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Direct Comparison of the Response of Bicyclic Sultam and Lactam Dienes to Photoexcitation. Concerning the Propensity of Differing Bond Types to Bridgehead Nitrogen for Homolytic Cleavage

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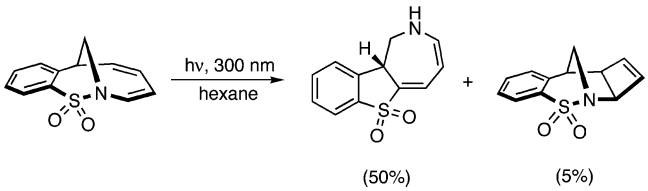
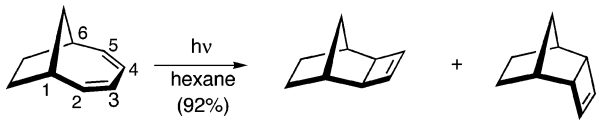


A convergent strategy has allowed access to bridgehead sultam **9** and the related carboxamides **10** and **11**. The synthetic routing proceeds via the coupling of a suitably constructed dienamine to either *o*-iodobenzenesulfonyl choride or *o*-iodobenzoyl chloride to generate the amides. The application in sequence of ring-closing metathesis and an intramolecular Heck reaction gave rise to advanced tricyclic intermediates. The final two steps involved bromination in liquid bromine and proper 2-fold dehydrobromination. The latter maneuver was best achieved with tetrabutylammonium fluoride in DMSO at elevated temperature. While the irradiation of **9** led principally via SO_2-N bond homolysis and [1,5] sigmatropic rearrangement to generate **37**, **10** proceeded via disrotatory cyclization to the exo cyclobutene **39**, and **11** resisted photoisomerization. The inertness of **11** may stem from its distorted structural features which force its conjugated diene double bonds to be rigidly oriented 32° out-of-plane. The unique ability of the sulfonamide linkage to excited-state homolysis holds comparative interest.

Introduction

In 1972, Jefford and Delay reported on the light-induced electrocyclic ring closure of bicyclo[4.2.1]nona-2,4-diene (**1**).[1] This study was based on orbital symmetry considerations[2] and viewed as an attempt to provide insight into the underlying cause of the exo selectivity exhibited by norbornene during electrophilic capture. Since the atoms defining the bridgehead atoms (C-1 and C-6) and the diene moiety (C-2 to C-5) reside in the same plane, the competitive disrotatory processes should be guided in their stereochemical outcome only by steric factors. Bond formation between C-2 and C-5 as in **2** and **3** was expected to be indifferent to those electronic considerations normally associated with exo and endo partitioning. The salient feature of the photoisomerization of **1** (hexane, 200 W Hanovia lamp, 25 °C) was the production of a 30:70 mixture of **2** and **3**. Irrespective of the inferences that can be drawn from this dichotomy, the lack of additional examples particularly from the heterocyclic realm motivated us to investigate the response of the structurally related bridgehead sultam **4** to photoactivation.[3]



1 **2** **3**

This particular extension caused us to become aware of the fact that **4** is subject to heretofore unprecedented light-induced SO_2-N bond cleavage with the ultimate generation of spirocycle **5** (Scheme 1). The structural intricacy of this photoproduct, with its combination of cyclobutene, thietane dioxide, and pyrrolidine rings, is quite striking. This excited-state transformation was best achieved in a 2:1 acetonitrile/acetone solvent system by irradiation through Pyrex with 350 nm light in a Rayonet reactor.

The behavior of **4** clearly represents a dramatic departure from the pathway adopted by **1**. At the mechanistic level, the first

(1) Jefford, C. W.; Delay, F. *J. Am. Chem. Soc.* **1972**, *94*, 4794.

(2) Woodward, R. B.; Hoffman, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, 1970; pp 38−68.

(3) Paquette, L. A.; Barton, W. R. S.; Gallucci, J. C. *Org. Lett.* **2004**, *6*, 1313.

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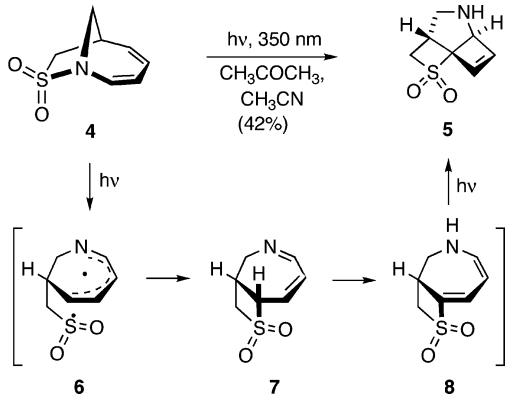
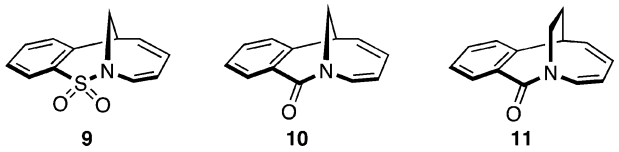
SCHEME 1



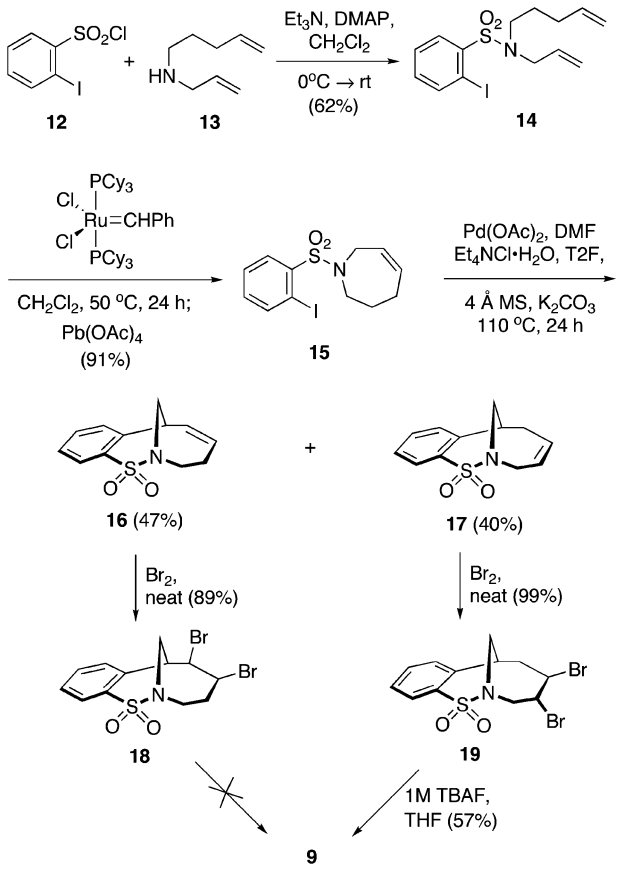
step appears to involve the formation of biradical **6** followed by rebonding to generate bicyclic isomer **7**. Generation of this intermediate allows for operation of a thermally induced suprafacial [1,5] sigmatropic hydrogen shift and arrival at **8**. The second leg of the biphotonic sequence now occurs with absorption by **8** of another quantum of light energy. These findings raise several issues pertinent to amide chemistry. For example, can it be inferred from the pathway adopted by **4** that the customarily robust sulfonamide linkage may be generally amenable to facile homolysis when reasonably good stereoelectronic overlap is available? Also, will similar architectural features have comparable consequences when carboxamides are involved? We report here our more recent investigation of the three benzo-fused systems **9**−**11** in order to determine if a related pattern of structural change emerges.



Synthetic Considerations

The strategy applied to the acquisition of **9** began with the coupling of 2-iodobenzenesulfonyl chloride (**12**)[4] to secondary amine **13**[5] (Scheme 2). The latter was generated in 40% overall yield by boric acid catalyzed amidation[6] involving 4-pentenoic acid and allylamine with subsequent lithium aluminum hydride reduction. Ring-closing metathesis represents a powerful strategy for the construction of medium-ring products.[7] In line with the tolerance of this process to a wide range of functionality including the sulfonamide group,[8] the conversion of **14** to **15** proceeded very well (in near-quantitative yield). This level of efficiency was made possible by effective removal of ruthenium-containing byproducts with lead tetraacetate.[9] Submission of **15**

SCHEME 2



to Heck reaction conditions[10,11] afforded a chromatographically separable two-component mixture consisting of **16** (47%) and **17** (40%). When the dibromination of **16** and **17** in various halogenated solvents was found to proceed slowly, recourse was made instead to liquid Br_2 as the reaction medium. These conditions led effectively to **18** and **19**. The 2-fold dehydromination of these dibromides was examined with a host of basic reagents.[12] While our inability to transform **18** into **9** was not unexpected, the sluggishness exhibited by **19** proved surprising. Ultimately, it was discovered that 1 M solutions of tetra-*n*-butylammonium fluoride in THF[13] were significantly superior in bringing about this transformation. The two-step route from **17** to **9** shown in Scheme 2 proceeds in 57% overall yield.

(4) Chau, M. M.; Kice, J. L. *J. Org. Chem.* **1977**, *42*, 3265.

(5) (a) Surzur, J. M.; Stella, L. *Tetrahedron Lett.* **1974**, 2191. (b) Newcomb, M.; Marquardt, D. J.; Deeb, T. M. *Tetrahedron* **1990**, *46*, 2329. (c) Bowman, W. R.; Clark, D. N.; Marmon, R. J. *Tetrahedron* **1994**, *50*, 1295. (d) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 707. (e) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 1757. (f) Evans, P.; Grigg, R.; Ramzan, M.; Imran, M.; Sridharan, V.; York, M. *Tetrahedron Lett.* **1991**, *40*, 3021.

(6) Tang, P. *Org. Synth.* **2004**, *81*, 262.

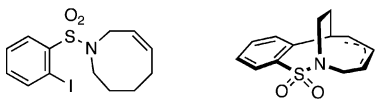
(7) *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Verlag GmbH, Weinheim, 2003; Vol. 2.

(8) For example: (a) Paquette, L. A.; Leit, S. *J. Am. Chem. Soc.* **1999**, *121*, 8126. (b) Paquette, L. A.; Ra, C. S.; Schloss, J. D.; Leit, S. M.; Gallucci, J. C. *J. Org. Chem.* **2001**, *66*, 3564. (c) Wanner, J.; Harned, A. M.; Probst, D. A.; Poon, K. W. C.; Klein, T. A.; Snelgrove, K. A.; Hanson, P. R. *Tetrahedron Lett.* **2002**, *43*, 917.

(9) Paquette, L. A.; Schloss, J. D.; Efremov, I.; Fabris, F.; Gallou, F.; Mendez-Andino, J.; Yang, J. *Org. Lett.* **2000**, *2*, 1259.

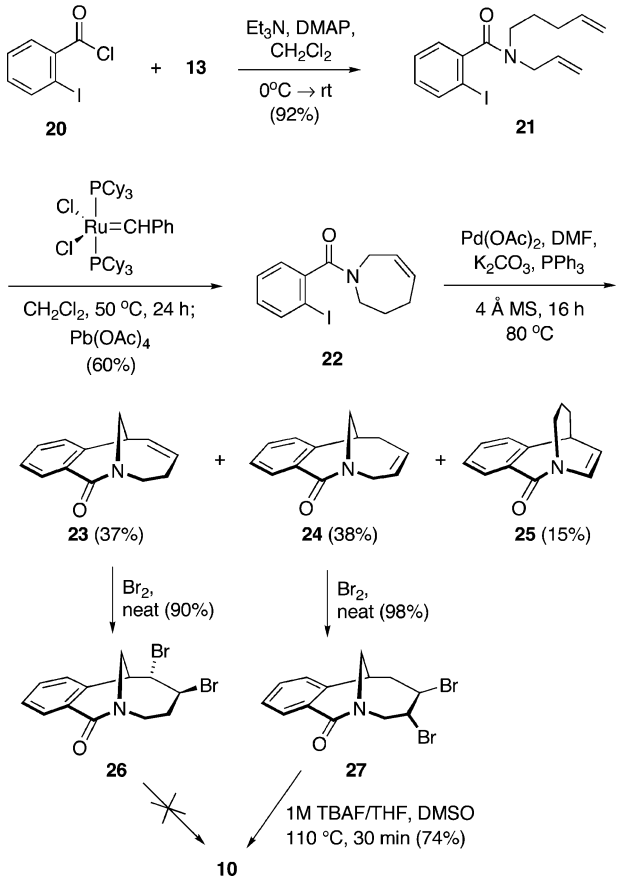
(10) (a) Grigg, R.; York, M. *Tetrahedron Lett.* **2000**, *41*, 7255. (b) Evans, P.; McCabe, T.; Morgan, B.; Reau, S. *Org. Lett.* **2005**, *7*, 43.

(11) This ring closure lacks generality and could not, for example, be successfully applied to the conversion of *i* to *ii*. Multicomponent mixtures resulted, and recourse to tris-3-furylphosphine (T2F) as a ligand was not particularly helpful.



(12) The reagent combinations included, but were not limited to, sodium hydride in THF at 25 °C, DBU in acetonitrile at reflux in a sealed tube, LiF and Li_2CO_3 in HMPA at 90 °C, and potassium *tert*-butoxide in THF at the reflux temperature.

SCHEME 3

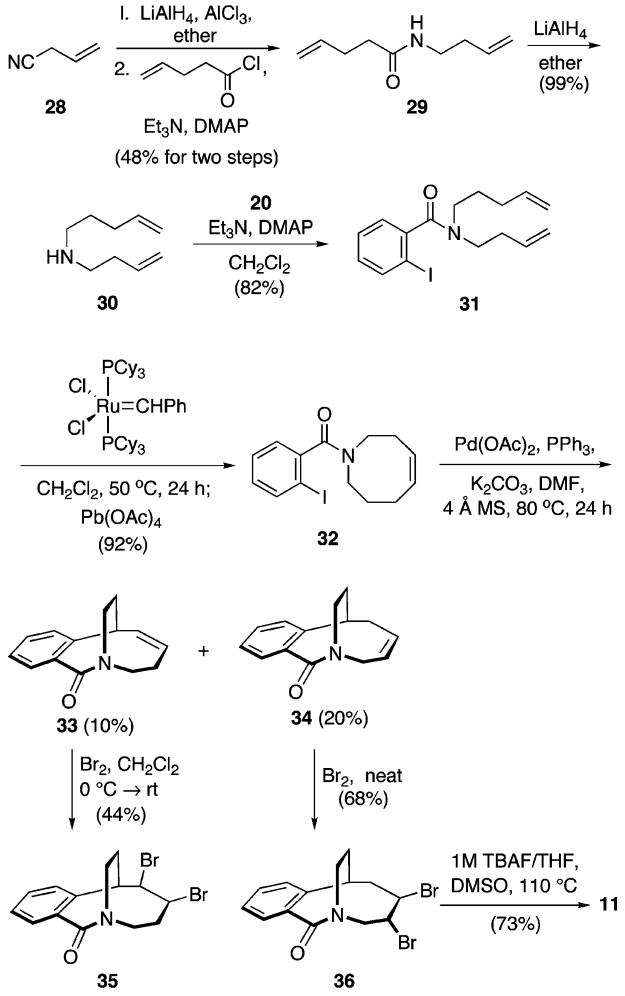


The conversion of 2-iodobenzoyl chloride to amide **22** was readily accomplished via a parallel sequence capped by ring-closing metathesis (Scheme 3). More advanced cyclization of this intermediate gave predominantly **23** and **24** alongside 15% of the [3.3.2] tricyclic isomer **25**. The first two lactams were individually brominated in neat bromine at room temperature to give **26** and **27**. Of these, only **27** proved to be a progenitor of **10**. The recalcitrance of **26** to the loss of HBr may stem from its conformational characteristics, corroborated by X-ray crystallographic analysis, that indicate no suitable trans-diaxial relationships to be readily attainable (see the Supporting Information).

At this juncture, it seemed advisable to introduce an additional methylene group so as to enlarge the methano bridge. To reach this goal, the commercially available nitrile **28** was reduced with $LiAlH_4$, and the amine so generated was acylated with 4-pentenoyl chloride. The doubly unsaturated amide **29** formed in this manner smoothly underwent conversion to the homologated secondary amine **30** upon further reduction. The program for accessing **11** continued with the action of **20** on **30** and the cyclization of **31** under Grubbs' conditions to deliver **32** in a remarkable 92% yield (Scheme 4). The product distribution realized from application of the intramolecular Heck reaction to **32** was closely related to that observed earlier. Thus, the azabicyclo[4.3.1]undecenone **34** having a double bond distal to the methano bridge is formed to an extent approximately twice that noted for the more proximal isomer **33**. All of the above assignments are undergirded by extensive NMR spectral data.

(13) (a) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429. (b) Dura, R. D.; Paquette, L. A. *Synthesis* **2006**, 2837.

SCHEME 4



Results of Photoactivation

As conditions for effecting the photorearrangement of **9** were researched, note was taken of the fact that triplet sensitization invariably resulted in slow polymer formation. Therefore, attention was profitably directed to the application of direct irradiation conditions such as those originally applied to hydrocarbon **1**. Under these experimental circumstances, two rearrangement pathways were operational. The predominant process gave rise to dihydroazepine **37** (50%), presumably via 1,5-migration of the sulfonyl group with cleavage of the SO_2-N linkage (Scheme 5). The structural assignment to **37** was corroborated by X-ray crystallographic analysis. The minor product proved to be cyclobutene **38** (5%), the likely consequence of disrotatory ring closure. The exo orientation of the four-membered ring in **38** was easily recognized on the basis of the coupling constants, or absence thereof, exhibited by the associated protons.[14]

These data demonstrate that **9** shows the same propensity as does **4** to undergo photoisomerization to the fused dihydro azepines **37** and **8**, respectively, despite the need to apply different irradiation conditions in the two examples. Interestingly, the subsequent ring closure of **8** to generate **5** is not mirrored by **37**. This divergence could possibly be a reflection

(14) Marchand, A. P. *Stereochemical Applications of NMR Studies in Rigid Bicyclic Systems*; Verlag Chemie International: Deerfield Beach, FL, 1982.

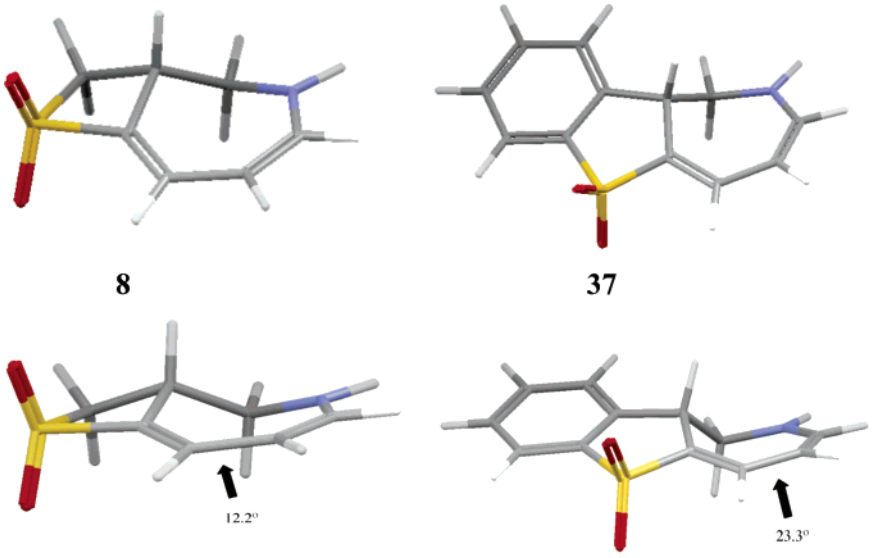


FIGURE 1. Ground-state geometries of **8** (left column) and **37** (right column) as visualized by the Mercury 1.4.1 program.

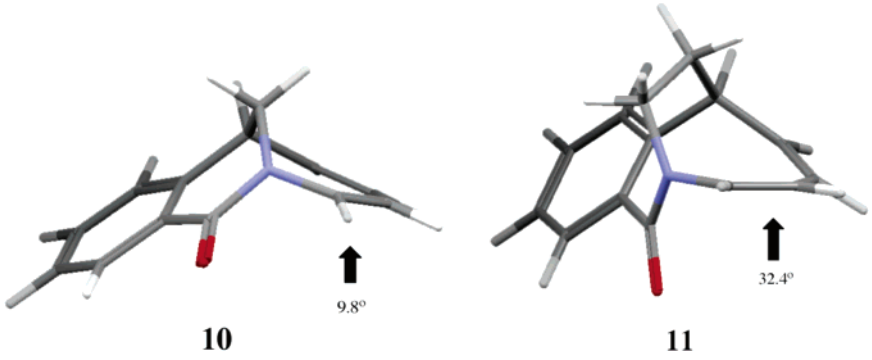
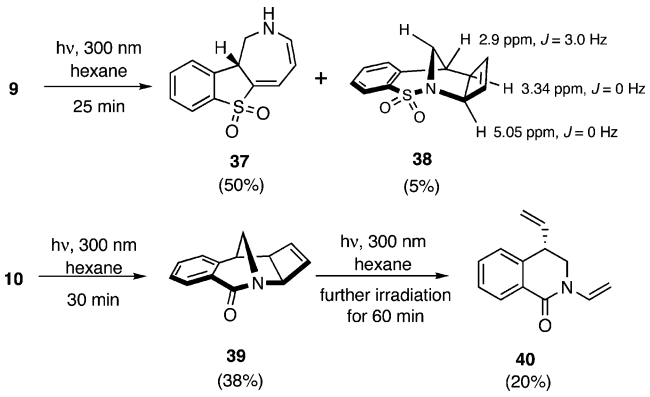


FIGURE 2. Ground-state geometries of **10** and **11** as visualized by the Mercury 1.4.1 program.

SCHEME 5



of the near-planarity of the conjugated diene unit in **8**, with the improved orbital overlap facilitating disrotatory cyclization to generate the cyclobutene ring. Some indication of the existing level of disparity in overlap was secured by making recourse to MacroModel version 8.6 calculations performed in conjunction with the MMFFs force field. As shown in Figure 1, the lowest minimum energy conformation of **37** features a dihedral angle (−23.3°) that is considerably wider than that exhibited by **8** (−12.2°).

Entirely comparable processing of lactam **10** afforded **39** as the major product (38%). Also formed was a less polar product identified as **40** on the basis of its ^{1}H and ^{13}C NMR spectra, especially at the 2D level. The progenitor of **40** was shown to be **39** by independent photoactivation of the latter for an extended 60 min time period. The conclusion that **38** and **39** share in common an exo-oriented cyclobutene ring stems from the similar features of their 2-D NMR spectra.

In contrast to the responsiveness of **10** to activation by light, **11** proved unreactive to comparable irradiation. More forcing photochemical conditions involving, for example, 200 and 450 W mercury lamp sources, brought about polymerization. We recognized that **10** and **11** differ appreciably in their ultraviolet absorption properties (see the Experimental Section) and that both compounds are characterized by very rigid molecular architectures. Once again, insight into the respective ground-state geometries was gained by computational means. As before, only one minimum energy conformer was found for each structure (Figure 2). The results show **10** to adopt a nicely shaped convex topography. The ethano bridge in **11** is much less well accommodated, and a significant level of structural distortion is consequently induced. This feature is most strikingly reflected in the dihedral angle adopted about the conjugated diene component, which is appreciably enlarged from 9.8° to 32.4° when progressing from **10** to **11**. This dichotomy is believed to be the root cause of the different chemical behavior and spectroscopic characteristics of this pair of bridgehead lactams.

Finally, it is noteworthy that attempts to carry out the irradiation of diene lactam **10** in the manner originally reported for **4** (350 nm, acetone, with and without CH_3CN as cosolvent) resulted exclusively in the recovery of unreacted starting material.

Overview

Three key reactions consisting of ring-closing metathesis, an intramolecular Heck cyclization, and bromination−dehydrobromination enabled a convergent and relatively abbreviated route to **9**−**11** to be developed. These platforms provided an excellent opportunity to compare the response of the related sulfonamide/carboxamide pair **9** and **10** to photoactivation. A second subset of probes involved **10** and its higher homologue **11**. Only in the bridgehead sulfonamide example was homolysis of the bond to nitrogen subject to homolytic cleavage with translocation to a site five atoms away. To our knowledge, an azepine substituted as in **37** has not been heretofore described. Also defined experimentally was the divergency in photoreactivity separating **10** from **11**. Seemingly, the marked structural distortion within the diene moiety of **11** is an apt deterrent either to valence isomerization or to CO−N bond fragmentation. Further elucidation of similarly dramatic reactivity differences in related systems is in progress.

Experimental Section

***N*-Allyl-2-iodo-*N*-pent-4-enylbenzenesulfonamide (14).** Amine **13** (1.7 g, 13.6 mmol), triethylamine (2.5 mL, 18.4 mmol), and a catalytic amount of DMAP were dissolved in a mixture of ether and dichloromethane (35 mL, 1:1). This mixture was cooled to 0 °C under Ar, a solution of 2-iodobenzenesulfonyl chloride (3.6 g, 12.2 mmol) in a mixture of ether and dichloromethane (20 mL, 1:1) was introduced via syringe over 2 h, and warming to rt was allowed to occur overnight. The reaction mixture was washed with 1 M HCl, saturated $NaHCO_3$ solution, and brine, dried, and purified over silica gel (elution with 20:1 hexane/ethyl acetate) to give **14** as a colorless oil (3.0 g, 62%): IR (neat, cm^{-1}) 1640, 1596, 1446; ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (dd, J = 2.6, 7.9 Hz, 1H), 8.07 (dd, J = 1.1, 7.8 Hz, 1H), 7.46 (td, J = 1.2, 7.7 Hz, 1H), 7.17 (td, J = 1.7, 6.9 Hz, 1H), 5.79−5.59 (m, 2H), 5.25−5.16 (m, 2H), 4.96−4.88 (m, 2H), 3.94 (d, J = 6.4 Hz, 2H), 3.26 (t, J = 7.6 Hz, 2H), 1.95 (quintet, J = 7.2 Hz, 2H), 1.58 (quintet, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 142.0, 137.2, 133.1, 132.9, 131.7, 128.1, 118.9, 115.1, 92.5, 49.7, 46.1, 30.5, 26.4; HRMS ES m/z $(M + Na)^+$ calcd 413.9995, obsd 413.9971.

1-(2-Iodobenzenesulfonyl)-2,3,4,7-tetrahydro-1*H*-azepine (15). Sulfonamide **14** (1.27 g, 3.75 mmol) was dissolved in 100 mL of dichloromethane and deoxygenated with Ar for 45 min. The reaction mixture was heated to 50 °C, Grubbs I catalyst (80 mg, 0.01 mmol) was added in one portion, and the mixture was stirred for 36 h. After the mixture was cooled to rt, lead tetraacetate (86 mg, 0.19 mmol) was added in one portion and stirring was maintained for an additional 6 h prior to concentration and purification over silica gel (elution with 20:1 hexane/ethyl acetate) to yield **15** as a white solid (1.24 g, 91%), mp 74−75 °C; IR (neat, cm^{-1}) 1567, 1445, 1325; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (dd, J = 1.5, 7.8 Hz, 1H), 8.08 (dd, J = 1.2, 7.8 Hz, 1H) 7.47 (td, J = 1.2, 7.6 Hz, 1H), 7.17 (td, J = 1.6, 7.7 Hz, 1H), 5.91−5.83 (m, 1H), 5.77−5.69 (m, 1H), 3.98 (dd, J = 1.1, 4.9 Hz, 2H), 3.48 (t, J = 6.0 Hz, 2H), 2.37−2.31 (m, 2H), 1.91−1.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 142.0, 133.1, 133.0, 131.6, 128.1, 127.6, 99.8, 92.1, 49.8, 46.5, 27.1, 26.9; HRMS ES m/z $(M + Na)^+$ calcd 385.9682, obsd 385.9665.

8-Thia-9-azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6,12-tetraene 8,8-Dioxide (16). Sulfonamide **15** (500 mg, 1.38 mmol), triphenylphosphine (144.8 mg, 0.55 mmol), K_2CO_3 (436 mg, 3.45 mmol), $Et_4NCl\cdot H_2O$ (228 mg, 1.38 mmol), and 150 mg of 4 Å MS were added to 15 mL of DMF and deoxygenated with Ar for 45 min. $Pd(OAc)_2$ (61.4 mg, 0.276 mmol) was introduced, and degassing was continued for 15 min prior to heating at 90 °C for 24 h. The reaction mixture was cooled to rt, ether was added, and the organic phase was washed with water, saturated NH_4Cl solution, and brine prior to solvent evaporation and purification over silica gel (elution with 4:1 hexane/ethyl acetate) to furnish **16** as a white solid (153 mg, 47%): mp 148−149 °C; IR (neat, cm^{-1}) 1476, 1441, 1322; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 1H), 7.44 (dt, J = 1.0, 7.5 Hz, 1H), 7.38−7.35 (m, 1H), 7.24 (d, J = 7.5 Hz, 1H), 5.79−5.74 (m, 1H), 5.51−5.46 (m, 1H), 4.70 (dd, J = 4.0, 15.5 Hz, 1H), 4.45 (dd, J = 6.5, 17.0 Hz, 1H), 3.71 (dd, J = 2.0, 16.5 Hz, 1H), 3.63 (d, J = 15.5 Hz, 1H), 3.16 (q, J = 3.5 Hz, 1H), 2.70−2.68 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.1, 131.7, 129.9, 128.8, 128.7, 127.7, 123.5, 54.4, 49.6, 37.3, 33.6; HRMS ES m/z $(M + Na)^+$ calcd 258.0559, obsd 258.0559.

8-Thia-9-azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6,11-tetraene 8,8-Dioxide (17). Continued elution furnished **17** as a white solid (141 mg, 40%): mp 141−143 °C; IR (neat, cm^{-1}) 1473, 1440, 1325; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, J = 1.0, 7.5 Hz, 1H), 7.45 (dt, J = 1.0, 6.5 Hz, 1H), 7.38 (dt, J = 1.0, 7.5 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 6.24−6.19 (m, 1H), 5.88−5.84 (m, 1H), 4.50 (dd, J = 4.5, 15.0 Hz, 1H), 4.01 (ddd, J = 3.5, 4.5, 14.5 Hz, 1H), 3.68 (d, J = 20.5 Hz, 1H), 3.50 (q, J = 4.5 Hz, 1H), 3.23−3.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.3, 136.6, 134.1, 131.9, 130.0, 127.6, 123.7, 50.6, 50.1, 36.8, 27.0; HRMS ES m/z $(M + Na)^+$ calcd 258.0559, obsd 258.0554.

12,13-Dibromo-8-thia-9-azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6-triene 8,8-Dioxide (18). Sulfonamide **16** (10 mg, 0.043 mmol) was dissolved in 1 mL of neat bromine and allowed to stir overnight. The next day, the residual bromine was removed under a constant stream of air for 2 h. The residue was partitioned between 5 mL of dichloromethane and 10 mL of saturated $NaHSO_3$ solution. The reaction mixture was stirred until it became colorless. The separated organic layer was washed further with 10% $NaHSO_3$ solution, water, and brine, dried, and evaporated. Chromatography of the residue on silica gel (elution with 4:1 hexane/ethyl acetate) afforded **18** as a tan solid (15 mg, 89%): mp 203−205 °C dec; IR ($CHCl_3$, cm^{-1}) 1463, 1442, 1326; ^1H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, J = 1.0, 7.5 Hz, 1H), 7.52 (td, J = 1.0, 7.5 Hz, 1H), 7.45 (m, 1H), 7.38 (d, J = 8.0 Hz, 1H), 5.01−5.00 (m, 1H), 4.69 (q, J = 4.0 Hz, 1H), 4.50 (dd, J = 4.5, 16.5 Hz, 1H), 4.29 (qd, J = 4.0, 11.5 Hz, 1H), 4.08 (d, J = 16.5 Hz, 1H), 3.55 (d, J = 4.0 Hz, 1H), 3.52 (t, J = 4.0 Hz, 1H), 2.84−2.78 (m, 1H), 2.11−2.05 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.8, 136.2, 132.0, 129.7, 128.8, 124.2, 59.5, 51.7, 45.4, 44.2, 42.4, 29.7; HRMS ES m/z $(M + Na)^+$ calcd 417.8911, obsd 417.8910.

11,12-Dibromo-8-thia-9-azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6-triene 8,8-Dioxide (19). Sulfonamide **17** (15 mg, 0.0638 mmol) was dissolved in 2 mL of neat bromine and allowed to stir overnight. The next morning, excess bromine was removed under a stream of air for 2 h. The residue was taken up in 10 mL of dichloromethane, treated with saturated $NaHSO_3$ solution, and stirred until it became colorless. The organic phase was washed with 10% $NaHSO_3$ solution, water, and brine and then dried. Chromatography of the residue on silica gel (elution with 4:1 hexane/ethyl acetate) gave **19** as a white solid (25 mg, 99%). The material was isolated as a 5:2 mixture of isomers that could not be separated by further chromatography or recrystalization: IR (neat, cm^{-1}) 1477, 1442, 1320; ^1H NMR (500 MHz, $CDCl_3$) δ 7.84−7.80 (m, 1.4H), 7.53−7.47 (m, 1.4H), 7.44−7.40 (m, 1.4H), 7.33 (d, J = 7.5 Hz, 1H), 7.23 (d, J = 7.5 Hz, 0.4H), 4.93 (dd, J = 5.0, 16.5 Hz, 1H), 4.77−4.75 (m, 1H), 4.64−4.61 (m, 1H), 4.57−4.56 (m, 0.4H), 4.54−4.52 (m, 0.8H), 4.50−4.46 (m, 0.4H), 4.45−4.38 (m, 1H), 4.22−

4.18 (m, 1.4H), 4.05 (dd, J = 0.5, 15.5 Hz, 0.4H), 3.90 (dd, J = 3.5, 16.5 Hz, 1H), 3.31 (q, J = 4.0 Hz, 1H), 3.23−3.22 (m, 0.4H), 3.14 (dt, J = 4.5, 16.0 Hz, 1H), 2.97−2.93 (m, 0.4H), 2.87−2.81 (m, 0.4H), 2.60 (ddd, J = 4.0, 7.0, 16.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.4, 138.4, 138.0, 137.9, 132.4, 131.8, 129.5, 129.2, 128.1, 124.1, 123.8, 53.2, 52.9, 52.18, 52.12, 51.6, 50.1, 47.4, 46.6, 44.0, 39.2, 36.2, 35.3.

8-Thia-9-azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6,10,12-pentaene 8,8-Dioxide (9). To a solution of dibromide **19** (500 mg, 1.26 mmol) in 7 mL of dry THF was added 1 M TBAF in THF (6.3 mL, 6.3 mmol). The resulting mixture was allowed to stir vigorously at rt for 1 h. The organic phase was washed with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (elution with 20:1 hexane/ethyl acetate) to give **9** (178 mg, 57%) as a white solid: mp 84.1−84.2 °C; IR (neat, cm^{-1}) 1635, 1598, 1568; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (m, 1H), 7.47 (m, 1H), 7.31 (m, 2H), 6.58 (d, J = 9.0 Hz, 1H), 6.41 (t, J = 9.5 Hz, 1H), 6.03 (dd, J = 7.5, 10.5 Hz, 1H), 5.59 (t, J = 8.5 Hz, 1H), 4.86 (m, 1H), 4.20 (dd, J = 5.0, 9.0 Hz, 1H), 3.20 (d, J = 14.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 135.8, 135.2, 132.5, 131.9, 131.0, 127.2, 125.0, 124.3, 114.2, 47.9, 39.8; HRMS ES m/z (M + Na)$^+$ calcd 256.0408, obsd 256.0406; λ 250 (ϵ 28 210) and 269 nm (ϵ 33 190).

***N*-Allyl-2-iodo-*N*-(pent-4-enyl)benzamide (21).** *N*-Allylpent-4-en-1-amine (1.7 g, 13.6 mmol), triethylamine (2.5 mL, 18.6 mmol), and DMAP (cat.) were dissolved in 55 mL of ether/dichloromethane (1:1) and brought to 0 °C under an argon atmosphere. 2-Iodobenzoyl chloride (3.26 g, 12.24 mmol) dissolved in dichloromethane (5 mL) was added dropwise over 30 min. The reaction mixture was allowed to warm to rt overnight. Workup consisted of washing the organic layer with 100 mL of 1 M HCl, saturated $NaHCO_3$ solution, and brine and then drying. Purification of the residue on silica gel (elution with 3:1 hexane/ethyl acetate) provided 4.0 g (92%) of **21** as a colorless oil: IR (neat, cm^{-1}) 1637, 1584, 1424; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82−7.79 (m, 1H), 7.39−7.32 (m, 1H), 7.19 (ddd, J = 1.5, 7.5, 12.0 Hz, 1H), 7.05 (ddd, J = 1.5, 7.5, 12.0 Hz, 1H), 6.00−5.81 (m, 1H), 5.71−5.54 (m, 1H), 5.34−4.85 (m, 4H), 4.48−4.46 (m, 0.3H), 3.89−3.82 (m, 1H), 3.69 (d, J = 5.0 Hz, 1H), 3.16−3.09 (m, 1.5H), 2.17 (s, 1H), 1.85−1.51 (m, 3.0H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 170.3, 142.48, 142.44, 139.1, 139.0, 137.8, 136.9, 132.9, 129.9, 128.0, 127.1, 126.9, 118.0, 117.7, 115.2, 115.0, 92.7, 92.5, 51.3, 47.3, 46.9, 44.1, 31.2, 30.5, 27.1, 26.0; HRMS ES m/z (M + Na)$^+$ calcd 378.0325, obsd 378.0325.

(*Z*)-(3,4-Dihydro-2*H*-azepin-1(7*H*)-yl)(2-iodophenyl)methanone (22). A solution of **21** (500 mg, 1.41 mmol) in 50 mL of dichloromethane was deoxygenated with argon for 30 min then heated to reflux. Grubbs generation I catalyst (17.3 mg, 0.021 mmol) was added, and the reaction mixture was refluxed for 36 h. After cooling, lead tetraacetate (13.4 mg, 0.029 mmol) was introduced, and the mixture was stirred for an additional 6 h, concentrated, and purified on silica gel (elution with 4:1 hexane/ethyl acetate) producing 300 mg (60%) of **22** as a viscous white semisolid: IR (neat, cm^{-1}) 1635, 1473, 1425; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82−7.81 (m, 1H), 7.38−7.33 (m, 1H), 7.19−7.16 (m, 1H), 7.07−7.03 (m, 1H), 5.92−5.87 (m, 0.5H), 5.85−5.81 (m, 1H), 5.41−5.37 (m, 0.5H), 4.44−4.40 (m, 0.5H), 4.25−4.20 (m, 0.5H), 4.07−4.04 (m, 0.5H), 3.84−3.80 (m, 0.5H), 3.70−3.65 (m, 0.5H), 3.54−3.49 (m, 0.5H), 3.39−3.35 (m, 1H), 2.35−2.27 (m, 2H), 2.03−1.96 (m, 1H), 1.81−1.72 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 169.8, 142.8, 142.7, 139.2, 139.1, 132.9, 132.0, 129.93, 129.92, 128.1, 128.0, 127.5, 127.1, 127.0, 126.5, 92.7, 92.6, 50.6, 47.8, 46.1, 42.4, 27.0, 26.9, 25.8; HRMS ES m/z (M + Na)$^+$ calcd 350.0012, obsd 350.0026.

Heck Cyclization of 22. 9-Azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6,11-tetraen-8-one (24). DMF was degassed under high vacuum for 30 min to remove any traces of dimethylamine. Lactam **22** (3.35 g, 8.85 mmol), triphenylphosphine (464 mg, 1.77 mmol), K_2CO_3 (2.44 g, 17.7 mmol), and 4 Å MS (500 mg) were added to 150 mL of DMF and deoxygenated with argon for 30 min. Palladium acetate (200 mg, 0.88 mmol) was added, and the reaction mixture was heated to 75−80 °C, stirred for 16 h, cooled, and filtered through Celite. Ethyl acetate was added, and the organic layer was washed exhaustively with water and brine prior to drying and concentration. The residue was chromatographed on silica gel to yield 670 mg (38%) of **24**, a pale orange oil: IR (neat, cm^{-1}) 1649, 1601, 1483; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (dd, J = 1.8, 7.5 Hz, 1H), 7.44−7.32 (m, 2H), 7.19 (dd, J = 1.8, 7.5 Hz, 1H), 5.53−5.51 (m, 2H), 4.61−4.51 (m, 1H), 3.87 (dd, J = 2.4, 13.5 Hz, 1H), 3.69 (d, J = 13.5 Hz, 1H), 3.56 (s, 1H), 3.31 (ddd, J = 2.0, 7.7, 13.5 Hz, 1H), 2.87−2.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 144.0, 131.7, 131.4, 130.5, 129.1, 127.5, 125.0, 123.7, 47.5, 46.6, 43.3, 25.5; HRMS ES m/z (M)$^+$ calcd 199.0991, obsd 199.1006.

9-Azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6,12-tetraen-8-one (23): isolated as 654 mg (37%) of a pale reddish oil; IR (neat, cm^{-1}) 1657, 1603, 1471; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (dd, J = 1.5, 8.8 Hz, 1H), 7.42−7.31 (m, 1H), 7.16 (dd, J = 1.5, 8.8 Hz, 1H), 5.60−5.53 (m, 2H), 5.16 (dd, J = 2.4, 17.1 Hz, 1H), 3.69−3.53 (m, 3H), 3.12−3.06 (m, 1H), 2.79−2.68 (m, 1H), 2.31−2.23 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 147.7, 131.5, 129.8, 128.9, 127.4, 127.1, 126.0, 125.3, 50.9, 50.0, 37.8, 32.7; HRMS ES m/z (M)$^+$ calcd 199.0991, obsd 199.1006.

9-Azatricyclo[7.3.2.0^{2,7}]tetradeca-2,4,6,13-tetraen-8-one (25): isolated as 266 mg (15%) of a pale yellow oil; IR (neat, cm^{-1}) 1662, 1630, 1602, 1458; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04−8.01 (m, 1H), 7.44−7.33 (m, 2H), 7.21−7.19 (m, 1H), 6.94 (dt, J = 3.2, 12.5 Hz, 1H), 5.49−5.44 (m, 1H), 3.69 (d, J = 3.8 Hz, 2H), 3.00−2.93 (m, 1H), 2.35−2.19 (m, 4H), 1.60−1.47(m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 147.8, 135.5, 131,7, 129.4, 129.3, 127.2, 125.5, 122.3, 53.7, 37.6, 32.8, 27.0.

12(*S),13(*S**)-Dibromo-9-azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6-trien-8-one (26).** A solution of **23** (25 mg, 0.125 mmol) in dichloromethane (5 mL) was brought to 0 °C. Bromine (40 μL, 0.25 mmol) was introduced, and the reaction mixture was allowed to warm to rt overnight. A 10% $NaHSO_3$ solution was added until the color was discharged. The organic layer was separated, washed with water and brine, and then dried to leave a residue that was purified on silica gel (elution with 95:5 hexane/ethyl acetate) to give 40 mg (90%) of a waxy solid that was crystallized from chloroform as colorless needles: mp 132−136 °C; IR ($CHCl_3$, cm^{-1}) 1653, 1558, 1540; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, J = 2.0, 6.0 Hz, 1H), 7.47−7.41 (m, 2H), 7.36 (dd, J = 2.0, 6.0 Hz, 1H), 4.63 (dd, J = 7.0, 9.5 Hz, 1H), 4.60−4.55 (m 1H), 4.20 (dt, J = 1.5, 10.0 Hz, 1H), 3.86 (dd, J = 2.0, 14.5 Hz, 1H), 3.69 (dd, J = 2.0, 14.5 Hz, 1H), 3.47 (td, J = 2.0, 7.0 Hz, 1H), 3.04 (ddd, J = 3.0, 6.5, 13.5 Hz, 1H), 2.94 (dddd, J = 2.0, 3.0, 7.0, 15.5 Hz, 1H), 2.53−2.45 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6, 140.3, 130.9, 130.3, 130.2, 128.4, 127.9, 60.6, 53.1, 47.8, 44.3, 43.2, 36.9; HRMS ES m/z (M + H) calcd 359.9422, obsd 359.9412.

11,12-Dibromo-9-azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6-trien-8-one (27). A solution of **24** (810 mg, 4.07 mmol) in neat bromine (3 mL) was stirred overnight. The residual bromine was removed under a stream of air. The residue was taken up into dichloromethane and washed with 10% $NaHSO_3$ solution until the organic layer was colorless. This solution was dried and evaporated to leave 1.4 g (98%) of **27** as a white foam: IR (neat, cm^{-1}) 1660, 1601, 1475; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, J = 1.0, 7.5 Hz, 1H), 7.47 (td, J = 1.0, 7.5 Hz, 1H), 7.41 (td, J = 1.0, 7.5 Hz, 1H), 7.33 (d, J = 7.5 Hz, 1H), 4.96 (t, J = 1.5 Hz, 1H), 4.69 (dd, J = 3.5, 6.0 Hz, 1H), 4.52−4.45 (m, 1H), 3.74−3.71 (m, 2H), 3.63 (s, 1H), 3.39 (dd, J = 7.5, 14.0 Hz, 1H), 3.10−3.03 (m, 1H), 2.17−2.11 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 140.7, 132.1, 131.3, 128.9, 128.4, 127.3, 58.6, 48.5, 47.0, 44.2, 43.7, 28.0; HRMS ES m/z (M + Na)$^+$ calcd 379.9261, obsd 379.9246.

9-Azatricyclo[7.4.1.0^{2,7}]tetradeca-2,4,6,10,12-pentaen-8-one (10). A solution of **27** (480 mg, 1.28 mmol) in 15 mL of dry DMSO

was treated with 1 M TBAF/THF (5.13 mL, 5.13 mmol) in one portion, and the mixture was heated at 110 °C for 25 min, cooled, and diluted with ethyl acetate. The organic layer was washed exhaustively with water and brine, dried, and evaporated. The residue was chromatographed on silica gel to yield 190 mg (74%) of **10** as a colorless film: IR (neat, cm^{-1}) 1662, 1601, 1457; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 7.5 Hz, 1H), 7.44 (td, J = 1.0, 7.0 Hz, 1H), 7.35−7.31 (m, 2H), 7.12−7.11 (m, 1H), 6.15−6.11 (m, 1H), 5.90−5.85 (m, 2H), 4.08 (dt, J = 2.0, 13.0 Hz, 1H), 3.73−3.72 (m, 1H), 3.33 (dd, J = 2.5, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4, 146.2, 140.2, 137.1, 132.1, 130.3, 129.2, 127.3, 126.4, 122.7, 121.4, 51.5, 43.9; HRMS ES m/z $(M + Na)^+$ calcd 220.0816, obsd 220.0801; λ 203 (ϵ 19 765) and 203 nm (ϵ 25 975).

***N*-(But-3-enyl)pent-4-enamide (29).** Homoallylamine (16.89 g, 238 mmol) and DMAP (cat.) were dissolved in 800 mL of ether under an argon atmosphere, the reaction mixture was brought to 0 °C, a solution of 4-pentenoic acid chloride (12.2 g, 108.2 mmol) in 10 mL of dichloromethane was introduced, and stirring was maintained for 16 h. Workup consisted of washing the reaction mixture with 1 M HCl, saturated $NaHCO_3$ solution, and brine prior to drying and chromatography of the residue on silica gel (elution with 7:3 hexane/ethyl acetate) to yield **29** as a colorless oil (8.0 g, 48%): IR (neat, cm^{-1}) 3079, 2928, 1646; ^1H NMR (500 MHz, $CDCl_3$) δ 5.91 (s, 1H), 5.82−5.68 (m, 2H), 5.07−4.94 (m, 4H), 3.28 (q, J = 7.0 Hz, 2H), 2.36−2.32 (m, 2H), 2.28 (t, J = 7.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 136.9, 135.2, 116.9, 115.3, 38.3, 35.7, 33.6, 29.5; HRMS ES m/z $(2M + Na)^+$ calcd 329.2199, obsd 329.2216.

***N*-(But-3-enyl)pent-4-en-1-amine (30).** Amide **29** (8.0 g, 52.2 mmol) was dissolved in 300 mL of ether under argon and brought to 0 °C. Lithium aluminum hydride (4.0 g, 104.5 mmol) was added portionwise over 20 min. The reaction mixture was stirred for 16 h, sequentially quenched with 4 mL of water, 4 mL of 2 M NaOH solution, and 12 mL of water, and stirred for an additional 3 h. After filtration and drying, the ether was distilled off to leave 7.2 g (99%) of **30** as a colorless oil: IR (neat, cm^{-1}) 3299, 1458, 1127; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85−5.69 (m, 2H), 5.09−4.90 (m, 4H), 2.62 (dt, J = 7.4, 17.0 Hz, 4H), 2.23 (qt, J = 1.2, 7.0 Hz, 2H), 2.10−2.02 (m, 2H), 1.56 (quintet, J = 7.5 Hz, 2H), 1.06 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 136.4, 116.1, 114.5, 49.2, 48.7, 34.2, 31.5, 29.1; HRMS ES m/z $(M)^+$ calcd 139.1355, obsd 139.1359.

***N*-(But-3-enyl)-2-iodo-*N*-(pent-4-enyl)benzamide (31).** Amine **30** (7.2 g, 51.9 mmol), diisopropylethylamine (9.03 mL, 51.9 mmol), and DMAP (cat.) were dissolved in 600 mL of ether and brought to 0 °C under an argon atmosphere. 2-Iodobenzoyl chloride (12.5 g, 47.2 mmol) was dissolved in dichloromethane (10 mL) and introduced to the ethereal solution via syringe over 1 h. The reaction mixture was allowed to warm to rt overnight and washed with 1 M HCl, saturated $NaHCO_3$ solution, water, and brine prior to drying and chromatography on silica gel (elution with 4:1 hexane/ethyl acetate) to yield 14.37 g (82%) of **31** as a yellowish oil: IR (neat, cm^{-1}) 1637, 1425, 1301; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, J = 1.2, 8.0 Hz, 1H), 7.40−7.36 (m, 1H), 7.19 (dt, J = 1.6, 7.2 Hz, 1H), 7.06 (dt, J = 1.6, 7.2 Hz, 1H), 5.95−5.82 (m, 1H), 5.64−5.49 (m, 1H), 5.19−4.87 (m, 4H), 3.81−3.79 (m, 1H), 3.37−3.04 (m, 3H), 2.56−2.46 (m, 1H), 2.29−2.18 (m, 2H), 1.89−1.81 (m, 2H), 1.66−1.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.45, 170.44, 142.6, 139.14, 139.11, 137.8, 136.9, 135.4, 134.1, 129.93, 129.90, 128.11, 128.10, 127.4, 127.1, 117.4, 116.7, 115.3, 115.1, 92.78, 92.76, 48.3, 48.1, 44.34, 44.30, 32.9, 31.5, 31.1, 30.6, 27.5, 26.1; HRMS ES m/z $(M + Na)^+$ calcd 392.0481, obsd 392.0488.

(*Z*)-(2-Iodophenyl)(3,4,7,8-tetrahydroazocin-1(2*H*)-yl)methanone (32). Amide **31** (5.0 g, 13.5 mmol) was dissolved in 1 L of dichloromethane and deoxygenated with Ar for 1 h. The reaction mixture was heated to reflux and treated with Grubbs generation I catalyst (89 mg, 0.108 mmol) in 2 mL of dichloromethane via syringe, stirred for 16 h, cooled to rt, and treated with lead tetraacetate (95.4 mg, 0.216 mmol). After an additional 6 h of stirring, the reaction mixture was concentrated and passed rapidly through a plug of silica gel (elution with 4:1 hexane/ethyl acetate) to yield 4.28 g (92%) of **32** as an off-white solid: mp 73−75 °C; IR (neat, cm^{-1}) 1632, 1476, 1418; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82−7.80 (m, 1.3H), 7.38−7.35 (m, 1.3H), 7.24 (dd, J = 1.5, 7.5 Hz, 0.3H), 7.16 (dd, J = 1.5, 7.5 Hz, 1H), 7.06−7.02 (m, 1.3H), 5.89−5.80 (m, 1H), 5.72−5.64 (m, 1.3H), 4.01 (s, 0.3H), 3.89 (m, 1H), 3.34 (s, 0.3H), 3.24−3.11, (m, 4H), 2.39 (q, J = 6.0 Hz, 0.6H), 2.28−2.03 (m, 6H), 1.81−1.74 (m, 1H), 1.29−1.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 170.8, 143.3, 142.6, 139.1, 139.0, 132.3, 130.1, 129.9, 129.7, 129.4, 128.1, 127.8, 127.7, 127.5, 127.1, 93.1, 92.6, 51.2, 48.4, 48.2, 46.7, 28.2, 27.1, 26.3, 25.7, 24.2, 23.4; HRMS ES m/z $(M + Na)^+$ calcd 364.0174, obsd 364.0185.

9-Azatricyclo[7.4.2.0^{2,7}]pentadeca-2,4,6,12-tetraen-8-one (33). DMF was degassed under high vacuum for 30 min to remove any residual dimethylamine. Lactam **33** (4.28 g, 12.5 mmol), triphenylphosphine (655 mg, 2.5 mmol), K_2CO_3 (3.46 g, 25.1 mmol), and 4 Å MS (500 mg) were added to 200 mL of DMF and deoxygenated further with Ar for 30 min. $Pd(OAc)_2$ (280 mg, 1.25 mmol) was introduced, and the mixture was heated to 75−80 °C overnight prior to cooling, filtration through Celite, dilution with ethyl acetate, and extensive washing with water and brine. The organic layer was dried and evaporated, and the residue was purified over silica gel to give 270 mg (10%) of a reddish oil alongside 670 mg of recovered **32**. For **33**: IR (neat, cm^{-1}) 1627, 1521, 1468; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72−7.70 (m, 1H), 7.37−7.31 (m, 2H), 7.16−7.14 (m, 1H), 5.86−5.82 (m, 1H), 5.68−5.61 (m, 1H), 5.29−5.24 (m, 1H), 3.46 (dd, J = 5.0, 17.3 Hz, 1H), 3.43−3.38 (m, 1H), 3.30−3.25 (m, 1H), 3.18 (dd, J = 7.3, 15.0 Hz, 1H), 2.76−2.68 (m, 1H), 2.53−2.47 (m, 1H), 2.46−2.40 (m, 1H), 1.75−1.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 144.5, 135.5, 131.0, 128.9, 128.3, 127.5, 127.1, 48.9, 47.5, 39.0, 33.8, 32.6; HRMS ES m/z $(M + Na)^+$ calcd 236.1051, obsd 236.1049.

9-Azatricyclo[7.4.2.0^{2,7}]pentadeca-2,4,6,11-tetraen-8-one (34): also isolated was **34** as a yellowish oil (543 mg, 20%); IR (neat, cm^{-1}) 1644, 1462, 1450; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65−7.63 (m, 1H), 7.41−7.32 (m, 2H), 7.16−7.14 (m, 1H), 5.74−5.69 (m, 1H), 5.63−5.55 (m, 1H), 4.43−4.34 (m, 1H), 3.74−3.71 (m, 1H), 3.52−3.43 (m, 1H), 3.29 (dd, J = 7.2, 15.0 Hz, 1H), 2.25−2.18 (m, 1H), 1.96 (quintet, J = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 140.4, 136.6, 136.1, 131.1, 128.7, 127.7, 127.6, 122.5, 46.4, 45.4, 44.3, 33.5, 26.8; HRMS ES m/z $(M + Na)^+$ calcd 236.1051, obsd 236.1046.

12,13-Dibromo-9-azatricyclo[7.4.2.0^{2,7}]pentadecatrien-8-one (35). Lactam **33** (30 mg, 0.139 mmol) was dissolved in dichloromethane (2 mL) at 0 °C and placed under an argon atmosphere, treated with bromine (14 μL, 0.278 mmol) via syringe, and allowed to warm to rt over 16 h. The next morning, 10% $NaHSO_3$ solution was added until the reaction mixture turned colorless. The separated organic layer was washed with water and brine and then dried. After evaporation, the residue was chromatographed on silica gel (elution with 4:1 hexane/ethyl acetate) to furnish 23 mg (44%) of **35** as a waxy yellow solid: IR (neat, cm^{-1}) 1638, 1470, 1452; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74−7.72 (m, 0.3H), 7.71−7.69 (m, 1H), 7.42−7.35 (m, 2.6H), 7.17−7.16 (m, 1.6H), 4.46−4.43 (m, 0.3H), 3.50−3.34 (m, 4H), 3.30−3.26 (m, 0.3H), 3.23 (dd, J = 11.0, 14.5 Hz, 1H), 3.13 (dd, J = 6.7, 15.0 Hz, 1H), 2.73−2.56 (m, 0.9H), 2.47−2.40 (m, 1H), 2.30−2.23 (m, 1H), 1.98−1.92 (m, 0.6), 1.90−1.83 (m, 1.3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 171.5, 142.8, 142.0, 135.2, 134.7, 131.5, 131.2, 129.4, 128.8, 128.5, 128.4, 127.92, 127.90, 74.14, 61.5, 55.2, 55.1, 53.6, 50.4, 48.4, 45.2, 42.5, 40.7, 40.0; HRMS ES m/z $(M + Na)^+$ calcd 395.9398, obsd 395.9395.

11,12-Dibromo-9-azatricyclo[7.4.2.0^{2,7}]pentadeca-2,4,6-trien-8-one (36). A solution of **34** (543 mg, 2.54 mmol) in dichloromethane (25 mL) was cooled to 0 °C and placed under an argon atmosphere, treated with bromine (262 μL, 5.09 mmol) via syringe,

and allowed to warm to rt overnight. The next morning, 10% $NaHSO_3$ solution was added until the reaction mixture turned a light yellow. The separated organic layer was washed exhaustively with water and brine, dried, and evaporated to leave **36** as a sticky yellow foam (650 mg, 68%): IR (neat, cm^{-1}) 1653, 1450, 1410; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, J = 1.0, 7.5 Hz, 1H), 7.46 (dt, J = 1.5, 7.5 Hz, 1H), 7.41 (dt, J = 1.5, 7.0 Hz, 1H), 7.36−7.35 (m, 1H), 4.58−4.53 (m, 1H), 4.36 (dd, J = 3.0, 8.5 Hz, 1H), 4.19 (dd, J = 8.0, 12.0 Hz, 1H), 3.39−3.28 (m, 3H), 3.06 (ddd, J = 5.5, 10.5, 10.5 Hz, 1H), 2.63−2.51 (m, 2H), 2.33−2.24 (m, 1H), 1.90−1.83 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 139.9, 131.6, 129.1, 128.6, 128.0, 127.4, 60.6, 44.6, 43.7, 40.7, 35.0, 31.0, 30.9; HRMS ES *m*/*z* $(M + H)^+$ calcd 371.9593, obsd 371.9594.

9-Azatricyclo[7.4.2.0^{2,7}]pentadeca-2,4,6,10,12-pentaen-8-one (11). A solution of **36** (250 mg, 0.642 mmol) in DMSO (10 mL) was treated with 1 M TBAF/THF (2.57 mL) and heated to 110 °C for 25 min, cooled to rt, added to 20 mL of ethyl acetate, and washed exhaustively with water and brine. The organic layer was dried and evaporated to leave a residue that was purified over silica gel (elution with ethyl acetate) to yield 98 mg (73%) of **11** as an off-white solid: mp 132−134 °C; IR (neat, cm^{-1}) 1648, 1620, 1593; ^1H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 9.0 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.65−7.62 (m, 1H), 7.44 (t, J = 7.5 Hz, 1H), 6.81 (dd, J = 11.0, 4.0 Hz, 1H), 5.56 (dd, J = 1.0, 11.0 Hz, 1H), 5.41 (dd, J = 1.5, 17.5 Hz, 1H), 4.23 (t, J = 7.0 Hz, 2H), 3.20 (t, J = 7.5 Hz, 2H), 2.18 (quintet J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 141.3, 136.9, 131.9, 130.9, 127.5, 125.6, 124.9, 123.0, 118.9, 110.1, 48.3, 31.5, 21.8; HRMS ES *m*/*z* $(M + H)^+$ calcd 212.1075, obsd 212.1063; λ 214 (ϵ 14 645), 232 (ϵ 13 335), and 296 nm (ϵ 7775).

Photoisomerization of 9. A sample of **9** (40 mg, 0.17 mmol) was dissolved in 170 mL of hexane (0.001 M) and placed in a quartz reaction vessel. The sample required 15 min of sonication to completely dissolve the reactant. The reaction mixture was then deoxygenated with Ar and irradiated at 3000 Å in a Rayonet reactor for 30 min. Concentration and purification of the residue on silica gel (elution with 1:1 hexane/ethyl acetate) yielded **37** as a crystalline solid (20 mg, 50%): mp 196−198 °C; IR (neat, cm^{-1}) 3372, 1633, 1582; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 7.7 Hz, 1H), 7.62 (td, J = 1.0, 7.7 Hz, 1H), 7.53−7.50 (m, 2H), 7.01 (dd, J = 2.2, 8.0 Hz, 1H), 6.62 (t, J = 7.2 Hz, 1H), 5.10 (s, 1H), 4.89 (m, 1H), 4.24 (qd, J = 2.2, 7.0 Hz, 1H), 3.97 (d, J = 7.1 Hz, 1H), 3.09 (qd, J = 2.7, 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 139.2, 135.3, 133.1, 130.8, 129.3, 129.2, 125.3, 121.6, 93.1, 50.3, 45.5; HRMS ES *m*/*z* $(M + Na)^+$ calcd 256.0405, obsd 256.0417. Also isolated was **38** as a colorless oil (3 mg, 5%): IR (neat, cm^{-1}) 1595, 1568, 1472; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, J = 0.5, 7.3 Hz, 1H), 7.45−7.41 (m, 2H), 7.20 (dd, J = 0.5, 7.5 Hz, 1H), 6.21 (s, 1H), 6.12 (d, J = 2.0 Hz, 1H), 5.06 (s, 1H), 4.34 (d, J = 13 Hz, 1H), 3.84 (dd, J = 3.5, 13 Hz, 1H), 3.34 (s, 1H), 2.98 (d, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.9, 139.6, 136.6, 135.9, 132.5, 128.6, 127.5, 126.3, 64.0, 55.9, 52.0, 39.3; HRMS ES *m*/*z* $(M + Na)^+$ calcd 256.0408, obsd 256.0385.

Photoisomerization of 10. A solution of **10** (140 mg, 0.7 mmol) in 750 mL of hexane was placed in a quartz reaction vessel. The reaction mixture was deoxygenated with Ar and irradiated at 3000 Å in a Rayonet reactor for 30 min. After concentration and purification of the residue on 10% deactivated silica gel (elution with 20:1 dichloromethane/ethyl acetate), **39** was isolated as a yellowish oil (53 mg, 38%): IR (neat, cm^{-1}) 1702, 1659, 1601, 1458; ^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 1H), 7.49 (dt, J = 1.5, 7.5 Hz, 1H), 7.33 (dt, J = 1.5, 7.5 Hz, 1H), 7.22 (d, J = 7.5 Hz, 1H), 6.23 (d, J = 2.0 Hz, 1H), 6.16 (d, J = 2.0 Hz, 1H), 4.31 (s, 1H), 3.53 (dd, J = 3.0, 12.5 Hz, 1H), 3.49 (d, J = 12.5 Hz, 1H), 3.29 (s, 1H), 2.90 (d, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.4, 148.1, 139.1, 136.6, 133.8, 130.1, 128.7, 127.5, 126.2, 67.3, 54.6, 54.1, 38.8; HRMS ES *m*/*z* $(M + Na)^+$ calcd 220.0738, obsd 220.0728.

2,4-Divinyl-3,4-dihydro-2*H*-isoquinolin-1-one (40). A solution of **39** (20 mg, 0.1 mmol) in 100 mL of hexane was placed in a quartz reaction vessel. The reaction mixture was deoxygenated with Ar and irradiated at 3000 Å in a Rayonet reactor for 60 min. After concentration and purification of the residue on 10% deactivated silica gel (elution with 20:1 dichloromethane/ethyl acetate), 4 mg (20%) of **40** was recovered as a yellowish film: IR (neat, cm^{-1}) 3285, 1665, 1473; ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, J = 1.0, 8.0 Hz, 1H), 7.70 (dd, J = 9.5, 17.0 Hz, 1H), 7.50 (dt, J = 1.5, 7.5 Hz, 1H), 7.40 (dt, J = 1.0, 7.5 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 5.92 (ddd, J = 7.5, 10.5, 17.5 Hz, 1H), 5.27 (d, J = 10.0 Hz, 1H), 5.14 (d, J = 17.5 Hz, 1H), 4.61 (dd, J = 1.0, 16.5 Hz, 1H), 4.57 (dd, J = 1.5, 9.2 Hz, 1H), 3.81−3.74 (m, 2H), 3.67 (dd, J = 6.5, 11.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 139.6, 136.8, 131.46, 132.43, 129.0, 128.4, 127.5, 126.6, 118.6, 93.9, 46.5, 41.4; HRMS ES *m*/*z* $(M + Na)^+$ calcd 222.0895, obsd 222.0891.

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Supporting Information Available: ORTEP diagram and tables of X-ray crystal data, atomic coordinates, bond lengths, and bond angles for **26** and **37**, as well as high-field ^1H and ^{13}C NMR spectra of all new compounds reported herein. This material is available free of charge via the Internet at http://pubs.acs.org.

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