meta* photocycloadduct **34** or **35** free of other coeluting contaminants.

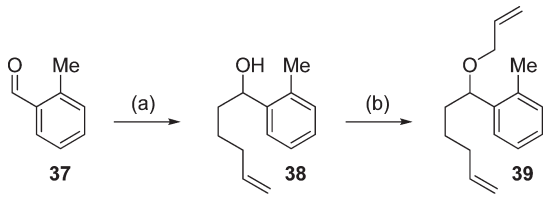
Investigations into the Formation of [5.5.5.6] Fenestranes. The fenestranes reported thus far have incorporated the same [5.5.5.5] structure. We therefore believed it would be prudent to attempt to expand the potential application of our double [3 + 2] photocycloaddition reaction by investigating the construction of a different type of fenestrane. For instance, a [5.5.5.6] fenestrane could be generated via the incorporation of an extra methylene group into one of the alkene tethers. We initially attempted the formation of photosubstrate **36** by alkylating **18** with butenyl bromide, but found, this to be a very ineffective process (Scheme 12).

Hence the alternative strategy of incorporating the extra methylene group into the all-carbon chain was adopted with

SCHEME 12. Failed Attempt To Convert Alcohol 18 into Arenyl−Diene 36

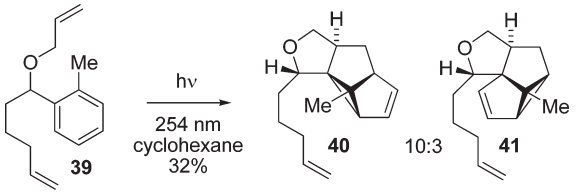


SCHEME 13. Formation of Photosubstrate 39[a]

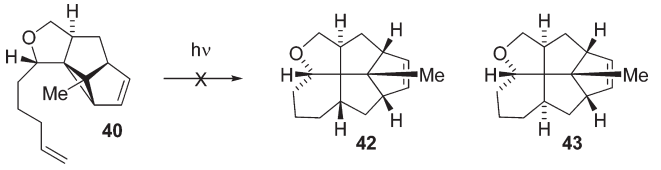


[a]Conditions: (a) pentenyl magnesium bromide, *o*-tolualdehyde, 0 °C, Et_2O, 81%; (b) Bu_4NHSO_4, $NaOH_{(aq)}$, CH_2Cl_2, allyl bromide, 74%.

SCHEME 14. *meta* Photoadducts 40 and 41 formed during Primary Photolysis Stage Involving Arenyl−Diene 39



SCHEME 15. Failed Attempt To Convert *meta* Photoadduct 40 into a [5.5.5.6] Fenestrane



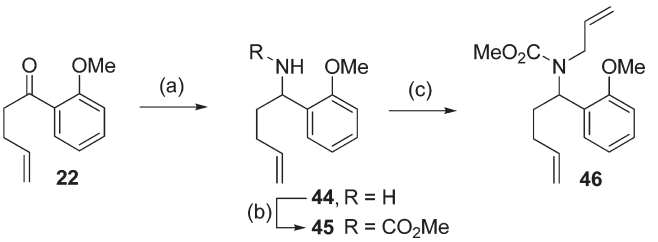
the preparation of **39** (Scheme 13). This was achieved by adding pentenyl magnesium bromide to *o*-tolualdehyde and then alkylating the secondary alcohol **38** with allyl bromide to afford ether **39**.

Cycloaddition of alkenes connected via a 3-atom chain are known to be kinetically favored over that of a 4-atom chain due to having fewer degrees of freedom.[5h] Hence as expected the shorter ether tethered alkene of **39** preferentially underwent *meta* photocycloaddition to afford the linear and angular *meta* photoadducts **40** and **41** in a ratio of 10:3 (Scheme 14).

The near coelution of these linear and angular products **40** and **41** hindered their separation and prevented the isolation of a pure sample of each. When a mixture rich in the linear *meta* photoadduct **40** was irradiated under triplet sensitized conditions using acetophenone, there was no evidence to indicate the formation of fenestranes **42** or **43** (Scheme 15).

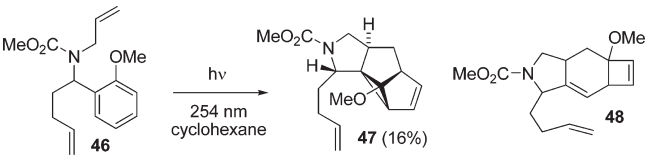
Significant decomposition took place during the course of this photoreaction. Only 11% of the original mixture of

SCHEME 16. Formation of Photosubstrate 46[a]



[a]Conditions: (a) NH_4OAc, $NaCNBH_3$, MeOH, rt, 3 days; (b) NEt_3, $ClCO_2Me$, Et_2O, rt, 62% over two steps; (c) NaH, allyl bromide, DMF, rt, 83%.

SCHEME 17. *meta* Photoadduct 47 formed during Primary Photolysis Stage Involving Arenyl−Diene 46



linear and angular primary photoadducts could be recovered from the crude residue, this time with the angular form **41** being the major component in a ratio of 5:1. It is likely that the longer alkene tether of **40** compared with **34** hindered the adoption of an appropriate conformation that would have allowed a secondary cycloaddition process to take place. [5.5.5.6] Fenestrane formation was too slow when compared with the interconversion between the linear and angular forms and the various other decomposition processes.

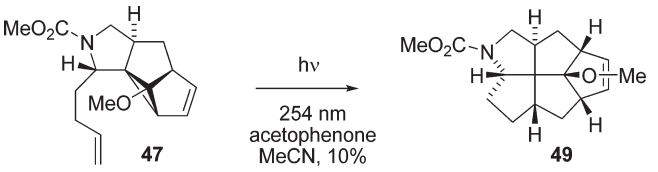
Aza-Fenestrane Formation. Gilbert and Blakemore[11] found, that an amino tethered variant of the intramolecular *meta* photocycloaddition reaction could be accomplished provided the nitrogen was protected with an electron-withdrawing group. Following this precedent we conceived that an aza-fenestrane[2d] could be created from the arenyl−diene photosubstrate **46**, which was synthesized from ketone **22**. Reductive amination of **22** using sodium cyanoborohydride[12] afforded the primary amine **44**, which was protected as the methoxy carbamate **45** and subsequently converted to **46** using allyl bromide and sodium hydride (Scheme 16).

Irradiation of **46** using 254 nm UV light provided mainly the linear *meta* photocycloadduct **47** along with an impure sample of the *ortho*-photocycloadduct **48** (Scheme 17). It is worth noting that only the nitrogen-tethered alkene underwent cycloaddition to a significant degree, even though both alkenes of amino arenyl−diene **46** were attached by three-atom tethers. This may have been due to the sp^2-hybridized nature of the protected nitrogen, which also added additional complexity to NMR interpretation due to the existence of two rotameric forms.

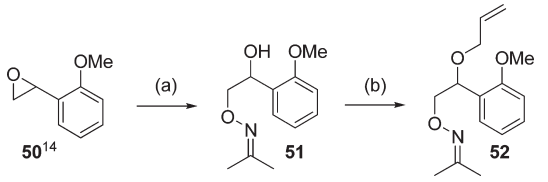
Irradiation of the linear *meta* adduct **47** in the absence of a triplet sensitizer rapidly resulted in its decomposition. However when **47** was irradiated in acetonitrile in the presence of acetophenone it underwent conversion to the amino fenestrane **49** (Scheme 18).

(11) Gilbert, A.; Blakemore, D. C. *Tetrahedron Lett.* **1994**, *35*, 5267.
(12) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748.

SCHEME 18. Conversion of Linear *meta* Photoadduct 47 into Aza-Fenestrane 49

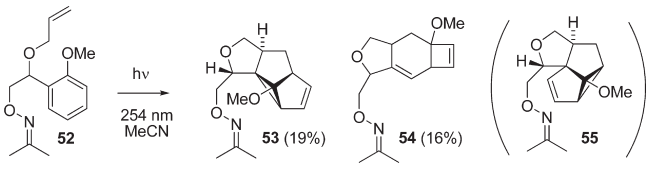


SCHEME 19. Formation of Photosubstrate 52[a]



[a]Conditions: (a) acetone oxime, KOH, DMSO, 80 °C, 94%; (b) Bu_4NHSO_4, $NaOH_{(aq)}$, CH_2Cl_2, allyl bromide, 83%.

SCHEME 20. Collection of Photoadducts Formed during Primary Photolysis Stage Involving Arenyl−Diene Photosubstrate 52

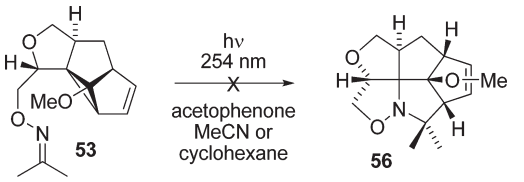


Investigations into Oxime Photocycloaddition Reactions. Booker−Milburn[13] recently showed the first example of a higher order [5 + 2] photocycloaddition to maleimides using an oxime or hydrazone in exchange for an alkene as the ground-state reacting partner. We postulated that an oxime could be substituted for an alkene during a double [3 + 2] photocycloaddition. To test this proposal, photosubstrate **52** was prepared by opening up the epoxide **50**[14] with acetone oxime using potassium hydroxide in DMSO and then allylating the resulting secondary alcohol **51** (Scheme 19). It is worth pointing out that oxime **51** failed to undergo intramolecular photocycloaddition when directly irradiated with 254 nm UV light.

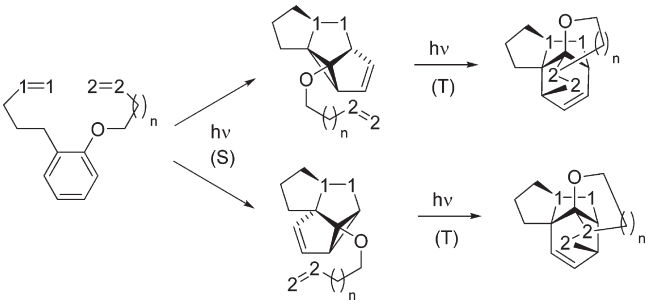
Irradiation of **52** using 254 nm UV light led to the formation of the linear *meta* photocycloadduct **53** and an impure sample of the *ortho*-derived photocycloadduct **54** as the two major products (Scheme 20), although traces of the angular *meta* photocycloadduct **55** could be observed in the ^{1}H NMR spectrum of the crude photolysis residue.

Irradiation of the linear adduct **53** was then performed in either cyclohexane or acetonitrile as the solvent under triplet sensitized conditions using acetophenone (Scheme 21). In cyclohexane this secondary photoreaction led to significant decomposition via polymerization, while in acetonitrile the linear adduct **53** simply photoequilibrated with the angular form **55**.

SCHEME 21. Failed Attempt to Convert *meta* Photoadduct 53 into Fenestrane 56



SCHEME 22. Proposed Strategy to form Criss-Cross Double *meta* Photocycloadducts



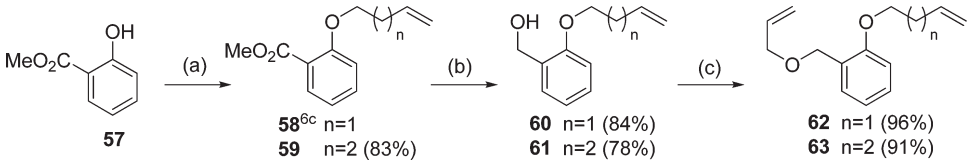
Investigations into the "Criss-Cross" Double *meta* Photocycloaddition Reaction. So far the focus of this research project was to assemble related fenestrane structures. This was achieved by attaching a bifurcating dienyl chain onto an aromatic ring adjacent to an electron-donating group. The electron-donating group directed the initial *meta* photocycloaddition onto the aromatic ring, while a second cycloaddition process led to the formation of a fenestrane by inserting the remaining tethered alkene into the external cyclopropane bond of the linear *meta* photocycloadduct. A variation on the double cycloaddition process using a different arrangement of tethered alkenes is presented in Scheme 22 that potentially would lead to the formation of criss-cross photocycloadducts.

The two tethered alkenes (−1 and −2) would be attached from different points about the aromatic ring, with alkene-1 being attached via a carbon atom to the aromatic ring and alkene-2 via an oxygen atom to the aromatic ring. The strongly electron-donating oxygen atom would control the initial *meta* photocycloaddition between the aromatic ring and the carbon-tethered alkene-1. The remaining oxygen-tethered alkene-2 would then undergo a secondary photocycloaddition process and insert into the internal cyclopropane bond of either the linear or angular *meta* photocycloadduct. The overall effect would be of a double *meta* photocycloaddition reaction taking place with the two alkenes sandwiching the former aromatic ring from above and beneath in a criss-cross fashion.

Two versions of the photosubstrate were prepared: one with an oxybut-3-enyl chain (**62**) and the other with an oxypent-4-enyl chain (**63**). Their synthesis began by etherification of methyl salicylate **57**[15] (oil of wintergreen) with either 4-bromobutene or 5-bromopentene, respectively. The methyl esters **58**[6c] and **59** were then reduced with DIBAL and the resulting primary alcohols **60** and **61** were allylated to

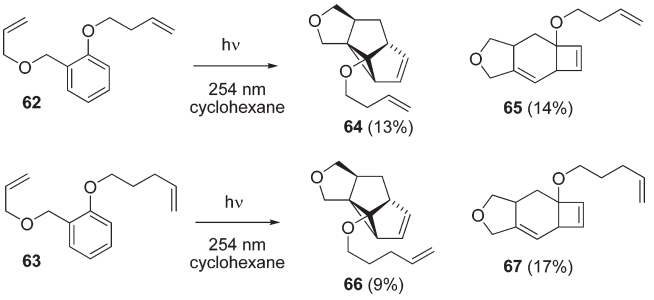
(13) Roscini, C.; Cubbage, K. L.; Berry, M.; Orr-Ewing, A. J.; Booker-Milburn, K. I. *Angew. Chem., Int. Ed.* **2009**, *48*, 8176.
(14) Guy, A.; Doussot, J.; Ferroud, C.; Garreau, R.; Godefroy-Falguieres, A. *Synthesis* **1992**, 821.
(15) Smith, K.; Morris, I. K.; Owen, P. G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 77.

SCHEME 23. Formation of Arenyl−Diene Photosubstrates 62 and 63[a]

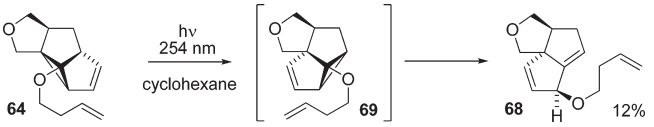


[a]Conditions: (a) 4-bromobutene or 5-bromopentene, K_2CO_3, acetone, reflux; (b) DIBAL, Et_2O, 0 °C; (c) Bu_4NHSO_4, $NaOH_{(aq)}$, CH_2Cl_2, allyl bromide.

SCHEME 24. Linear *meta* and *ortho*-Derived Photoadducts Formed during Primary Photolysis Stages Involving Arenyl−Diene Photosubstrates 62 and 63



SCHEME 25. The Conversion of Linear *meta* Photoadduct 64 into the 1,2-Alkoxy Rearranged Product 68



afford the two arenyl−diene photosubstrates **62** and **63**, respectively (Scheme 23).

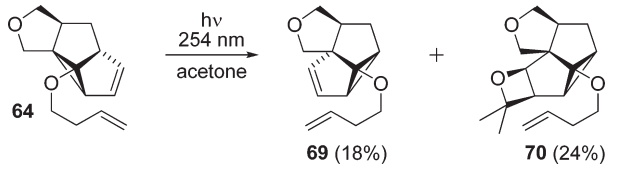
Direct irradiation of the oxybut-3-enyl analogue **62** with 254 nm UV light until it had all been consumed afforded the linear *meta* photocycloadduct **64** and the *ortho*-derived photocycloadduct **65**. Similarly irradiation of the oxypent-4-enyl variant **63** gave the linear *meta* photocycloadduct **66** and the *ortho*-derived photocycloadduct **67** (Scheme 24).

Secondary photolysis of the oxybut-3-enyl linear *meta* photoadduct **64** without triplet sensitization in cyclohexane resulted in decomposition and conversion to the 1,2-alkoxy rearranged product **68** (c.f. compound **7**). This could be derived from a photoequilibration of linear adduct **64** to its angular form **69**, then a 1,2-translocation of the oxygen linked alkenyl chain to afford **68** (Scheme 25).

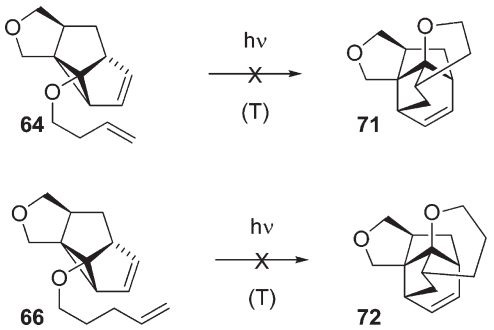
Photolysis of the linear adduct **64** in the presence of acetophenone with cyclohexane as the solvent only resulted in interconversion between the linear (**64**) and angular (**69**) forms; no 1,2-alkoxy rearranged product **68** was generated during this procedure. Repeating this process with acetonitrile as the solvent achieved a similar result, albeit with less decomposition of the photosubstrate. When photolysis of the linear adduct **64** was performed in neat acetone to act as a triplet sensitizer, photoequilibration to the angular form **69** occurred and a Paterno−Büchi cycloaddition process[16] took

(16) (a) Paternò, E.; Chieffi, G. *Gazz. Chim. Ital.* **1909**, *39−1*, 341. (b) Büchi, G.; Inman, C. G.; Lipinsky, E. S. *J. Am. Chem. Soc.* **1954**, *76*, 4327. (c) Bach, T. *Synthesis* **1998**, 683.

SCHEME 26. The Conversion of Linear *meta* Photoadduct 64 into the Angular *meta* Photoadduct 69 and the Paterno−Büchi Cycloadduct 70



SCHEME 27. Failed Attempts to Convert *meta* Photoadducts 64 and 66 into Double *meta* Cycloadducts 71 and 72



place between acetone and the angular isomer **69** to afford the oxetane **70**. Again no 1,2-alkoxy rearranged product **68** was derived from this triplet-sensitized reaction and interestingly there was no product derived from Paterno−Büchi cycloaddition between acetone and the linear *meta* photocycloadduct **64** (Scheme 26).

A similar series of secondary photolytic studies were performed using the oxypent-4-enyl linear *meta* photoadduct **66** in the hope that a longer tether might favor the formation of an appropriate conformation to allow secondary cycloaddition. However rapid decomposition of **66** hindered subsequent purification procedures and disappointingly no evidence could be established to support the formation of double *meta* cycloaddition products **71** or **72** from either the oxybut-3-enyl or the oxypent-4-enyl *meta* adducts **64** or **66** (Scheme 27).

Conclusion

The flexibility of the double [3 + 2] photocycloaddition reaction to assemble a range of ether and aza [5.5.5.5] fenestrane structures has been demonstrated with the formation of compounds **2**,[1] **16**,[1] **30**, **31**, **32**, **33**, and **49**. Their respective ^1H and ^{13}C NMR spectra are compared on pages S267 and S268 of the Supporting Information. Thermolysis properties of linear *meta* photoadduct **3** were investigated

and resulted in a fragmentive elimination−addition reaction to afford tricyclic acetal **11**. The insertion of an additional methylene group into the basic arenyl−diene skeleton failed to afford the desired [5.5.5.6] fenestrane structure. The presence of an oxime moiety in the aromatic photosubstrate did not prevent the primary *meta* photocycloaddition reaction from taking place; however, the highly substituted compound **53** failed to undergo a secondary photocycloaddition reaction to afford polyheterocyclic fenestrane **56**. Also investigations into the formation of criss-cross double *meta* photocycloadducts **71** and **72** failed to achieve the desired result. During the course of these investigations a Paterno−Büchi cycloaddition reaction between acetone and an angular *meta* photocycloadduct was discovered.

Experimental Section

Representative Procedures. Full experimental procedures and spectroscopic data for all compounds can be found in the Supporting Information. Some standard examples are provided here.

Compound 11. The major linear *meta* photoadduct **3**[1] (50 mg) was dissolved in toluene-d_8 (0.7 mL) and added to a resealable Young's tap NMR tube. This was sealed under a nitrogen atmosphere and heated to 200 °C for approximately 1.75 h. The major product was isolated by flash column chromatography (40:1 SiO_2; diethyl ether/pentane 10:90) yielding **11** (30 mg, 59%) as a colorless semisolid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.19 (1H, d, J = 2.5 Hz); 5.83−5.92 (1H, m); 5.87 (1H, dd, J = 3.3, 6.4 Hz); 5.78 (1H, dd, J = 3.1, 6.3 Hz); 5.25 (1H, dm, J = 17.2 Hz); 5.09 (1H, dm, J = 10.3 Hz); 4.41 (1H, dd, J = 8.3, 9.4 Hz); 3.93 (2H, dm, J = 5.4); 3.70 (1H, dd, J = 8.3, 12.9 Hz); 3.33 (1H, d, J = 3.1 Hz); 3.21 (3H, s); 2.92 (1H, ddddd, J = 2.5, 7.7, 9.4, 9.6, 12.9 Hz); 2.73 (1H, ddd, J = 2.7, 3.3, 3.6 Hz); 1.72 (1H, ddd, J = 3.6, 7.7, 12.5 Hz); 1.49 (1H, ddd, J = 2.7, 9.6, 12.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.1, 134.9, 130.9, 130.3, 116.2, 114.5, 111.4, 76.0, 63.0, 48.7, 44.0, 43.7, 36.9, 28.4. IR (thin film, cm^{-1}) 3061, 2941, 2862, 1765, 1667, 1646, 1598, 1463, 1368, 1348, 1320, 1288, 1238, 1189, 1126, 1059, 1006, 949, 921, 787, 771, 704. HRMS (ESI) m/z calcd for $C_{14}H_{18}NaO_3$ [M + Na]$^+$, 257.1154; found, 257.1150.

Compound 17. To a stirred solution of alcohol **24**[10] (2.92 g, 15.2 mmol) and allyl bromide (6.58 mL, 76.1 mmol) in dichloromethane (10 mL) under a nitrogen atmosphere, was added 50% NaOH (25 mL) and tetrabutylammonium hydrogen sulfate (10.33 g, 30.4 mmol). This was allowed to stir for 3 days until TLC showed complete conversion of the starting material. The reaction was quenched with saturated ammonium chloride solution (50 mL) and extracted with diethyl ether (2 × 50 mL). The combined organic layers were dried over magnesium sulfate, the solvents were removed under reduced pressure, and the resulting residue was purified by flash column chromatography (diethyl ether/petrol 10:90) to yield the ether **17** (2.81 g, 80%) as a yellow oil. R_f = 0.63 (diethyl ether/petrol 10:90). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (1H, br d, J = 7.4 Hz); 7.24 (1H, br t, J = 7.8 Hz); 6.99 (1H, t, J = 7.4 Hz); 6.87 (1H, br d, J = 8.2 Hz); 5.81−5.98 (2H, m); 5.26 (1H, d, J = 17.2 Hz); 5.14 (1H, d, J = 10.4 Hz); 5.03 (1H, d, J = 17.2 Hz); 4.95 (1H, d, J = 10.2 Hz) 4.80 (1H, dd, J = 5.1, 7.7 Hz); 3.93 (1H, dd, J = 5.2, 12.7 Hz); 3.82 (3H, s); 3.79 (1H, dd, J = 5.9, 12.7 Hz); 2.09−2.28 (2H, m); 1.72−1.85 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.9, 138.7, 135.3, 130.9, 128.0, 126.7, 120.7, 116.3, 114.2, 110.3, 74.4, 69.8, 55.3, 36.1, 30.0. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ [M + Na]$^+$, 255.1361; found, 255.1364.

Synthesis of Compounds 26, 27, 28, and 29. A solution of ether **17** (3.00 g, 12.9 mmol) in dry cyclohexane (150 mL) was degassed with nitrogen for 15 min in a quartz immersion-well photoreactor. The apparatus was cooled with water, and the solution was irradiated for 32 h using a 6 W low-pressure mercury vapor lamp (λ_{max} = 254 nm) until NMR analysis showed the complete consumption of starting material. The solvent was removed under reduced pressure, and the resulting yellow residue was subjected to flash column chromatography (100:1 silica, ethyl acetate/petroleum ether 10:90) to afford linear *meta* adduct **27** (145 mg, 4.8%). A second separation (diethyl ether/pentane 4:94 to 20:80) gave linear *meta* photocycloadduct **26** (250 mg, 8.3%). Angular adduct **28** (55 mg, 1.8%) and *ortho* derived adduct **29** (540 mg, 18%) were also isolated pure from the reaction mixture. Other impure adducts that included further *ortho* derivatives and degradation products from apparent Norrish-type reactions also existed in the crude photolysis residue but could not be obtained in a satisfactorily purified form.

Compound 26. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.84 (1H, dddd, J = 6.7, 6.7, 10.4, 17.1 Hz); 5.66 (1H, dd, J = 2.4, 5.6 Hz); 5.56 (1H, ddd, J = 1.2, 2.7, 5.6 Hz); 5.03 (1H, d, J = 17.1 Hz); 4.95 (1H, d, J = 10.4 Hz); 4.07 (1H, dd, J = 7.7, 8.9 Hz); 4.00 (1H, dd, J = 3.3, 9.4 Hz); 3.57 (1H, dd, J = 4.7, 9.0 Hz); 3.41 (3H, s); 3.40−41 (1H, m); 2.32−2.38 (1H, m); 2.20−2.28 (1H, m); 2.14−2.16 (1H, m); 2.07−2.15 (1H, m); 1.94 (1H, ddd, J = 5.4, 9.2, 11.7 Hz); 1.87 (1H, dd, J = 6.7, 11.7 Hz); 1.63 (1H, dddd, J = 5.1, 9.6, 10.0, 14.1 Hz); 1.46 (1H, dddd, J = 3.4, 6.3, 9.9, 14.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.5, 133.1, 127.9, 114.4, 88.3, 75.2, 71.9, 56.6, 56.2, 53.6, 44.2, 43.1, 37.0, 31.9, 29.9. IR (thin film, cm^{-1}) 3055, 2935, 2855, 1640, 1586, 1450, 1401, 1356, 1340, 1325, 1305, 1246, 1231, 1193, 1170, 1133, 1097, 1071, 1008, 911, 864, 748, 734. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ [M + Na]$^+$, 255.1361; found, 255.1347.

Compound 27. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.92 (1H, dddd, J = 5.6, 5.7, 10.4, 17.2 Hz); 5.71 (1H, dd, J = 2.0, 5.7 Hz); 5.51 (1H, ddd, J = 1.3, 2.7, 5.6 Hz); 5.26 (1H, dddd, J = 1.6, 1.7, 1.7, 17.2 Hz); 5.14 (1H, dddd, J = 1.4, 1.4, 1.7, 10.4 Hz); 4.02 (1H, dddd, J = 1.5, 1.5, 5.5, 12.9 Hz); 3.93 (1H, dddd, J = 1.4, 1.5, 5.7, 12.9 Hz); 3.76 (1H, dd, J = 2.2, 4.3 Hz); 3.38 (3H, s); 3.24 (1H, dd, J = 2.7, 5.6 Hz); 2.47 (1H, m); 2.20−2.26 (1H, m); 2.04−2.11 (1H, m); 1.97−2.03 (1H, m); 1.82−1.89 (2H, m); 1.73 (1H, ddd, J = 5.5, 9.7, 11.7 Hz); 1.34 (1H, dddd, J = 2.9, 2.9, 7.5, 12.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.6, 132.6, 128.6, 116.4, 90.4, 78.5, 69.7, 56.9, 56.2, 52.5, 45.4, 40.2, 37.9, 33.1, 28.5. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ [M + Na]$^+$, 255.1361; found, 255.1348.

Compound 28. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.87−5.94 (1H, m); 5.74 (1H, dd, J = 1.2, 5.7 Hz); 5.55 (1H, dd, J = 2.4, 5.7 Hz); 5.27 (1H, d, J = 17.2 Hz); 5.14, (1H, d, J = 10.4 Hz); 4.13 (1H, dd, J = 4.1, 7.1 Hz); 3.96−4.03 (2H, m); 3.32 (3H, s); 2.24−2.31 (2H, m); 2.19 (1H, d, J = 8.5); 2.08 (1H, dd, J = 6.3, 8.5 Hz); 1.71 (1H, dd, J = 6.1, 8.8, 9.3 Hz); 1.61−1.68 (2H, m); 1.52−1.57 (1H, m); 1.46 (1H, dd, J = 6.2, 13.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.2, 133.7, 124.0, 116.2, 91.0, 78.9, 71.7, 70.7, 57.0, 56.7, 37.1, 35.9, 34.7, 28.1, 26.8. IR (thin film, cm^{-1}) 2935, 1646, 1584, 1448, 1379, 1210, 1157, 1089, 1005, 920, 760, 700. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ [M + Na]$^+$, 255.1361; found, 255.1354.

Compound 29. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.13 (1H, d, J = 2.7 Hz); 6.06 (1H, d, J = 2.7 Hz); 5.91 (1H, dddd, J = 5.7, 5.7, 10.4, 17.2 Hz); 5.82 (1H, dd, J = 2.8, 6.1 Hz); 5.26 (1H, d, J = 17.2 Hz); 5.14 (1H, d, J = 10.4 Hz); 4.20 (1H, dddd, J = 5.1, 5.3 Hz); 3.95 (1H, dddd, J = 1.5, 1.5, 5.6, 12.8 Hz); 3.91 (1H, dddd, J = 1.4, 1.5, 5.9, 12.8 Hz); 3.29−3.36 (1H, m); 3.32 (3H, s); 2.33−2.40 (1H, m); 2.08−2.15 (1H, m); 2.04 (1H, dd, J = 5.3, 12.4 Hz); 1.87−1.93 (1H, m); 1.68 (1H, dddd, J = 4.8, 7.2, 7.2, 12.2 Hz); 1.30 (1H, dddd, J = 7.3, 7.3 7.4, 12.6 Hz); 1.15 (1H, t, J = 12.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.5, 138.4, 136.3, 135.4, 121.5, 116.7, 85.0, 81.3, 69.1, 51.8, 46.9, 37.1, 34.4, 31.8, 29.1. IR (thin film, cm^{-1}) 3075, 3043, 2975, 2931, 2846, 2244, 1826, 1679, 1640, 1586, 1563, 1449, 1377, 1342, 1292,

1257, 1208, 1172, 1098, 1021, 989, 911, 830, 767, 730. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ $[M + Na]^+$, 255.1361; found, 255.1356.

Compound 30. The linear *meta* adduct **26** (81 mg, 0.349 mmol) and acetophenone (62.8 mg, 0.523 mmol) were dissolved in dry cyclohexane (200 mL) in a quartz immersion-well photoreactor. Nitrogen was bubbled through the solution for 20 min in order to remove dissolved oxygen. The mixture was then irradiated for 11 h using a 6 W low pressure mercury vapor lamp. Cyclohexane was removed under reduced pressure, and the resulting residue was subjected to flash column chromatography (100:1 silica; ether/dichloromethane/pentane 10:5:85); to yield the double [3 + 2] product **30** as a pale yellow oil (22 mg, 27%). $R_f = 0.22$ (diethyl ether/dichloromethane/pentane 10:5:85). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.67 (1H, ddd, J = 1.6, 2.5, 6.0 Hz); 5.46 (1H, ddd, J = 1.4, 2.6, 6.0 Hz); 4.53 (1H, d, J = 7.9 Hz); 3.65 (1H, dd, J = 4.5, 8.8 Hz); 3.52 (1H, d, J = 8.8 Hz); 3.24 (1H, dddd, J = 1.4, 2.5, 7.9, 8.5 Hz); 3.21 (3H, s); 3.11 (1H, dm, J = 10.1 Hz); 2.29 (1H, ddd, J = 4.6, 8.1, 11.0 Hz); 2.14−2.26 (2H, m); 1.96 (1H, ddd, J = 5.4, 7.9, 11.2 Hz); 1.87 (2H, dd, J = 6.9, 14.5 Hz); 1.75 (1H, ddd, J = 10.2, 10.9, 13.1 Hz); 1.64 (1H, ddd, J = 1.3, 8.0, 13.0 Hz); 1.51 (1H, ddd, J = 5.0, 7.3, 11.5 Hz); 1.20 (1H, dddd, J = 7.1, 11.4, 11.4, 13.5 Hz); 1.06 (1H, ddd, J = 8.5, 11.2, 13.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 133.4, 132.6, 102.4, 77.3, 77.2, 72.4, 60.0, 53.4, 51.9, 48.2, 43.6, 40.0, 36.6, 31.5, 23.3. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ $[M + Na]^+$, 255.1361; found, 255.1356.

Compound 31. The linear *meta* adduct **27** (35 mg, 0.151 mmol) and acetophenone (27.2 mg, 0.226 mmol) were dissolved in dry cyclohexane (200 mL) in a quartz immersion-well photoreactor. Nitrogen was bubbled through the solution for 20 min in order to remove dissolved oxygen. The mixture was then irradiated for 17 h using a 6 W low pressure mercury vapor lamp. Cyclohexane was removed under reduced pressure, and the resulting residue was subjected to flash column chromatography (100:1 silica; ether/pentane 20:80) to yield the double [3 + 2] product **31** as a yellow oil (11 mg, 31%). $R_f = 0.29$ (diethyl ether/pentane 20:80); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.65 (1H, dm, J = 5.9 Hz); 5.47 (1H, dm, J = 5.8 Hz); 4.28 (1H, br. s.); 3.67 (1H, t, J = 6.7 Hz); 3.35 (1H, t, J = 8.2 Hz); 3.21 (1H, dd, J = 7.1, 12.1 Hz); 3.19 (3H, s); 3.10 (1H, dm, J = 10.0 Hz); 2.81−2.89 (1H, m); 2.26−2.32 (1H, m); 1.95 (1H, ddd, J = 5.3, 7.7, 11.2 Hz); 1.78−1.89 (2H, m); 1.68−1.76 (1H, m); 1.62 (1H, dd, J = 8.3, 13.3 Hz); 1.52−1.57 (1H, m); 1.42 (1H, dd, J = 5.7, 12.4 Hz); 1.16 (1H, ddd, J = 8.9, 11.3, 13.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 133.7, 132.0, 103.5, 80.3, 76.8, 66.9, 62.1, 55.1, 52.0, 48.6, 41.4, 36.3, 32.6, 31.3, 28.9. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ $[M + Na]^+$, 255.1361; found, 255.1356.

Compound 60. Ester **58**[6c] (2.8 g, 13.6 mmol) was dissolved in diethyl ether (50 mL) under a nitrogen atmosphere and cooled to 0 °C. DIBAL (1 M, 40.8 mL, 40.8 mmol) was added dropwise via syringe over 30 min. The reaction was stirred until analysis by TLC showed none of the ester remained. With the temperature maintained at 0 °C, the reaction was diluted with diethyl ether (100 mL) followed by the cautious addition of water (100 mL). The two layers were partitioned in a separating funnel; the organic layer was washed with brine (2 × 50 mL) and dried over anhydrous magnesium sulfate. The ether was removed under reduced pressure to yield alcohol **60** (2.04 g, 84%) as a colorless oil that was used without further purification. $R_f = 0.11$ (diethyl ether/petrol 10:90). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24−7.28 (2H, m); 6.94 (1H, td, J = 1.1, 7.4 Hz); 6.88 (1H, dd, J = 1.0, 8.5 Hz); 5.86−5.95 (1H, ddt, J = 6.8, 10.2, 17.0 Hz); 5.22 (1H, dm, J = 17.0 Hz); 5.16 (1H, dm, J = 10.2 Hz); 4.68 (2H, br. s); 4.09 (2H, t, J = 6.3 Hz); 2.56−2.61 (2H, m); 2.52−2.58 (1H, br. s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.8, 134.6, 129.3, 128.8, 128.7, 120.7, 117.4, 111.0, 66.8, 62.3, 33.7. IR (thin film, cm^{-1}) 3392, 3076, 2926, 2873, 1642, 1603, 1590, 1492, 1456, 1432, 1389, 1289, 1240, 1196, 1114, 1045, 917, 752. HRMS (ESI) m/z calcd for $C_{11}H_{14}NaO_2$ $[M + Na]^+$, 201.0891; found, 201.0884.

Compound 62. To a stirred solution of alcohol **60** (2.04 g, 11.5 mmol) and allyl bromide (4.96 mL, 57.3 mmol) in dichloromethane (10 mL) under a nitrogen atmosphere at 0 °C, was added 50% NaOH (30 mL) and tetrabutylammonium hydrogen sulfate (3.9 g, 11.5 mmol). This was allowed to warm to ambient temperature and to stir for 24 h until TLC showed complete conversion of the starting material. The reaction was quenched with saturated ammonium chloride solution (50 mL) and extracted with diethyl ether (2 × 50 mL). The combined organic layers were dried over magnesium sulfate, the solvents were removed under reduced pressure and the resulting residue was purified by flash column chromatography (ethyl acetate/petrol 3:97) to yield the ether **62** (2.4 g, 96%) as a pale yellow oil. $R_f = 0.39$ (diethyl ether/hexane 20:80). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (1H, dd, J = 1.8, 7.5 Hz); 7.24 (1H, td, J = 1.8, 7.8 Hz); 6.96 (1H, td, J = 1.0, 7.4 Hz); 6.85 (1H, dd, J = 1.0, 8.1 Hz); 5.95−6.04 (1H, ddt, J = 5.6, 10.5, 17.2 Hz); 5.88−5.97 (1H, ddt, J = 6.7, 10.2, 17.0 Hz); 5.34 (1H, dm, J = 17.2 Hz); 5.21 (1H, dm, J = 10.2 Hz); 5.18 (1H, dm, J 17.1 Hz); 5.11 (1H, dm, J = 10.2 Hz); 4.58 (2H, s); 4.09 (2H, ddd, J = 1.4, 1.5, 5.6 Hz); 4.04 (2H, t, J = 6.6 Hz); 2.54−2.59 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.4, 135.1, 134.6, 128.9, 128.5, 120.5, 116.9, 116.7, 111.2, 71.5, 67.3, 66.9, 33.7. IR (thin film, cm^{-1}) 2627, 2848, 1641, 1433, 1374, 1344, 1292, 1258, 1156, 1094, 1057, 914, 883, 820, 758, 743. HRMS (ESI) m/z calcd for $C_{14}H_{18}NaO_2$ $[M + Na]^+$, 241.1204; found, 241.1199.

Synthesis of Compounds 64 and 65. A solution of ether **62** (2.10 g, 9.63 mmol) in dry cyclohexane (400 mL) was degassed with nitrogen for 15 min in a quartz immersion-well photoreactor. The apparatus was cooled with water and the solution was irradiated for 18 h using a 16 W low-pressure mercury vapor lamp (λ_{max} = 254 nm) until NMR analysis showed the complete consumption of starting material. The solvent was removed under reduced pressure, and the resulting orange residue was subjected to flash column chromatography (100:1 silica, dichloromethane/diethyl ether/petrol 5:10:85) to afford *meta* adduct **64** (280 mg, 13%) and *ortho*-derived adduct **65** (301 mg, 14%) both with minor coeluting impurities.

Compound 64. R_f = 0.39 (dichloromethane/diethyl ether/petrol 5:10:85). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.81 (1H, ddt, J = 6.7, 10.2, 17.1 Hz); 5.69 (1H, dd, J = 2.3, 5.8 Hz); 5.56 (1H, dm, J = 5.8 Hz); 5.09 (1H, dm, J = 17.1 Hz); 5.03 (1H, dm, J = 10.2 Hz); 3.90 (1H, d, J = 9.1 Hz); 3.89 (1H, dd, J = 7.8, 8.9 Hz); 3.70 (1H, dd, J = 3.5, 8.9 Hz); 3.69 (1H, d, J = 9.1 Hz); 3.63 (1H, dt, J = 6.8, 9.2 Hz); 3.57 (1H, dt, J = 6.8, 9.2 Hz); 3.37 (1H, dd, J = 2.7, 5.0 Hz); 2.34 (2H, q, J = 6.8 Hz); 2.25−2.31 (1H, m); 2.21 (1H, br. s); 1.96 (1H, dd, J = 5.3, 9.4 Hz); 1.92 (1H, dd, J = 6.2, 10.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.0, 132.8, 128.1, 116.4, 87.7, 73.4, 68.7, 66.1, 53.8, 52.6, 44.7, 42.4, 36.8, 34.4. IR (thin film, cm^{-1}) 3055, 2930, 2851, 1658, 1641, 1586, 1465, 1456, 1430, 1376, 1330, 1277, 1246, 1188, 1169, 1138, 1077, 1057, 1015, 909, 860, 743. HRMS (ESI) m/z calcd for $C_{14}H_{18}NaO_2$ $[M + Na]^+$, 241.1204; found, 241.1198.

Compound 65. R_f = 0.30 (dichloromethane/diethyl ether/petrol 5:10:85). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.15 (1H, dm, J = 1.9 Hz); 6.02 (1H, dm, J = 1.9 Hz); 5.75−5.84 (1H, m); 5.60 (1H, br. s); 5.06 (1H, dm, J = 17.1 Hz); 5.00 (1H, dm, J = 10.2 Hz); 4.36 (1H, d, J = 13.4 Hz); 4.25 (1H, d, J = 13.4 Hz); 4.18 (1H, t, J = 8.3 Hz); 3.50 (2H, t, J = 6.9 Hz); 3.37 (1H, t, J = 8.4 Hz); 3.30 (1H, d, J = 6.0 Hz); 2.47−2.56 (1H, m); 2.28 (2H, q, J = 7.0 Hz); 2.09 (1H, dd, J = 5.2, 12.3 Hz); 1.25 (1H, t, J = 12.3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.5, 138.1, 136.6, 135.2, 116.2, 115.2, 84.7, 73.8, 63.5, 47.4, 37.0, 34.9, 33.5. IR (thin film, cm^{-1}) 2926, 2847, 1640, 1586, 1459, 1474, 1434, 1374, 1344, 1291, 1157, 1097, 1058, 1029, 994, 918, 821, 785, 760, 721, 693,

652. HRMS (ESI) m/z calcd for $C_{14}H_{18}NaO_2$ $[M + Na]^+$, 241.1204; found, 241.1198.

Compound 68. A solution of linear *meta* adduct **64** (100 mg, 0.460 mmol) in dry cyclohexane (400 mL) was degassed with nitrogen for 15 min in a quartz immersion-well photoreactor. The apparatus was cooled with water, and the solution was irradiated for 48 h using a 16 W low-pressure mercury vapor lamp ($\lambda_{max} = 254$ nm) until NMR analysis showed the complete consumption of starting material. The solvent was removed under reduced pressure, and the resulting residue was subjected to flash column chromatography (100:1 SiO_2, diethyl ether/hexane 20:80) to afford 1,2-alkenyloxy migration adduct **68** (12.0 mg, 12%) alongside other isomers that could not be obtained in a satisfactorily purified form. $R_f = 0.36$ (diethyl ether/hexane, 20:80). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.20 (1H, d, $J = 5.9$ Hz); 5.96 (1H, dd, $J = 2.4$, 5.9 Hz); 5.78 (1H, dddd, $J = 6.9$, 6.9, 10.2, 17.2 Hz); 5.61 (1H, br. s.); 5.06 (1H, dm, $J = 17.2$ Hz); 5.00 (1H, dm, $J = 10.2$ Hz); 4.49 (1H, d, $J = 2.4$ Hz); 3.90 (1H, d, $J = 9.1$ Hz); 3.87 (1H, d, $J = 9.4$ Hz); 3.67 (1H, dd, $J = 4.4$, 9.0 Hz); 3.58 (1H, ddd, $J = 7.1$, 7.1, 9.0 Hz); 3.42−3.47 (1H, m); 3.42 (1H, d, $J = 9.4$ Hz); 2.75−2.84 (2H, m); 2.59 (1H, ddd, $J = 1.7$, 5.0, 15.9 Hz); 2.55 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.7, 140.9, 135.2, 133.3, 125.5, 116.3, 76.9, 76.9, 74.8, 70.4, 68.3, 47.6, 42.8, 34.4. IR (thin film, cm^{-1}) 2926, 2847, 1640, 1586, 1459, 1474, 1434, 1374, 1344, 1291, 1157, 1097, 1058, 1029, 994, 918, 821, 785, 760, 721, 693, 652. HRMS (ESI) m/z calcd for $C_{14}H_{18}NaO_2$ $[M + Na]^+$, 241.1204; found, 241.1198.

Synthesis of Compounds 69 and 70. A solution of linear *meta* adduct **64** (50.0 mg, 0.229 mmol) in acetone (150 mL) was degassed with nitrogen for 15 min in a quartz immersion-well photoreactor. The apparatus was cooled with water, and the solution was irradiated for 3 h using a 6 W low-pressure mercury vapor lamp ($\lambda_{max} = 254$ nm) until NMR analysis showed the complete consumption of starting material. The solvent was removed under reduced pressure, and the resulting residue was subjected to flash column chromatography (ether/hexane 20:80 to 40:60) to afford angular *meta* adduct **69** (9 mg, 18%) and Paterno−Büchi adduct **70** (12.0 mg, 24%) alongside other isomers that could not be obtained in a satisfactorily purified form.

Compound 69. $R_f = 0.34$ (diethyl ether/hexane 20:80). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.81 (1H, ddt, $J = 6.9$, 10.3, 17.0 Hz); 5.63 (1H, dd, $J = 2.3$, 5.6 Hz); 5.55 (1H, d, $J = 5.6$ Hz); 5.08 (1H, dm, $J = 17.0$ Hz); 5.04 (1H, dm, $J = 10.3$ Hz); 4.23 (1H, d, $J = 8.9$ Hz); 3.85 (1H, dd, $J = 7.9$, 8.0 Hz); 3.81 (1H, d, $J = 8.9$ Hz); 3.68 (1H, dd, $J = 8.2$, 10.7 Hz); 3.50−3.60 (2H, m); 2.42−2.47 (1H, m); 2.31−2.37 (2H, m); 2.16−2.24 (2H, m); 1.81 (1H, dd, $J = 5.8$, 14.0 Hz); 1.58 (1H, dd, $J = 6.4$, 14.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.9, 133.2, 125.9, 116.6, 89.3, 70.0, 69.3, 68.9, 68.2, 58.1, 37.4, 36.9, 34.5, 23.6. HRMS (ESI) m/z calcd for $C_{14}H_{18}NaO_2$ $[M + Na]^+$, 241.1204; found, 241.1197.

Compound 70. $R_f = 0.29$ (diethyl ether/hexane, 40:60) ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.85 (1H, ddt, $J = 6.8$, 10.2, 17.2 Hz); 5.09 (1H, dm, $J = 17.2$ Hz); 5.03 (1H, dm, $J = 10.2$ Hz); 4.69 (1H, dm, $J = 4.2$ Hz); 4.26 (1H, d, $J = 9.3$ Hz); 4.01 (1H, t, $J = 8.1$ Hz); 3.83 (1H, d, $J = 9.3$ Hz); 3.76 (1H, ddd, $J = 6.8$, 6.8, 8.9 Hz); 3.64 (1H, ddd, $J = 7.0$, 7.0, 8.9 Hz); 3.47 (1H, dd, $J = 8.3$, 10.5 Hz); 2.48 (1H, d, $J = 4.1$ Hz); 2.37 (2H, q, $J = 6.9$ Hz); 2.21 (1H, ddd, $J = 7.3$, 7.3, 10.3 Hz); 2.03 (1H, d, $J = 9.8$ Hz); 1.97 (1H, dd, $J = 6.0$, 9.8 Hz); 1.72 (1H, dd, $J = 6.0$, 14.1 Hz); 1.51 (3H, s); 1.38 (3H, s); 1.37 (1H, ddm, $J = 6.7$, 14.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.1, 116.5, 89.1, 83.3, 82.1, 72.8, 69.1, 68.5, 68.2, 53.0, 45.4, 34.6, 33.9, 31.6, 28.9 24.5, 23.1. HRMS (ESI) m/z calcd for $C_{17}H_{24}NaO_3$ $[M + Na]^+$, 299.1623; found, 299.1614.

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Supporting Information Available: Complete experimental procedures, full characterization including ^{1}H and ^{13}C NMR spectra and where relevant COSY or DQF-COSY, multiplicity-edited HSQC, standard HMBC and ROESY correlation spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.