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A Tin-Free Route to *trans*-Diels–Alder Motifs by Visible Light Photoredox Catalysis

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Supporting Information

ABSTRACT: A tin-free *trans*-Diels–Alder paradigm for the stereoselective synthesis of *trans*-fused polycyclic systems was developed through the photocatalytic reductive dehalogenation of α-haloketones promoted by visible light. Good to excellent diastereoselectivities were observed in the stereoselective construction of *trans*-fused octalone derivatives under mild reaction conditions.

Stereoselective construction of *trans*-fused bicyclic systems is an important task in organic synthesis, because they are among the most versatile intermediates for the synthesis of various polycyclic natural products and relevant compounds. Danishefsky and co-workers developed a two-step *trans*-Diels–Alder (DA) protocol, which provides expeditious access to *trans*-fused octalins and hydrindanes from nitroalkene dienophiles and simple dienes.[1] This conceptually novel strategy involves equipping cyclohexenes with a nitro group as a traceless activating group, thereby enhancing the dienophilicity of the otherwise unreactive dienophiles to yield *cis*-fused DA adducts. Subsequent free radical-mediated reduction of this angular functionality using AIBN and $n\mathrm{Bu_3SnH}$ furnishes the target *trans*-fused bicyclic systems with good to excellent selectivity.[1] The research groups of Danishefsky and Yamamoto have independently reported that the Lewis acid catalyzed DA reactions of α-halogentated 2-cycloalkenones with 1,3-butadienes can provide efficient access to *cis*-fused bicyclic systems with a halogenated quaternary stereogenic center.[2] The halogenated *cis*-fused cycloadducts were then successfully converted to the *trans*-fused octalones in a highly stereoselective fashion by tin-mediated free radical reduction and reductive alkylation.[2b,3,4] In contrast with traditional reductive dehalogenation reactions, which are nonstrategic from the standpoint of *redox economy*,[5] the dehalogenation step in the *trans*-DA paradigm can be considered strategic, since the reduction of carbon–halogen bond would be compensated by the concomitant inversion of configuration at the ring junction stereogenic center.

Despite these advances, there still exists a need for developing new and green methods for the stereoselective synthesis of *trans*-fused polycyclic systems, because organotin hydride-mediated radical reactions have two major disadvantages: the intrinsic toxicity of tin-based reagents and the difficulty of removing their residues from the products. These practical considerations have proved to be a serious hurdle to industrial applications. Inspired by the reports from the laboratories of Stephenson, Zeitler and Reiser,[6] we envisaged that visible-light-induced photocatalytic dehalogenation might be an ideal platform for the development of a green and environmentally benign *trans*-DA protocol that is free of organotin reagent. Visible-light-mediated photoredox catalysis has recently emerged as a powerful tool for a range of organic transformations owing to its inherent features of sustainability and green chemistry as well as promising potential for use in industry.[7] Herein, we report a tin-free methodology using visible-light-induced photoredox catalysis for the stereoselective synthesis of *trans*-fused polycycles.[8]

We began our investigation by examining the photocatalytic reductive dehalogenation of α-bromoketone **1a**. By employing the reaction conditions recently disclosed by Stephenson and co-workers,[6a] a degassed solution of **1a** in DMSO (0.05 M) was irradiated by blue LEDs at room temperature with Ru(bpy)$_3$Cl$_2$·6H$_2$O (**3**) (2.0 mol %, bpy = 2,2′-bipyridine) as a photocatalyst in the presence of formic acid (10 equiv) and $i\mathrm{Pr_2NEt}$ (10 equiv). Under these conditions, the desired product **2a** was obtained in 31% yield with a 3:1 ratio of *trans*-**2a** to *cis*-**2a**, as established by comparison with authentic reference compounds (Table 1, entry 1).[3] Fortunately a more substantial improvement in both the yield and diastereoselectivity was realized when we turned to the Hantzsch ester (HEH) **4** as a hydrogen-atom donor. Accordingly, by fixing **4** as the hydrogen source, we carefully optimized other reaction parameters such as bases, solvents, concentration and the stoichiometry of the reagents and photocatalysts. As for the bases, $n\mathrm{Bu_3N}$ proved to be superior over other organic and inorganic bases, providing **2a** as a 9:1 *trans*/*cis* mixture in 84% yield (entry 5 vs entries 2–4). Intriguingly, the ratio of *trans*-**2a** to *cis*-**2a** was further improved to 12:1, albeit with a slightly diminished yield of 68%, when the reaction was carried out in the absence of a base (entry 6). Although at this point it is difficult to know whether the superior result achieved in the absence of an additional base is primarily due to a subtle electronic effect in the nature of the hydrogen atom transfer event, this result apparently demonstrates that **4** can act as both the reductive quencher and the hydrogen donor in this

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Table 1. Reductive Dehalogenation: Optimization of Reaction Conditions[a]

entry	catalyst	base	trans/cis[b]	yield (%)[c]
1[d]	3	iPr$_2$NEt	3:1	31
2	3	iPr$_2$NEt	8:1	72
3	3	Et_3N	7:1	70
4	3	$CaCO_3$	9:1	49
5	3	nBu$_3$N	9:1	84
6	3	–[e]	12:1	68
7	–[f]	nBu$_3$N	9:1	47
8[g]	3	nBu$_3$N	–	0
9[g]	3	iPr$_2$NEt	–	0
10[h]	3	nBu$_3$N	–	0
11	Ru(bpy)$_3$(PF$_6$)$_2$	nBu$_3$N	9:1	90
12	Ru(bpy)$_3$(PF$_6$)$_2$	–[e]	11:1	96
13	Ru(phen)$_3$Cl$_2$	nBu$_3$N	5:1	82
14	Ir(ppy)$_3$	nBu$_3$N	ND[i]	20

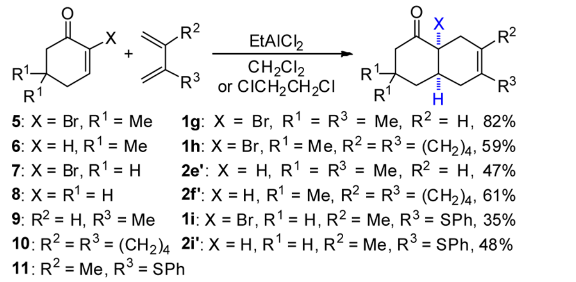
[a]Reaction conditions: **1a** (0.150 mmol), catalyst (3.00 μmol), **4** (0.225 mmol), base (0.225 mmol) in degassed solvent (3 mL) under irradiation with blue LEDs at rt for 8–11 h. [b]Determined by ^{1}H NMR (500 MHz) analysis. [c]Yield of isolated **2a**. [d]Instead of **4**, a mixture of HCO_2H (1.50 mmol) and iPr$_2$NEt (1.50 mmol) was used as the hydrogen donor. [e]In the absence of a base. [f]In the absence of a catalyst. [g]In the absence of visible-light. [h]In the absence of **4**. [i]Not determined.

photoreductive process. Control experiments revealed that a photocatalyst, **4** and visible light were essential for the efficient conversion of **1a** into **2a** (entries 7–10). Finally, we evaluated several frequently employed photocatalysts in the debromination of **1a** under otherwise identical conditions. While Ru(bpy)$_3$(PF$_6$)$_2$ compared favorably with **3** in terms of yield (entry 11 vs entry 5), Ru(phen)$_3$Cl$_2$ (phen = 1,10-phenanthroline) and Ir(ppy)$_3$ (ppy = 2-phenylpyridine) proved to be less effective than **3** in terms of diastereoselectivity and yield, respectively (entries 13 and 14). Notably, the highest yield of **2a** was obtained when the reaction was catalyzed by Ru(bpy)$_3$(PF$_6$)$_2$ under base-free conditions (entry 12). Considering its commercial availability and high reproducibility, we decided to use **3** as the photocatalyst for further studies.

Having the optimized reaction conditions in hand, we next explored the scope and limitations of this photocatalytic dehalogenation reaction with a range of known α-haloketones[2a,3] and newly synthesized α-bromoketones **1g**–**1h** as well. The latter were both prepared by the Lewis-acid catalyzed DA reaction of **5** with appropriate dienes (Scheme 1). The results of these studies are summarized in Table 2.

Initially, we sought to probe the effect of the α-halogen substituents on the diastereoselectivity, and a series of octalone derivatives **1a**–**1c** with three different α-halogen substitutions were evaluated under the optimized conditions (Table 2). The use of α-iodoketone **1b** resulted in a significant decrease in the yield of **2a**, while maintaining a similar diastereoselectivity. The reaction could also be extended to α-chloroketones, but the use of 2.0 equiv of **4** was necessary in order to achieve complete conversion for these substrates. For example, subjecting **1c** to irradiation with blue LEDs in the presence of **4** (2.0 equiv)

Scheme 1. Diels–Alder Routes to α-Bromoketones and *cis*-Fused Reference Compounds



cleanly afforded **2a** in a good yield of 86%, although a slightly elevated temperature (40 °C) was necessary for improving efficiency. Surprisingly, a remarkable erosion in the diastereoselectivity (*trans*/*cis* = 3:1) was observed for **1c** regardless of the temperatures. Although a full understanding of decisive factors that control the diastereoselectivity must await further mechanistic studies, the dehalogenation step for **1c** might be an exothermic reaction (early transition state), whereas the similar step for both **1a** and **1b** seems to be an endothermic reaction (late transition state).[9] As anticipated, the *cis*-fused product **2h** was predominant (*trans*/*cis* = 1:4) in the case of the α-chlorohydrindanoid **1k**. Gratifyingly, we found that the reductive dehalogenation reaction can be easily carried out at gram scale without significantly eroding either yield or diastereoselectivity, as exemplified with **1a**.

Importantly, we found that the steric bulk of a geminal dimethyl pattern at the β-position relative to the carbonyl group was compatible with a range of substrates, and profoundly affected diastereoselectivity to favor the *trans*-bicyclic systems in all cases (Table 2), presumably because of a bigger difference in free-energy between transoid and cisoid conformers (see Scheme 2).[10] For both of the unprecedented *trans*-octalones (i.e., **2e** and **2f**), the structures were unambiguously determined by preparation of the corresponding *cis*-fused products (i.e., **2e′** and **2f′**) as reference samples by the Lewis acid catalyzed DA reaction of **6** with isoprene (**9**) and 1,2-dimethylenecyclohexane (**10**), respectively (Scheme 1).[11] In accord with Casadevall's observation,[12] the ^{13}C NMR chemical shifts of the two ring junction carbons of *cis*-**2e′** appear at 47.7 and 30.7 ppm as singlets, whereas two singlets are observed at 49.5 and 36.1 ppm in the ^{13}C NMR spectrum of *trans*-**2e**. The debromination of **1j** exhibited complete diastereoselectivity to afford the *trans*-bicyclic **2g** as a single diastereomer.[3,13]

Several experiments were carried out in order to gain a better understanding of the reaction mechanism. First, we resubmitted a stereochemically pure sample of *trans*-**2a** to the photocatalytic reaction under otherwise identical conditions. Even after an extended reaction time of 14 h, the *trans*-**2a** was recovered unchanged and any traces of the corresponding *cis*-isomer were not detected by either TLC or ^{1}H NMR spectroscopy. Carefully monitoring the course of the debromination of **1a** indicated that the ratio of *trans*-**2a** to *cis*-**2a** is not changing and remains constant. These experiments lead us to believe that (1) the photocatalytic product **2a** does not undergo a secondary photochemical reaction, such as Norrish type I fragmentation reaction under these conditions, and (2) the process involving inversion of configuration, namely the hydrogen abstraction step, is irreversible and might be the rate-determining step of the overall process; slow conversion of **1a** and low yielding of

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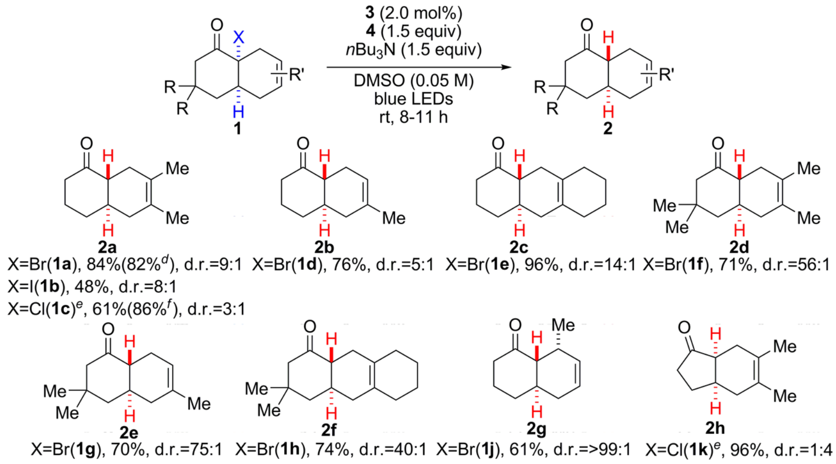
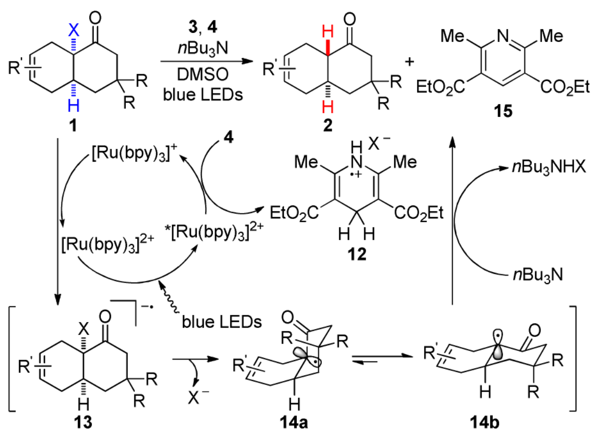
Table 2. Reductive Dehalogenation: Substrate Scope[a,b,c]



[a]Reaction conditions: **1** (0.150 mmol), **3** (3.00 μmol), **4** (0.225 mmol), nBu$_3$N (0.225 mmol) in degassed DMSO (3 mL) under irradiation with blue LEDs at rt for 8−11 h. [b]Yield of isolated **2**. [c]Determined by ^{1}H NMR (500 MHz) analysis. [d]4.00 mmol scale (1.03 g) of **1a**. [e]With 2.00 equiv (0.300 mmol) of **4**. [f]The reaction was carried out at 40 °C for 8 h.

Scheme 2. Proposed Mechanism for Reductive Dehalogenation

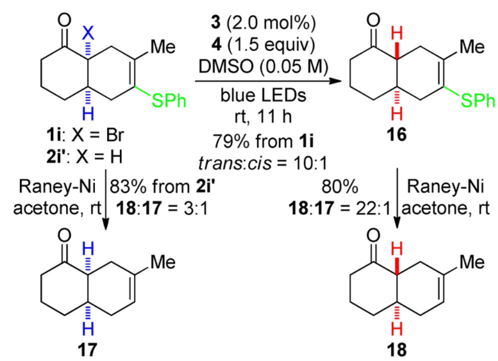


2a (18% yield, *trans*/*cis* = 6:1) by employing 4-methyl Hantzsch ester in place of **4** is also consistent with this mechanistic proposal.

On the basis of these results and previous reports,[6,14] we propose a plausible mechanism in Scheme 2. Upon irradiation with blue LEDs (~450 nm), **3** will readily absorb a photon to generate the excited state *[Ru(bpy)$_3$]$^{2+}$, which would be reductively quenched by **4** to provide the strong reductant [Ru(bpy)$_3$]$^+$ with concomitant formation of the nitrogen radical cation **12**. The crucial step of this mechanism is the single-electron transfer (SET) from the electron-rich Ru(I) species to the electron deficient α-haloketone **1** to induce the reductive scission of the C-X bond, rapidly furnishing the alkyl radical species **14** via the radical anion **13** while returning the [Ru(bpy)$_3$]$^{2+}$ **3** to the catalytic cycle. Subsequent irreversible hydrogen atom transfer from the radical cation **12** to this electron deficient intermediate **14** would generate the *trans*-fused bicyclic **2** and the pyridine byproduct **15**. The selective formation of *trans*-**2** could be explained by a preferential formation of conformer **14a** over conformer **14b** (Scheme 2).

Since visible-light-induced reductive debrominaiton occurs under mild reaction conditions, we decided to apply this technology to the case wherein chemodifferentiation is required in executing the reductive cleavage of the angular and the vinyl leaving groups. Pleasingly, the chemoselective debromination of **1i** prepared from diene **11**[15] delivered a 10:1 separable mixture of **16** and **2i′** in a combined yield of 79% without touching the phenylthio group when the reaction was carried out in the absence of nBu$_3$N (Scheme 3). Somewhat diminished

Scheme 3. Access to *iso*-Diels−Alder Motifs



diastereoselectivity (**16**:**2i′** = 6:1) was observed when the same reaction was conducted by using nBu$_3$N as the base. Finally, we examined removal of the sulfur auxiliary from **16** to gain access to an angularly nonfunctionalized *trans*-IDA(s) motif (cf., **18**).[16] Treatment of diastereomerically pure **16** with an excess of Raney Ni in acetone afforded the desired **18** along with a tiny amount of **17** in a combined yield of 80% (**18**:**17** = 22:1). A pure sample of **18** was readily isolated by column chromatography. In order to gain access to a diastereomeric pair of IDA(s), **2i′** was exposed to Raney Ni to yield a separable 3:1 mixture of **18** and **17** in a combined yield of 83%. A pure sample of **17** was also readily available by column chromatography. The relative stereochemistry of **16** and **18** as well as **2i′** and **17** was firmly confirmed by their ^{13}C NMR spectroscopy.[12]

In summary, we have developed a tin-free *trans*-DA paradigm for the stereoselective synthesis of *trans*-fused polycycles through the photocatalytic reductive dehalogenation of α-haloketones promoted by visible light. The good to excellent diastereoselectivity observed in this reaction represents a considerable advance in the stereoselective construction of

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trans-fused octalone derivatives under mild reaction conditions. This reaction is also highlighted by its chemoselectivtiy in executing the reductive cleavage of the α-activated carbon–bromine bond without touching the vinyl leaving group. Our current efforts are directed toward further improvement of photoredox catalysis in the context of the stereoselective synthesis of *trans*-fused bicyclic systems, specifically to replace the organometallic complexes with less expensive and less toxic organic photocatalysts.[17]

■ EXPERIMENTAL SECTION

General Experimental Methods. Unless otherwise noted, all reagents were purchased at the highest commercial quality from commercial suppliers and used without further purification. Dichloromethane and 1,2-dichloroethane were distilled over CaH_2 under an atmosphere of nitrogen just prior to use. Dimethyl sulfoxide (DMSO) was distilled over CaH_2 under a reduced pressure and stored over 3 Å molecular sieves. *N*,*N*-Diisopropylethylamine (Hünig base) and tri-*n*-butylamine were dried over KOH overnight, distilled from zinc dust and stored over 3 Å molecular sieves. All reactions were carried out in flame-dried glassware under an atmosphere of nitrogen unless otherwise noted. Analytical TLC was performed on silica gel 60 F254 plates and visualized by UV fluorescence quenching and $KMnO_4$ staining. Flash column chromatography was performed on silica gel 60 (40–63 mm). Unless otherwise noted, products were isolated as a mixture of diastereomers. Diastereomeric ratios were determined by ^{1}H NMR. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 500 MHz spectrometer at ambient temperature unless otherwise stated. Chemical shifts are reported in parts per million relative to residual solvent $CDCl_3$ (7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C). The multiplicities of ^{1}H NMR are reported as follows: s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, t = triplet, ddt = doublet of doublet of triplets, td = triplet of doublets, dq = doublet of quartets, m = multiplet, br = broad. IR spectra were recorded on a FT-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High-resolution mass spectrometry (HRMS) were performed on a TOF system for the electrospray ionization (ESI) experiment. Melting points are reported uncorrected.

General Procedure for the Diels–Alder Reaction of Cycloalkenones. To a solution of cycloalkenone (1.00 equiv) in anhydrous CH_2Cl_2 or 1,2-dichloroethane (0.20 M) at an appropriate temperature was added ethylaluminum dichloride (1.0 M solution in hexanes, 0.100–1.00 equiv) via syringe. The reaction mixture was stirred at the same temperature for 10 min and then diene (4.00 or 10.0 equiv) was added in one portion via syringe. The resultant mixture was stirred until the reaction was complete as judged by TLC analysis. At this point the reaction was quenched by a small amount of triethylamine and a saturated solution of potassium sodium tartrate (Rochelle salt) was added to the mixture. After being stirred vigorously for 5 min at room temperature, the mixture was poured into water and extracted with CH_2Cl_2 three times. The combined extract was washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated using a rotary evaporator. The crude mixture thus obtained was purified by flash column chromatography on silica gel to afford the desired cycloadduct.

***cis*-1-Bromo-4,8,8-trimethylbicyclo[4.4.0]dec-3-en-10-one (1g).** Prepared using 2-bromo-5,5-dimethylcyclohex-2-enone (**5**, 203 mg, 1.00 mmol, 1.00 equiv), ethylaluminum dichloride (0.20 mL, 0.20 mmol, 0.20 equiv) and distilled isoprene (**9**, 681 mg, 10.0 mmol, 10.0 equiv) in CH_2Cl_2 (5.0 mL) at −10 °C for 6 h, **1g** was isolated as a white solid (223 mg, 82%) after flash column chromatography (hexanes/EtOAc = 30:1 → 25:1) on silica gel. Mp 82.7–85.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.32 (s, 1H), 2.93 (dd, J = 18.9, 1.6 Hz, 1H), 2.70–2.54 (m, 3H), 2.50 (d, J = 17.2 Hz, 1H), 2.27 (dd, J = 14.5, 2.7 Hz, 1H), 1.81–1.71 (m, 2H), 1.73 (s, 3H), 1.33 (dt, J = 14.0, 3.3 Hz, 1H), 1.05 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.4, 131.5, 114.3, 74.0, 50.4, 42.7, 40.7, 34.3, 34.2, 34.0, 31.6, 26.4, 23.7; IR (cm^{-1}) ν 2959, 2926, 2883, 2829, 1713, 1201; HRMS (ESI, TOF) calcd for $C_{13}H_{19}BrNaO$ $[M + Na]^+$ 293.0517, found 293.0511.

***cis*-9a-Bromo-3,3-dimethyl-3,4,4a,5,6,7,8,9,9a,10-decahydroanthracen-1(2*H*)-one (1h).** Prepared using 2-bromo-5,5-dimethylcyclohex-2-enone (**5**, 203 mg, 1.00 mmol, 1.00 equiv), ethylaluminum dichloride (0.10 mL, 0.10 mmol, 0.10 equiv) and 1,2-dimethylenecyclohexane[18] (**10**, 433 mg, 4.00 mmol, 4.00 equiv) in CH_2Cl_2 (5.0 mL) at room temperature for 15 h, **1h** was isolated as a white solid (166 mg, 59%) after flash column chromatography (hexanes/EtOAc = 30:1 → 25:1) on silica gel. Mp 78.9–82.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.80 (d, J = 18.5 Hz, 1H), 2.66–2.49 (m, 3H), 2.32–2.21 (m, 2H), 1.96–1.84 (m, 4H), 1.79–1.65 (m, 4H), 1.63–1.49 (m, 2H), 1.33 (dt, J = 14.0, 3.2 Hz, 1H), 1.05 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.2, 125.2, 121.4, 75.0, 50.4, 42.7, 40.6, 38.5, 34.4, 34.3, 31.5, 30.0, 29.6, 26.5, 23.0, 22.9; IR (cm^{-1}) ν 2925, 2908, 2829, 1717, 1457, 1366, 1201; HRMS (ESI, TOF) calcd for $C_{16}H_{23}BrNaO$ $[M + Na]^+$ 333.0830, found 333.0822.

***cis*-4,8,8-Trimethylbicyclo[4.4.0]dec-3-en-10-one (2e′).** Prepared using 5,5-dimethylcyclohex-2-enone (**6**, 62.1 mg, 0.500 mmol, 1.00 equiv), ethylaluminum dichloride (0.15 mL, 0.15 mmol, 0.15 equiv) and distilled isoprene (**9**, 341 mg, 5.00 mmol, 10.0 equiv) in 1,2-dichloroethane (2.5 mL) at 33 °C for 2 days, **2e′** was isolated as a colorless oil (55.0 mg, 47%) after flash column chromatography (hexanes/EtOAc = 28:1 → 25:1) on silica gel. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.33 (s, 1H), 2.50 (d, J = 5.7 Hz, 1H), 2.54–2.40 (m, 1H), 2.34–2.16 (m, 3H), 2.06–2.03 (m, 1H), 1.92 (d, J = 14.2 Hz, 1H), 1.75 (t, J = 13.3 Hz, 1H), 1.69 (s, 1H), 1.66 (s, 3H), 1.20 (d, J = 13.5 Hz, 1H), 1.05 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.6, 131.9, 116.9, 49.9, 47.7, 40.0, 35.0, 34.2, 32.3, 30.7, 26.6, 24.3, 23.9; IR (cm^{-1}) ν 2955, 2915, 1702, 1459, 1234; HRMS (ESI, TOF) calcd for $C_{13}H_{20}NaO$ $[M + Na]^+$ 215.1412, found 215.1400.

***cis*-3,3-Dimethyl-3,4,4a,5,6,7,8,9,9a,10-decahydroanthracen-1(2*H*)-one (2f′).** Prepared using 5,5-dimethylcyclohex-2-enone (**6**, 62.1 mg, 0.500 mmol, 1.00 equiv), ethylaluminum dichloride (0.15 mL, 0.30 mmol, 0.30 equiv) and 1,2-dimethylenecyclohexane (**10**, 216 mg, 2.00 mmol, 4.00 equiv) in 1,2-dichloroethane (2.5 mL) at 50 °C for 2 days, **2f′** was isolated as a white solid (71.3 mg, 61%) after flash column chromatography (hexanes/EtOAc = 30:1) on silica gel. Mp 53.9–57.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.58–2.47 (m, 2H), 2.32–2.18 (m, 2H), 1.92 (d, J = 14.2 Hz, 1H), 1.84 (br s, 5H), 1.75 (t, J = 13.3 Hz, 1H), 1.72–1.64 (m, 2H), 1.64–1.46 (m, 4H), 1.18 (d, J = 13.5 Hz, 1H), 1.06 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.5, 125.9, 123.8, 49.9, 48.7, 39.9, 35.0, 34.8, 32.3, 30.7, 30.3, 29.9, 28.9, 26.6, 23.1, 23.0; IR (cm^{-1}) ν 2955, 2918, 2828, 1694, 1436, 1269, 1237; HRMS (ESI, TOF) calcd for $C_{16}H_{24}NaO$ $[M + Na]^+$ 255.1725, found 255.1719.

***cis*-1-Bromo-3-methyl-4-(phenylthio)bicyclo[4.4.0]dec-3-en-10-one (1i).** Prepared using 2-bromocyclohex-2-enone (**7**, 175 mg, 1.00 mmol, 1.00 equiv), ethylaluminum dichloride (1.0 mL, 1.0 mmol, 1.0 equiv) and 3-methyl-2-(phenylthio)buta-1,3-diene[15] (**11**, 705 mg, 4.00 mmol, 4.00 equiv) in dichloromethane (10 mL) at 0 °C for 6 h, **1i** was isolated as a white solid (123 mg, 35%) after flash column chromatography (hexanes/Et_2O = 99:1 → 98:2) on silica gel. Mp 56.3–59.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (t, J = 7.8 Hz, 2H), 7.16–7.13 (m, 3H), 3.34 (d, J = 17.8 Hz, 1H), 3.26 (dt, J = 15.0, 9.5 Hz, 1H), 2.84 (d, J = 17.8 Hz, 1H), 2.70 (dq, J = 6.7, 3.9 Hz, 1H), 2.47–2.32 (m, 3H), 2.31–2.21 (m, 1H), 1.99 (s, 3H), 1.92–1.87 (m, 2H), 1.60–1.55 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.7, 139.5, 135.8, 129.0, 128.0, 125.6, 120.7, 68.8, 44.5, 43.0, 36.0, 34.1, 26.1, 22.2, 20.9; IR (cm^{-1}) ν 2947, 2931, 2911, 2889, 1707, 1471, 1439, 1222; HRMS (ESI, TOF) calcd for $C_{17}H_{19}BrNaOS$ $[M + Na]^+$ 373.0238, found 373.0229.

***cis*-3-Methyl-4-(phenylthio)bicyclo[4.4.0]dec-3-en-10-one (2i′).** Prepared using cyclohex-2-enone (**8**, 223 mg, 2.32 mmol, 1.00 equiv), ethylaluminum dichloride (2.3 mL, 2.3 mmol, 1.0 equiv) and 3-methyl-2-(phenylthio)buta-1,3-diene[15] (**11**, 1.64 g, 9.28 mmol, 4.00 equiv) in dichloromethane (12 mL) at room temperature for 23 h, **2i′** was isolated as a white solid (303 mg, 48%) after flash column chromatography (hexanes/EtOAc = 15:1 → 14:1 → 13:1) on silica gel. Mp 97.7–100.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.23

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J. Org. Chem. 2015, 80, 3309–3314

(m, 2H), 7.17–7.08 (m, 3H), 2.85–2.76 (m, 1H), 2.69 (d, J = 17.5 Hz, 1H), 2.51–2.43 (m, 1H), 2.43–2.37 (m, 1H), 2.36–2.26 (m, 1H), 2.22–2.14 (m, 1H), 2.12–2.10 (m, 2H), 1.99 (s, 3H), 1.97–1.81 (m, 3H), 1.76–1.67 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.7, 139.8, 136.5, 128.9, 127.6, 125.1, 120.7, 48.5, 40.3, 37.5, 33.5, 31.2, 28.3, 23.7, 21.3; IR (cm^{-1}) ν 2965, 2942, 2922, 2904, 1697, 1579, 1475; HRMS (ESI, TOF) calcd for $C_{17}H_{20}NaOS$ [M + Na]$^+$ 295.1133, found 295.1128.

General Procedure for the Dehalogenation of α-Haloketones. A flame-dried 15 mL Schlenk-type flask fitted with a magnetic stir bar was charged with **1** (0.150 mmol, 1.00 equiv), **4** (57.0 mg, 0.225 mmol, 1.50 equiv) and **3** (2.2 mg, 3.0 μmol, 2.0 mol %). The flask was sealed with a rubber septum, evacuated and backfilled with N_2. To this mixture was added dry DMSO (3 mL, 0.05 M) followed by tri-*n*-butylamine (41.7 mg, 0.225 mmol, 1.50 equiv). The resultant mixture was degassed for 20 min by nitrogen purging and irradiated at room temperature with blue LEDs (at a distance of approximately 10 cm so that the reaction mixture did not heat up during the course of the reaction). After stirring for 8–11 h at room temperature, the reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 × 10 mL). The combined extract was washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated using a rotary evaporator. The crude mixture thus obtained was purified by flash column chromatography on silica gel to afford the dehalogenated product **2**.

3,4-Dimethylbicyclo[4.4.0]dec-3-en-10-one (2a). Prepared from *cis*-1-bromo-3,4-dimethylbicyclo[4.4.0]dec-3-en-10-one (**1a**, 38.6 mg, 0.150 mmol, 1.00 equiv), **2a** (22.3 mg, 84%, *trans*/*cis* = 9:1) was isolated (hexanes/EtOAc = 15:1 → 14:1) as an off-white solid. The spectral data matched those in the literature.[3]

4-Methylbicyclo[4.4.0]dec-3-en-10-one (2b). Prepared from *cis*-1-bromo-3-methylbicyclo[4.4.0]dec-3-en-10-one (**1d**, 36.5 mg, 0.150 mmol, 1.00 equiv), **2b** (18.8 mg, 76%, *trans*/*cis* = 5:1) was isolated (hexanes/EtOAc = 15:1 → 14:1) as a colorless oil. The spectral data matched those in the literature.[3]

3,4,4a,5,6,7,8,9,9a,10-decahydroanthracen-1(2*H*)-one (2c). Prepared from *cis*-9a-bromo-3,4,4a,5,6,7,8,9,9a,10-decahydroanthracen-1(2*H*)-one (**1e**, 42.5 mg, 0.150 mmol, 1.00 equiv), **2c** (29.5 mg, 96%, *trans*/*cis* = 14:1) was isolated (hexanes/EtOAc = 12:1 → 10:1) as a white solid. The spectral data matched those in the literature.[3]

3,4,8,8-Tetramethylbicyclo[4.4.0]dec-3-en-10-one (2d). Prepared from *cis*-1-bromo-3,4,8,8-tetramethylbicyclo[4.4.0]dec-3-en-10-one (**1f**, 42.8 mg, 0.150 mmol, 1.00 equiv), **2d** (22.0 mg, 71%, *trans*/*cis* = 56:1) was isolated (hexanes/EtOAc = 14:1 → 13:1) as a colorless oil. The spectral data matched those in the literature.[3]

4,8,8-Trimethylbicyclo[4.4.0]dec-3-en-10-one (2e). Prepared from *cis*-1-bromo-4,8,8-trimethylbicyclo[4.4.0]dec-3-en-10-one (**1g**, 40.7 mg, 0.150 mmol, 1.00 equiv), **2e** (20.3 mg, 70%, *trans*/*cis* = 21:1) was isolated (hexanes/EtOAc = 14:1 → 13:1) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40 (s, 1H), 2.29 (d, J = 13.0 Hz, 1H), 2.22–2.08 (m, 3H), 2.08–1.94 (m, 2H), 1.94–1.80 (m, 2H), 1.71–1.59 (m, 4H), 1.46–1.40 (m, 1H), 1.06 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.2, 132.6, 120.0, 54.9, 49.5, 46.0, 38.5, 36.1, 35.8, 32.1, 25.6, 24.6, 23.3; IR (cm^{-1}) ν 2957, 2905, 2831, 1706, 1439, 1368, 1194; HRMS (ESI, TOF) calcd for $C_{13}H_{20}NaO$ [M + Na]$^+$ 215.1412, found 215.1402.

3,3-Dimethyl-3,4,4a,5,6,7,8,9,9a,10-decahydroanthracen-1(2*H*)-one (2f). Prepared from *cis*-9a-bromo-3,3-dimethyl-3,4,4a,5,6,7,8,9,9a,10-decahydroanthracen-1(2*H*)-one (**1h**, 46.7 mg, 0.150 mmol, 1.00 equiv), **2f** (25.9 mg, 74%, *trans*/*cis* = 40:1) was isolated (hexanes/EtOAc = 13:1 → 12:1 → 11:1) as a white solid. Mp 53.4–55.8; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.28 (d, J = 13.0 Hz, 1H), 2.18–2.05 (m, 3H), 1.99–1.76 (m, 8H), 1.72–1.59 (m, 2H), 1.63 (d, J = 13.4 Hz, 1H), 1.52–1.37 (m, 3H), 1.05 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.5, 127.0, 126.6, 54.8, 50.2, 45.8, 39.0, 36.3, 35.9, 32.1, 30.0, 29.9, 29.5, 25.6, 23.0, 23.0; IR (cm^{-1}) ν 2955, 2920, 2869, 2829, 1706, 1437, 1367, 1237; HRMS (ESI, TOF) calcd for $C_{16}H_{24}NaO$ [M + Na]$^+$ 255.1725, found 255.1718.

***trans*-*trans*-2-Methylbicyclo[4.4.0]dec-3-en-10-one (2g).** Prepared from *cis*-*cis*-1-bromo-2-methylbicyclo[4.4.0]dec-3-en-10-one (**1j**, 36.5 mg, 0.150 mmol, 1.00 equiv), **2g** (15.0 mg, 61%, *trans*/*cis* = >99:1) was isolated (hexanes/EtOAc = 13:1 → 12:1) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.70 (dddd, J = 9.6, 5.2, 2.4, 1.6 Hz, 1H), 5.57–5.48 (m, 1H), 2.71–2.61 (m, 1H), 2.42 (ddt, J = 15.7, 4.4, 2.3 Hz, 1H), 2.31–2.14 (m, 3H), 2.04–1.93 (m, 3H), 1.89 (dddd, J = 17.2, 10.3, 4.5, 2.2 Hz, 1H), 1.72–1.60 (m, 1H), 1.43–1.33 (m, 1H), 0.96 (d, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.1, 133.4, 124.2, 54.3, 41.8, 34.4, 32.9, 32.1, 29.0, 24.0, 16.6; IR (cm^{-1}) ν 3020, 2956, 2925, 2853, 1703, 1650, 1449, 1365; HRMS (ESI, TOF) calcd for $C_{11}H_{16}NaO$ [M + Na]$^+$ 187.1099, found 187.1094.

3,4-Dimethylbicyclo[4.3.0]non-3-en-9-one (2h). Prepared from *cis*-1-bromo-3,4-dimethylbicyclo[4.3.0]non-3-en-9-one (**1k**, 29.8 mg, 0.150 mmol, 1.00 equiv), **2h** (23.7 mg, 96%, *trans*/*cis* = 1:4) was isolated (hexanes/EtOAc = 13:1 → 12:1) as a pale yellow oil. The spectral data matched those in the literature.[11]

3-Methyl-4-(phenylthio)bicyclo[4.4.0]dec-3-en-10-one (16). Prepared from *cis*-1-bromo-3-methyl-4-(phenylthio)bicyclo[4.4.0]dec-3-en-10-one (**1i**, 56.0 mg, 0.159 mmol, 1.00 equiv), **3** (2.4 mg, 3.2 mmol, 2.0 mol %) and **4** (60.6 mg, 0.239 mmol, 1.50 equiv) in DMSO (3.2 mL, 0.050 M), **16** (34.4 mg, 79%, *trans*/*cis* = 10:1) was isolated (hexanes/EtOAc = 15:1 → 14:1 → 13:1) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.23 (m, 2H), 7.21–7.11 (m, 3H), 2.54–2.40 (m, 2H), 2.40–2.26 (m, 4H), 2.21–2.11 (m, 1H), 2.07 (ddd, J = 13.0, 5.8, 2.9 Hz, 1H), 1.99 (s, 3H), 1.85 (d, J = 14.6 Hz, 1H), 1.81–1.64 (m, 2H), 1.41 (ddd, J = 25.0, 13.3, 3.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.5, 140.7, 136.2, 128.9, 128.2, 125.4, 121.5, 50.4, 41.8, 41.7, 39.7, 32.0, 31.9, 26.1, 21.5; IR (cm^{-1}) ν 2960, 2937, 2921, 2853, 1698, 1581, 1474, 1370; HRMS (ESI, TOF) calcd for $C_{17}H_{20}NaOS$ [M + Na]$^+$ 295.1133, found 295.1128.

Procedure for the Dehalogenation of 1a at Gram Scale. A flame-dried 250 mL one-necked, round-bottomed flask fitted with a magnetic stir bar was charged with **1a** (1.03 g, 4.00 mmol, 1.00 equiv), **4** (1.52 g, 6.00 mmol, 1.50 equiv) and **3** (60.0 mg, 0.0800 mmol, 2.00 mol %). The flask was sealed with a rubber septum, evacuated and backfilled with N_2 (three cycles). To this mixture was added dry DMSO (80 mL, 0.05 M) followed by tri-*n*-butylamine (1.11 g, 6.00 mmol, 1.50 equiv). The resultant mixture was degassed for 30 min by nitrogen purging and irradiated at room temperature with blue LEDs (at a distance of approximately 10 cm so that the reaction mixture did not heat up during the course of the reaction). After stirring for 13 h at room temperature, the reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 × 25 mL). The combined extract was washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated using a rotary evaporator. The crude mixture thus obtained was purified by flash column chromatography on silica gel to afford the desired product **2a** (588 mg, 82%, *trans*/*cis* = 9:1) as an off-white solid. A diastereomerically pure sample of *trans*-**2a** was isolated as a white solid by column chromatography (hexanes/EtOAc = 15:1).

Preparation of a 22:1 Mixture of *trans*- (18) and *cis*-3-Methylbicyclo[4.4.0]dec-3-en-10-one (17). A solution of *trans*-3-methyl-4-(phenylthio)bicyclo[4.4.0]dec-3-en-10-one (**16**, 42.0 mg, 0.154 mmol, 1.00 equiv) in acetone (3.1 mL, 0.050 M) at room temperature was treated with an excess of Raney Ni (washed with acetone 5 times just prior to use). The resultant mixture was stirred vigorously for 4.5 h. At this point the mixture was diluted with CH_2Cl_2 and filtered on a pad of Celite. The filtrate was dried over anhydrous Na_2SO_4, filtered and concentrated using a rotary evaporator. The crude mixture thus obtained was purified by flash column chromatography (hexanes/EtOAc = 19:1 → 17:1) on silica gel to afford a 22:1 diastereomeric mixture of **18** and **17** (20.3 mg, 80%) as a colorless oil. A pure sample of **18** was obtained as a colorless oil by flash column chromatography (hexanes/EtOAc = 19:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.31 (s, 1H), 2.46–2.39 (m, 1H), 2.35 (td, J = 13.7, 5.9 Hz, 1H), 2.24–2.15 (m, 3H), 2.12–1.97 (m, 2H), 1.96–1.85 (m, 2H), 1.74–1.56 (m, 2H), 1.66 (s, 3H), 1.43 (ddd, J = 25.1, 13.3, 3.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.4, 133.1, 119.3, 50.7, 42.0, 40.1, 33.7, 32.5, 29.2, 26.2, 23.5; IR (cm^{-1}) ν 2923, 2901, 2846,

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2828, 1698, 1428, 1315, 1236; HRMS (ESI, TOF) calcd for $C_{11}H_{16}NaO$ $[M + Na]^+$ 187.1099, found 187.1089.

Preparation of a 3:1 Mixture of *trans*- (18) and *cis*-3-Methylbicyclo[4.4.0]dec-3-en-10-one (17). A solution of *cis*-3-methyl-4-(phenylthio)bicyclo[4.4.0]dec-3-en-10-one (**2i′**, 48.0 mg, 0.176 mmol, 1.00 equiv) in acetone (3.5 mL, 0.050 M) at room temperature was treated with an excess of Raney Ni (washed with acetone 5 times just prior to use). The resultant mixture was stirred vigorously for 3.5 h. At this point the mixture was diluted with CH_2Cl_2 and filtered on a pad of Celite. The filtrate was dried over anhydrous Na_2SO_4, filtered and concentrated using a rotary evaporator. The crude mixture thus obtained was purified by flash column chromatography (hexanes/EtOAc = 19:1 → 17:1) on silica gel to afford a 3:1 diastereomeric mixture of **18** and **17** (24.1 mg, 83%) as a colorless oil. A pure sample of **17** was obtained as a colorless oil by flash column chromatography (hexanes/EtOAc = 18:1). ^1H NMR (500 MHz, $CDCl_3$) δ 5.31 (s, 1H), 2.73 (dd, J = 9.9, 4.8 Hz, 1H), 2.46–2.16 (m, 4H), 2.02–1.83 (m, 5H), 1.82–1.77 (m, 1H), 1.76–1.70 (m, 1H), 1.67 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.8, 131.2, 119.0, 48.9, 39.9, 35.6, 28.5, 28.3, 27.4, 24.1, 23.4; IR (cm^{-1}) ν 2912, 1710, 1445, 1375, 1312, 1202; HRMS (ESI, TOF) calcd for $C_{11}H_{16}NaO$ $[M + Na]^+$ 187.1099, found 187.1089.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra of all new products. This material is available free of charge at http://pubs.acs.org.This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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