whereupon a homogeneous pale brown oil was isolated. The product is identified as the previously reported[17] 7-methylenebicyclo[4.1.0]hept-2-ene (17) (1.23 g, 41%), identical to a sample prepared independently: ^{1}H NMR δ 0.85–2.2 (m, 6 H), 5.2–6.2 (m, 4 H); ^{13}C NMR[21] δ 15.0, 17.2 (C1/C6), 17.0, 21.1 (C5/C4), 103.0 (=CH_2), 124.0, 126.0 (C2/C3), 135.7 (C7). No evidence was obtained to support the formation of [4 + 2] adduct.

D. From 9,9-Dichlorobicyclo[6.1.0]nonane (8d).[19] **8d** (5 g, 26 mmol) with furan gave one fraction from column chromatography that provided spectroscopic data identical to those reported[17] for bicyclo[6.1.0]nona-1,6-diene (**20**) (1.7 g, 61%). No evidence was obtained for the formation of a [4 + 2] adduct.

(21) The earlier report (see ref 16) quotes eight distinct signals for 17 but does not give the chemical shifts.

7-Methylenebicyclo[4.1.0]hept-2-ene (17). This was prepared from **8c** (1.0 g, 5.6 mmol) according to the method of Billups et al.[17] Yield: 185 mg, 31% (lit.[17] 42%). The compound was identical to that obtained in the presence of furan.

Attempted Addition of 7-Methylenebicyclo[4.1.0]hept-2-ene (17) to 1,3-Diphenylisobenzofuran. Reaction of **17** (120 mg, 1.1 mmol) with DPIBF (300 mg, 1.1 mmol) in DMSO (25 mL) as described for **9** above gave, as the only characterizable product, *o*-dibenzoylbenzene (262 mg, 83%), mp 146–147 °C (lit.[20] mp 147–148 °C).

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Diels–Alder Cycloadditions Using Nucleophilic 3-(*p*-Tolylthio)-2-pyrone. Regiocontrolled and Stereocontrolled Synthesis of Unsaturated, Bridged, Bicyclic Lactones

Gary H. Posner,* Todd D. Nelson, Chris M. Kinter, and Neil Johnson

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

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Captodative 3-(tolylthio)-2-pyrone (1) is shown to be reactive as a nucleophilic diene undergoing 2 + 4-cycloadditions with various electrophilic alkenes under sufficiently *mild thermal conditions* (≤90 °C) so that the initial bicyclic lactone adducts can be isolated on gram scale in moderate to very good yields (42–82%) *without loss of* CO_2. These bicyclic adducts are formed regiospecifically and often with excellent stereoselectivity. These Diels–Alder cycloadditions are *the first examples of a captodative unsaturated sulfide acting as an enophile.* NMR data (^{13}C) are presented correlating the electron density in the pyrone diene systems with their Diels–Alder reactivity, and some transformations of the bicyclic lactone adducts are shown to illustrate the value and versatility of these richly functionalized synthetic intermediates.

Introduction

Typically, 2-pyrones cycloadd to various alkenes at temperatures so high (~100–200 °C) that loss of CO_2 from the initial bicyclic lactone adducts occurs in situ.[1] Attempts to isolate these initial nonaromatic bicyclic adducts generally have failed. Some exceptions exist.[2] For example, 3-hydroxy-2-pyrone has been reported to undergo thermal and high-pressure cycloadditions with maleic anhydride and with acrylate and acrylonitrile derivatives, and the bicycloadducts have been isolated but without characterization of their stereochemistry; in several instances, these bicycloadducts decomposed on attempted chromatographic purification.[3] Also, carboxylate esters of 3-hydroxy-2-pyrone have been reported to undergo high-pressure, stereoselective, inverse-electron-demand cycloaddition with electron-rich vinyl ethers,[4] and pyrone itself has been reported to undergo some cycloadditions with alkenes at 19 kbar.[5] Because unsaturated, bridged, bicyclic lactones are structurally rich and versatile building units having fixed and useful stereochemical relationships, we have sought simple and direct ways to synthesize these valuable compounds. Success has been achieved using *electrophilic* 3-sulfinyl- and especially 3-sulfonyl-2-pyrones that reliably undergo mild and stereocontrolled 2 + 4-cycloadditions with nucleophilic dienophiles such as enol ethers.[6] The stable bicyclic lactones so formed have served effectively as key polyfunctional building units in construction of shikimate,[7] chorismate,[8] and vitamin D_3 de-

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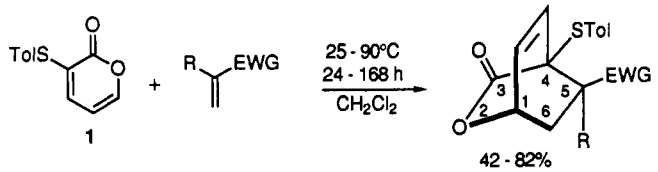
Table I. ^{13}C NMR Chemical Shift Data

Y	^{13}C (ppm)	^{13}C (ppm)
$ArSO_2^-$	157.1[a]	133.6[b]
MeO_2C^-	156.5	132.8
Br^-	150.9	127.0
H^-	Δ 4.7 { 151.7	Δ 1.6 { 128.5
ArS^-	147.0[a]	126.9[b]
R_3SiO^-	144.0[c] } Δ 9.6	121.4[d] } Δ 7.1
HO^-	142.1	121.4

[a] Ar = Tol. [b] Ar = Ph. [c] R_3 = t-$BuMe_2$. [d] R_3 = Me_3.

rivatives.[9] Now we report that *nucleophilic* 3-sulfenyl-2-pyrone 1 undergoes mild, thermal Diels–Alder cycloadditions with diverse electrophilic dienophiles CH_2=C(R)EWG in which R is hydrogen, methyl, or methylene and the electron-withdrawing group (EWG) is nitro, nitrile, aldehyde, ketone, or carboxylate ester (eq 1). Full details



1

42 - 82%

EWG	R
$-NO_2$	-H
-CN	-Me
-CHO	$-CH_2-$
-COMe	
-COOMe	

(1)

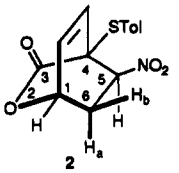
of these regiospecific and stereoselective Diels–Alder cycloadditions are recorded here, including ^{13}C NMR data correlating chemical reactivity with electron density in the reactant pyrone ring and including some subsequent chemical transformations illustrating the value of these richly functionalized bicycloadducts as versatile synthetic intermediates.

Results and Discussion

A series of 3-substituted 2-pyrones was studied by ^{13}C NMR spectroscopy in order to generate a *quantitative* measurement of electron density in the pyrone diene system;[10a] these data (Table I) were expected to confirm our *qualitative* generalization that electron-withdrawing groups (e.g., $ArSO_2$) would diminish electron density in the pyrone diene unit whereas electron-releasing groups (e.g., ArS) would enhance electron density. To avoid any proximity effects between the substituent Y and the ring carbon atom being examined, only the carbon atom para to the Y-substituent was considered. For comparison, Table I also includes ^{13}C NMR data for the para position in Y-substituted benzenes.[10b]

The data in Table I deserve comment. A strikingly similar trend in ring electron density is seen in *both* the Y-substituted pyrones and the Y-substituted benzenes; arylsulfonyl and methoxycarbonyl groups are the strongest electron-withdrawing substituents, whereas arylthio groups are strong electron-donors. In the 3-Y-2-pyrone series, in which the ^{13}C NMR chemical shift values at C_6 range from 151.7 ppm for Y = H to 142.1 ppm (Δ 9.5 ppm) for Y = OH, the arylthio group with C_6 at 147.0 ppm (4.7/9.6) appears to be even more effective than an arylthio group attached to a benzene ring (1.6/7.1) in increasing ring electron density (see the lower part of Table I). Furthermore, the ^{13}C NMR chemical shift data for the pyrone series parallel the relative reactivities found in competition experiments for Diels–Alder cycloadditions with 2,2-dimethyl-1,3-dioxole, an electron-rich dienophile: 3-Tol-SO_2/3-MeOOC/3-Br = 20/7/1. Finally, these ^{13}C NMR measurements suggested that 3-(*p*-tolylthio)-2-pyrone (1) would be an excellent candidate as a *nucleophilic* diene in polar 2 + 4-cycloadditions with electron-poor alkenes, as (arylthio)benzenes are excellent nucleophiles in electrophilic aromatic substitution reactions. Electron-rich pyrone diene 1 was prepared as a stable solid from 3-bromo-2-pyrone according to our published procedure.[11] Table II lists the successful reaction conditions used and the results obtained in cycloaddition of electron-rich pyrone sulfide 1 with various electron-poor dienophiles. Benzene was used as solvent in all cases in part to avoid temperatures above 90 °C; control reactions using THF and hexane as solvents in sealed tubes at 85–90 °C proceeded much more slowly than the corresponding cycloaddition in benzene.

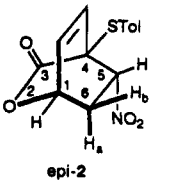
With very reactive nitroethylene as dienophile, smooth 2 + 4-cycloaddition occurred *at room temperature* giving pure bicycloadduct 2, having an endo stereochemical relationship of the nitro substituent relative to the 2-carbon ethylenic bridge, in 82% yield with no exo-isomer detectable by 400-MHz ^1H NMR spectroscopy (i.e., >98:2 endo–exo stereochemistry). The regiochemistry and the endo orientation of the nitro substituent in bicycloadduct 2 were established in two ways. First, excellent literature precedent[2d,12] using ^1H NMR decoupling experiments indicated unambiguously that, for such 4,5-disubstituted (but not 4,6-disubstituted) endo-functionalized bicyclic lactones, $J_{1,6a}$ is larger than $J_{1,6b}$ and that $J_{5,6a}$ is larger than $J_{5,6b}$; NMR data for bicyclic lactone 2 are shown here. Second, rather than the expected reduction of the nitro group, epimerization of the nitro group from the endo → exo orientation was achieved using ammonium formate/palladium on charcoal;[13] the exo-nitro epimer (*epi*-2) had the coupling constants shown here. Similar endo → exo epimerizations were achieved using only ammonium formate (without palladium on charcoal) and using diazabicycloundecane (DBU) in THF.



2

$J_{1,6a}$ = 3.85 Hz; $J_{1,6b}$ = 1.4 Hz

$J_{5,6a}$ = 9.3 Hz; $J_{5,6b}$ = 3.35 Hz



epi-2

$J_{1,6a}$ = 3.7 Hz; $J_{1,6b}$ = 1.6 Hz

$J_{5,6a}$ = 4.3 Hz; $J_{5,6b}$ = 10.15 Hz

(9) (a) Posner, G. H.; Kinter, C. M. *J. Org. Chem.* **1990**, *55*, 3967. (b) Posner, G. H.; Nelson, T. D. *Ibid.* **1991**, *56*, 4339.

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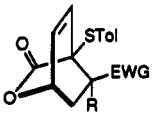
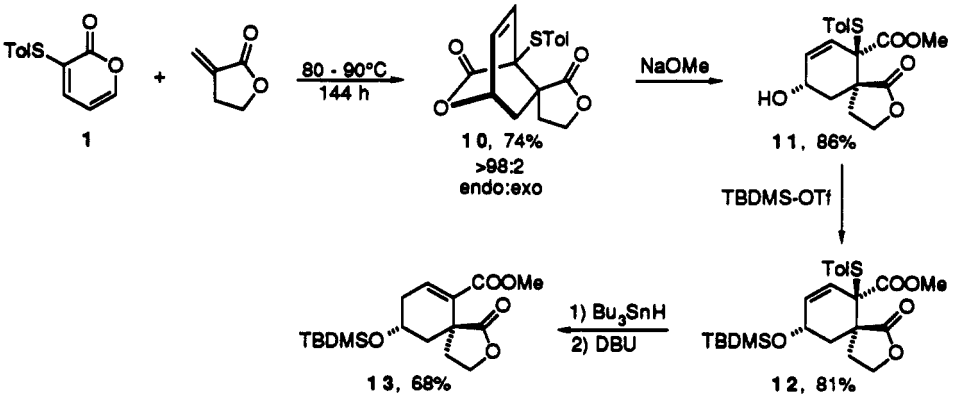
Table II. Formation of Cycloadducts 2–9 According to eq 1



dienophile	condns °C, h	cycloadduct	R	EWG	endo:exo	yield,[b] %
	25, 36	2	H	$-NO_2$	>98:2[a]	82
	85, 24	3	H	–CN	2:1	53
	88, 34	4	H	–CHO	>98:2[a]	44
	85–90, 168	5	Me	–CHO	>98:2[a]	70
	85–90, 96	6	H	–COMe	>98:2[a]	70
	85, 72	7	H	$-CO_2Me$	3:1	65
	85, 192	8	H	$-CO_2Bn$	9:1	64
	85–90, 215	9	Me	$-CO_2Me$	3:1	42

[a] No evidence of exo formation by examination of 400-MHz ^1H NMR spectrum of crude reaction product. [b] Yield of purified endo product.

Scheme I



Likewise, the regiochemistry and the orientation of the electron-withdrawing groups in the major bicycloadducts formed from other electron-poor dienophiles and pyrone sulfide 1 were established as 3-endo based on ^1H NMR data including decoupling experiments (see Experimental Section for details).

Methacrolein was found to undergo cycloaddition with 3-(*p*-tolylthio)-2-pyrone (1) stereospecifically to give a chromatographically stable bicyclic lactone adduct in contrast to the corresponding less stable adduct formed from 3-bromo-2-pyrone.[14]

Acrylonitrile and methyl acrylate both underwent cycloaddition with pyrone sulfide 1 at 85 °C for 1 day to form the corresponding bicyclic lactones in good yields with complete 3-regiospecificity but with only small (2.1-3.5:1.0) endo stereoselectivity. The endo stereochemistry of, for example, the methyl methacrylate adduct, 5,5-disubstituted bicyclic lactone 9, was assigned by ^1H NMR decoupling experiments in analogy to previous results from us[6-9] and from others.[2] In contrast, acrolein cycloadded to pyrone sulfide 1 with essentially complete endo stereocontrol; at this time, no convincing argument is obvious to explain these dramatically different stereochemical outcomes.

Pyrone sulfide 1 is more reactive as a nucleophilic diene than 3-bromo-2-pyrone.[14] Evidence supporting this statement comes from the ^{13}C NMR data in Table I and from a comparison of rates of cycloaddition. Table I shows C_6 for pyrone sulfide 1 at 147.0 ppm and C_6 for 3-bromo-2-pyrone at 150.9 ppm, indicating a higher electron density in the diene component of pyrone sulfide 1. Also, whereas cycloaddition of acrylonitrile with pyrone sulfide 1 was complete within 24 h at 85 °C, the comparable reaction with 3-bromo-2-pyrone was not complete even after 1 week at 85 °C.

We have found previously that increasing the size of the dienophile even slightly dramatically retards the rate of cycloaddition with 2-pyrones. For example, in cycloaddition with 3-tolylsulfinyl-2-pyrone, *ethyl* vinyl thioether was considerably more sluggish than *methyl* vinyl thioether.[7] Likewise, we have found now that *benzyl* acrylate is considerable more sluggish than *methyl* acrylate in cycloaddition to pyrone sulfide 1 (see Table II).

Virtually complete regiocontrol and stereocontrol, although much slower rates of reaction, were obtained in cycloadditions of α-substituted CH_2=C(R)EWG systems such as methacrolein and α-methylene-γ-butyrolactone with pyrone sulfide 1.

Several electron-poor alkenes failed to undergo cycloaddition with pyrone sulfide 1 even after prolonged heating: tolyl vinyl sulfone, 1,4-naphthoquinone, diethyl ethylidenemalonate, 2-butenolide, 2-pentenolide, and 2-cyclohexenone. Thus, substituents on the alkene double bond of CH_2=CHEWG apparently exert a strong steric impediment toward cycloaddition with pyrone sulfide 1.

(14) Posner, G. H.; Nelson, T. D.; Kinter, C. M.; Afarinkia, K. *Tetrahedron Lett.* **1991**, *32*, 5295.

Pyrone sulfide 1 can be considered a captodative diene in which C_3 is attached to an electron-accepting lactone carbonyl group and also to an electron-releasing arylthio group.[15] Several examples have been reported in which a vinyl sulfide *geminally* substituted with an electron-withdrawing group shows unusually high Diels–Alder reactivity toward dienes.[16] As far as we know, cycloadditions of pyrone sulfide 1 with the alkenes in Table I, along with the results in the accompanying article,[17] represent the *first examples of a captodative unsaturated sulfide acting as an enophile.*

To illustrate the potential of many of the richly functionalized bicycloadducts shown in Table I as versatile synthetic intermediates,[5-8] spirolactone 10 was subjected to basic methanolysis and then to alcohol protection producing pentasubstituted cyclohexene 11 as a single diastereomer (Scheme I); IR spectroscopy confirmed that only the 6-membered lactone was cleaved and that the 5-membered lactone (1770 cm^{-1}) remained intact. Reductive cleavage of the allylic carbon–sulfur bond of 12 under neutral radical conditions using tributyltin hydride proceeded well. Double-bond isomerization gave unsaturated spirolactone 13 that we are in the process of converting into a ring-A modified vitamin D_3 for biological evaluation.[9] The sulfur-free compound thus obtained (13) represents a formal cycloaddition of pyrone itself to α-methylene-γ-butyrolactone, a reaction that cannot be achieved above 100 °C without loss of CO_2 from the initial cycloadduct and that proceeds very sluggishly below 100 °C; *thus, 3-(p-tolylthio)-2-pyrone (1) is a highly reactive synthetic equivalent of 2-pyrone in thermal (i.e., not high-pressure) Diels–Alder cycloadditions with some electron-poor alkenes.*

Conclusion

In conclusion, pyrone sulfide 1 has been established as a reactive electron-rich heteroaromatic diene that undergoes effective thermal 2 + 4-cycloadditions with some electron-poor alkenes. Reaction conditions are sufficiently mild so that the initial bicyclic lactone adducts can be isolated in moderate to very good yields. These bicycloadducts, formed regiospecifically and often with outstanding stereocontrol, represent compact and multifunctional synthetic intermediates of considerable value. Of special practical importance, these cycloadducts generally are more stable and are formed more rapidly than those prepared from ambiphilic 3-bromo-2-pyrone.[14] Finally, by adjusting the oxidation state of the sulfur atom in 3-sulfur-substituted pyrones, we have now shown that captodative 3-(arylthio)-2-pyrone 1 is a useful *electron-rich* diene complementing 3-(arylsulfonyl)-2-pyrones as *electron-poor* dienes in diverse 2 + 4-cycloaddition reactions producing unsaturated, bridged, bicyclic lactones.

Experimental Section

General. Tetrahydrofuran and diethyl ether were distilled from benzophenone ketyl prior to use. Methylene chloride and triethylamine were distilled from calcium hydride immediately prior to use. Commercially available anhydrous solvents were used in other instances. All reagents were purchased from Aldrich Chemical Co. (Milwaukee, WI) and unless otherwise specified were used as received without further purification. FT-IR spectra were determined using a Perkin-Elmer Model 1600 FT-IR spectrophotometer. The ^1H NMR spectra were recorded on a Varian XL-400 spectrometer and Bruker AMX-300 spectrometer operating at 400 and 300 MHz, respectively. The ^{13}C NMR spectra were recorded of the same instruments operating at 100 and 75 MHz, respectively. High-resolution mass spectra were obtained on a two sector high-resolution VG-70S mass spectrometer run at 70 eV. Elemental analyses were performed by Atlantic Microlab, Norcross, GA. A Leco Corp. Model No. PG-200-HPC 13 kbar apparatus was used for the high-pressure experiments. Melting points are uncorrected.

4-(4′-Methylbenzenesulfenyl)-5-*endo*-nitro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene (2). To a CH_2Cl_2 solution of 874 mg (4.0 mmol) of sulfenyl pyrone 1 was added 0.29 mL of nitroethylene[18] and the solution stirred for 24 h. Additional nitroethylene was added (ca. 0.15 mL) and stirred for 12 h. The reaction was checked every 12 h by TLC, and 0.15 mL of nitroethylene was subsequently added until the pyrone was consumed. Usually 2–5 more additions at 12-h intervals were necessary to give complete cycloaddition. The solvent was evaporated, and purification by column chromatography (silica gel, 30–70% Et_2O/hexane) afforded 957 mg (3.3 mmol, 82%) of the endo bicycloadduct 2 as an off-white solid: mp 124–125 °C (R_f = 0.77, 75% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ 7.64 (d, J = 8 Hz, 2 H), 7.15 (d, J = 8 Hz, 2 H), 6.68 (dd, J = 7.9, 5.3 Hz, 1 H), 6.18 (d, J = 7.9 Hz, 1 H), 5.28 (ddd, J = 5.3, 3.85, 1.4 Hz, 1 H), 4.88 (ddd, J = 9.3, ≈3.35, 1.2 Hz, 1 H), 2.95 (ddd, J = ≈14.35, 9.3, 3.85 Hz, 1 H), 2.35 (s, 3 H), 2.25 (ddd, J = ≈14.35, ≈3.35, 1.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 167.8, 140.5, 137.3 (2), 131.5, 131.0, 129.9 (2), 124.1, 79.3, 71.9, 59.5, 36.1, 21.3; IR ($CDCl_3$) 1762 cm^{-1}; HRMS m/e calcd for $C_{14}H_{13}O_4SN$ 291.0565, found 291.0567.

4-(4′-Methylbenzenesulfenyl)-5-*exo*-nitro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene (*epi*-2). A flame-dried round-bottomed flask was charged with 152 mg (0.52 mmol) of 2, 60 mg of 10% Pd on carbon, 304 mg of HCO_2NH_4, 1.0 mL of anhydrous CH_2Cl_2, and 3.8 mL of MeOH. After the mixture was stirred at room temperature for 12 h an additional 40 mg of HCO_2NH_4 were added and stirred for 10 h. This was then filtered through a plug of Celite with MeOH. Evaporation of the solvent and purification by column chromatography (silica gel, 30–60% Et_2O/hexane) afforded 99 mg (0.34 mmol, 65%) of ***epi*-2** as an off-white solid: mp 129–131 °C (R_f = 0.6, 75% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ 7.56 (d, J = 8 Hz, 2 H), 7.23 (d, J = 8 Hz, 2 H), 6.62 (dd, J = ≈7.85, 5.0 Hz, 1 H), 6.33 (dd, J = ≈7.85, 1.8 Hz, 1 H), 5.31 (dddd, J = 5.0, 3.7, 1.8, 1.6 Hz, 1 H), 4.74 (dd, J = ≈10.15, 4.3, 1 H), 2.62 (ddd, J = 14, 4.3, 3.7 Hz, 1 H), 2.44 (ddd, J = 14, ≈10.15, 1.6 Hz, 1 H), 2.38 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 167.1, 140.9, 137.7 (2), 134.6, 132.2, 130.5 (2), 123.7, 83.7, 71.7, 58.4, 34.1, 21.3; IR ($CDCl_3$) 1765 cm^{-1}; MS m/e (EI) 291 (M^+, 22), 201 (24), 200 (27), 123 (100), 109 (10), 91 (11), 45 (12); HRMS m/e calcd for $C_{14}H_{13}O_4SN$ 291.0565, found 291.0570.

5-*endo*-Cyano-4-(4′-methylbenzenesulfenyl)-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene (3). To a 5.0 mL hydrolysis tube was added 83.6 mg (0.38 mmol) of sulfenyl pyrone 1, 0.60 mL (9.1 mmol, 24 equiv) of acrylonitrile, and 0.60 mL of anhydrous CH_2Cl_2. This was sealed under argon and was heated at 85 °C for 21.5 h. After the solution was cooled, an additional 0.75 mL (11.4 mmol, 30 equiv) of acrylonitrile was added. The tube was resealed and warmed to 85 °C for 7.5 h. Removal of the solvent and purification by PTLC (1000 μm, Et_2O) afforded 55.2 mg (0.20 mmol, 53%) of the bicycloadduct 3 as a light yellow solid: mp 106 °C (forms a new solid that does not completely melt even at 137 °C): ^1H NMR ($CDCl_3$) δ 7.79 (dt, J = 8, 2 Hz, 2 H), 7.20–7.17 (m, 2 H), 6.73 (dd, J = 7.9, 5.1 Hz, 1 H), 6.37 (dd, J = 7.9, 1 Hz, 1 H), 5.23 (ddd, J = 5.1, 3.6, 1.6 Hz, 1 H), 2.91 (ddd, J = 9.6, 3.2, 1 Hz, 1 H), 2.66 (ddd, J = 13.6, 9.6, 3.6 Hz, 1 H), 2.36 (s, 3 H), 2.13 (ddd, J = 13.6, 3.2, 1.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.1, 140.7, 137.2 (2), 133.6, 133.2, 130.0 (2), 124.1, 118.5, 71.7, 57.2, 34.0,

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29.8, 21.3; IR ($CDCl_3$) 2254, 1770 cm^{-1}; HRMS *m/e* calcd for $C_{15}H_{13}O_2SN$ 271.0673, found 271.0667.

4-(4'-Methylbenzenesulfenyl)-3-oxo-2-oxabicyclo[2.2.2]-oct-7-ene-5-*endo*-carboxaldehyde (4). A 5.0-mL hydrolysis tube was charged with 0.648 g (2.97 mmol) of sulfenyl pyrone 1, 1.0 mL of anhydrous CH_2Cl_2, and 1.735 g (30.9 mmol, 10.4 equiv) of acrolein. This was sealed under argon and heated at 87–90 °C for 34 h. Purification by silica gel chromatography (10–20% EtOAc/hexane) gave 0.358 g (1.31 mmol, 44%) of the bicyclo-adduct 4 as a yellow oil. Addition of Et_2O/hexane (ca. 1:1) caused solidification. The solvent was removed and the solid further triturated with Et_2O to give a white solid: mp 91–92 °C; ^1H NMR ($CDCl_3$) δ 9.88 (d, J = 2 Hz, 1 H), 7.62 (d, J = 8 Hz, 2 H), 7.15 (d, J = 8 Hz, 2 H), 6.61 (dd, J = 7.9, 5.1 Hz, 1 H), 6.22 (dd, J = 7.9, 2.0 Hz, 1 H), 5.22 (ddd, J = 5.1, 4, 3, 2.0 Hz, 1 H), 2.83 (ddd, J = 9.4, 2, 2 Hz, 1 H), 2.45 (ddd, J = 14, 9.4, 4 Hz, 1 H), 2.19 (ddd, J = 14, 3, 2 Hz, 1 H); IR ($CHCl_3$) 1759, 1727 cm^{-1}. Anal. Calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; S, 11.69. Found: C, 65.78; H, 5.14; S, 11.68.

4-(4'-Methylbenzenesulfenyl)-3-oxo-2-oxabicyclo[2.2.2]-oct-7-ene-5-*exo*-methyl-5-*endo*-carboxaldehyde (5). Methacrolein (87 μL and 87 μL after 72 h, 2.0 mmol) was added to a solution of 1 (23 mg, 0.1 mmol) in benzene (0.3 mL) in a sealed tube, and the solution was heated at 90 °C for 7 days. Chromatography (silica gel, 0–20% Et_2O/hexane) afforded the endo adduct 5 as a white solid (20 mg, 70%): mp 102–103 °C; ^1H NMR ($CDCl_3$) δ 7.52 (d, J = 8 Hz, 2 H), 7.13 (d, J = 8 Hz, 2 H), 6.53 (dd, J = 7.9, 5.1 Hz, 1 H), 6.13 (dd, J = 7.9, 1.9 Hz, 1 H), 5.19 (ddd, J = 5.1, 3.8, 1.5 Hz, 1 H), 2.40 (dd, J = 13.8, 1.5 Hz, 1 H), 2.33 (s, 3 H), 2.05 (dd, J = 13.8, 3.8 Hz, 1 H), 1.40 (s, 3 H); IR ($CHCl_3$) 1758, 1726 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O_3S$: C, 66.64; H, 5.59; S, 11.12. Found: C, 66.63; H, 5.64; S, 11.03.

5-*endo*-Acetyl-4-(4'-methylbenzenesulfenyl)-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene (6). Methyl vinyl ketone (52 μL and 52 μL after 72 h, 1.24 mmol) was added to a solution of 1 (27 mg, 0.21 mmol) in benzene (1.0 mL) in a sealed tube, and the solution was heated at 90 °C for 4 days. Chromatography (silica gel, 0–10% Et_2O/hexane) afforded the endo adduct 6 as a clear oil (24.3 mg, 70%): R_f = 0.27 (2:1 Et_2O/hexane); ^1H NMR ($CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 2 H), 7.12 (d, J = 8.0 Hz, 2 H), 6.49 (dd, J = 7.95, 5.18 Hz, 1 H), 6.21 (ddd, J = 7.95, 1.17, 1.17 Hz, 1 H), 5.2 (ddd, J = 5.18, 3.7, 1.32 Hz, 1 H), 3.1 (dd, J = 10.14, 4.44 Hz, 1 H), 2.6 (ddd, J = 13.1, 9.7, 3.7 Hz, 1 H), 2.34 (s, 3 H), 2.19 (s, 3 H), 1.77 (ddd, J = 13.1, 4.48, 1.32 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 204.71, 171.07, 139.59, 136.18 (2), 132.95, 131.08, 129.85 (2), 126.27, 73.08, 46.22, 33.56, 31.17, 21.23, 18.26; IR ($CHCl_3$) 3025, 1760, 1725 cm^{-1}; HRMS *m/e* calcd for $C_{16}H_{16}O_3S$ 288.0820, found 288.0826.

Methyl 4-(4'-Methylbenzenesulfenyl)-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*endo*-carboxylate (7). Methacrylate (100 μL and 100 μL after 48 h, 2.2 mmol) was added to a solution of 1 (24 mg, 0.1 mmol) in benzene (0.3 mL) in a sealed tube, and the solution was heated at 85–90 °C for 4 days. Chromatography (silica gel, 0–20% Et_2O/hexane) afforded endo adduct 7 as a white solid (21.7 mg, 65%): mp 145 °C (R_f = 0.43, 2:1 Et_2O/hexane)); ^1H NMR ($CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2 H), 7.12 (d, J = 8.0 Hz, 2 H), 6.54 (dd, J = 7.95, 5.16 Hz, 1 H), 6.21 (ddd, J = 7.95, 1.52, 1.52 Hz, 1 H), 5.20 (ddd, J = 5.16, 4.1, 1.36 Hz, 1 H), 3.74 (s, 3 H), 2.99 (ddd, J = 9.7, 4.1, 0.82 Hz, 1 H), 2.64 (ddd, J = 13.36, 9.7, 4.1 Hz, 1 H), 2.34 (s, 3 H), 1.93 (ddd, J = 13.36, 4.17, 1.36 Hz, 1 H); IR ($CHCl_3$) 3019, 1756, 1742 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O_4S$: C, 63.16; H, 5.30; S, 10.54. Found: C, 62.90; H, 5.33; S, 10.46.

Benzyl 4-(4'-Methylbenzenesulfenyl)-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*endo*-carboxylate (8). Benzyl acrylate (280 mg, 1.6 mmol) was added to a solution of 1 (70 mg, 0.31 mmol) in CH_2Cl_2 (0.75 mL) in a sealed tube and was heated at 75–85 °C for 9 days. Chromatography (silica gel, 0–20% Et_2O/hexane) afforded endo adduct 8 as a white solid (76 mg, 0.19 mmol, 64%): mp 77.5–78.5 °C (R_f = 0.32, 2:1 Et_2O/hexane)); ^1H NMR ($CDCl_3$) δ 7.52 (d, J = 8.0 Hz, 2 H), 7.38 (m, 5 H), 7.06 (d, J = 8.0 Hz, 2 H), 6.53 (dd, J = 7.9, 5.16 Hz, 1 H), 6.02 (dd, J = 7.9, 1.15 Hz, 1 H), 5.16 (ddd, J = 5.16, 4.1, 1.25 Hz, 1 H), 3.04 (ddd, J = 9.5, 4.1, 0.96 Hz, 1 H), 2.64 (ddd, J = 13.2, 9.5, 4.0 Hz, 1 H), 2.32 (s, 3 H), 1.93 (ddd, J = 13.2, 4.1, 1.25 Hz, 1 H); IR ($CHCl_3$) 1760, 1741, 1519 cm^{-1}. Anal. Calcd for $C_{22}H_{20}O_4S$: C, 69.45; H, 5.30; S, 8.40. Found: C, 69.23; H, 5.25; S, 8.25.

Methyl 4-(4'-Methylbenzenesulfenyl)-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*exo*-methyl-5-*endo*-carboxylate (9). Methyl methacrylate (58 μL and 116 μL after 72 h, 1.65 mmol) was added to a solution of 1 (24 mg, 0.11 mmol) in benzene (1.0 mL) in a sealed tube, and the solution was heated at 85–90 °C for 9 days. Chromatography (silica gel, 0–20% Et_2O/hexane) afforded endo adduct 9 as a white solid (14.7 mg, 42%): mp 120–121 °C (R_f = 0.32, 2:1 Et_2O/hexane); ^1H NMR ($CDCl_3$) δ 7.53 (d, J = 8.1 Hz, 2 H), 7.12 (d, J = 8.1 Hz, 2 H), 6.42 (dd, J = 7.97, 5.19 Hz, 1 H), 6.14 (dd, J = 7.97, 1.87 Hz, 1 H), 5.16 (ddd, J = 5.19, 4.0, 1.4 Hz, 1 H), 3.72 (s, 3 H), 2.35 (dd, J = 13.3, 1.4 Hz, 1 H), 2.33 (s, 3 H), 2.24 (dd, J = 13.3, 4.0 Hz, 1 H), 1.53 (s, 3 H); IR ($CHCl_3$) 3025, 2954, 1754, 1731 cm^{-1}. Anal. Calcd for $C_{17}H_{18}O_4S$: C, 64.13; H, 5.70; S, 10.07. Found: C, 63.98; H, 5.73; S, 9.96.

Bicycloadduct 10. α-Methylene-γ-butyrolactone (Aldrich Chem. Co., 44 μL and 44 μL after 24 h, 1.0 mmol) was added to a solution of 1 (22 mg, 0.1 mmol) in benzene (0.7 mL) in a sealed tube, and the solution was heated at 80–90 °C for 6 days. Chromatography (silica gel, 0–10% Et_2O/hexane) afforded endo adduct 10 as a white solid (23.4 mg, 74%): mp 139–141 °C; ^1H NMR ($CDCl_3$) δ 7.54 (d, J = 8 Hz, 2 H), 7.14 (d, J = 8 Hz, 2 H), 6.51 (dd, J = 8.0, 5.2 Hz, 1 H), 6.18 (dd, J = 8.0, 1.9 Hz, 1 H), 5.24 (m, 1 H), 4.57 (m, 1 H), 4.32 (m, 1 H), 2.88 (ddd, J = 13.6, 8.6, 6.8 Hz, 1 H), 2.42–2.36 (m, 2 H), 2.34 (s, 3 H), 2.21 (ddd, J = 13.6, 8.2, 5.3 Hz, 1 H); IR ($CHCl_3$) 1762 and 1744 cm^{-1}; HRMS, *m/e* calcd for $C_{17}H_{16}O_4S$ 316.0769, found 316.0774. Anal. Calcd for $C_{17}H_{16}O_4S$: C, 64.54; H, 5.10; S, 10.14. Found: C, 64.44; H, 5.13; S, 10.05.

Hydroxy Ester 11. A flame-dried 10-mL round-bottomed flask was charged with 63.9 mg (0.20 mmol) of the cycloadduct 10, 1.0 mL of anhydrous MeOH and 1 mL of anhydrous CH_2Cl_2 under argon. After the solution was cooled to 0 °C, 8 μL of a freshly prepared NaOMe solution (30.1 mg Na/5.0 mL MeOH) was added and stirred for 30 min. The reaction was warmed to room temperature, an additional 25 μL of the NaOMe solution was added, and the reaction was stirred overnight at room temperature. The reaction was quenched with two drops of aqueous saturated NH_4Cl, diluted with methylene chloride, dried over magnesium sulfate, and filtered, the solvent removed by rotary evaporation, and the solution finally passed through a plug of silica gel with ethyl acetate to quantitatively give the hydroxy ester 11 as an off-white solid. Trituration with 50% Et_2O/hexane followed by 100% Et_2O gave 59.5 mg (0.17 mmol, 86%) of 11 as a white solid: mp 167–168 °C; ^1H NMR ($CDCl_3$) δ 7.30 (d, J = 8 Hz, 2 H), 7.10 (d, J = 8 Hz, 2 H), 5.84 (ddd, J = 10.2, 3.6, 1.2 Hz, 1 H), 5.68 (dd, J = 10.2, ~1.65 Hz, 1 H), 4.52–4.47 (m, 1 H), 4.33–4.21 (m, 1 H), 3.77 (s, 3 H), 2.99–2.85 (m, 2 H), 2.35 (s, 3 H), 2.07–1.98 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 178.0, 170.7, 140.1, 137.9 (2), 129.5, 129.4 (2), 128.5, 126.5, 64.8, 63.0, 58.0, 52.7, 45.6, 35.6, 32.1, 21.3; IR ($CHCl_3$) 3607, 1770, 1730 cm^{-1}; MS *m/e* (EI) 348 (M^+, 13), 224 (47), 193 (79), 165 (36), 124 (100), 121 (78), 91 (76), 77 (54); HRMS *m/e* calcd for $C_{18}H_{20}O_5S$ 348.1031, found 348.1027.

Siloxy Ester 12. A flame-dried 25-mL round-bottomed flask was charged with 48.1 mg (0.14 mmol) of alcohol 11 and 5.0 mL of anhydrous CH_2Cl_2 under argon. To this was added 25 μL (0.21 mmol, 1.5 equiv) of 2,6-lutidine followed by 50 μL (0.22 mmol, 1.6 equiv) of *tert*-butyldimethylsilyl triflate (TBDMS-OTf). This mixture was stirred at room temperature for 5 h and then quenched with dilute aqueous HCl. The mixture was diluted with CH_2Cl_2, and the organic layer was separated. After back-extraction, the organic portions were combined, washed with brine, dried over $MgSO_4$, and filtered and the solvent removed by rotary evaporation. Purification by flash silica gel chromatography (0–20% EtOAc/hexane) afforded 52.3 mg (0.11 mmol, 82%) of silyl ether 12 as an off-white solid: mp 115–115.5 °C; ^1H NMR ($CDCl_3$) δ 7.30 (d, J = 8 Hz, 2 H), 7.11 (d, J = 8 Hz, 2 H), 5.72 (ddd, J = 10.2, 3.8, 1.4 Hz, 1 H), 5.62 (dd, J = 10.2, 1.5 Hz, 1 H), 4.39–4.36 (m, 1 H), 4.27–4.22 (m, 2 H), 3.77 (s, 3 H), 3.04–2.94 (m, 2 H), 2.35 (s, 3 H), 1.97–1.91 (m, 2 H), 0.86 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H); IR ($CDCl_3$) 1770, 1729 cm^{-1}; HRMS *m/e* (M^+ – *t*-Bu) calcd for $C_{24}H_{34}O_5SSi$ 405.1192, Found 405.1186.

α,β-Unsaturated Ester 13. A flame-dried 10-mL round-bottomed flask was charged with 28.3 mg (0.061 mmol) of sulfide 12, 21 μL (0.078 mmol, 1.3 equiv) of tributyltin hydride, 3.0 mg (0.018 mmol, 0.3 equiv) of AIBN, and 1.0 mL of anhydrous

benzene under argon. The flask was then immersed in a preheated oil bath and refluxed for 50 min. After the solution was cooled, 20 μL of DBU was added and the reaction mixture stirred for 15 min. The solvent was then removed and the mixture purified by flash silica gel chromatography (10–50% EtOAc/hexane) to afford 17.5 mg (0.051 mmol, 84%) of α,β-unsaturated ester **13** as a colorless oil: R_f = 0.6 (50% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.15 (t, J = 4.1 Hz, 1 H), 4.52–4.47 (m, 1 H), 4.35–4.28 (m, 2 H), 3.74 (s, 3 H), 2.58–2.48 (m, 3 H), 2.29 (ddd, J = 19.3, 4.3, 1.1 Hz, 1 H), 2.04–1.91 (m, 2 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR ($CDCl_3$) 180.6, 165.8, 141.0, 130.3, 65.9, 63.6, 51.9, 44.0, 39.3, 34.7, 34.2, 25.8, 18.0, -4.8; IR ($CHCl_3$) 1759, 1709 cm^{-1}; HRMS m/e (M^+ - t-Bu) calcd for $C_{17}H_{28}O_5Si$ 283.1002, found 283.1005.

3-(*tert*-Butyldimethylsiloxy)-2-pyrone. A 25-mL round-bottomed flask was charged with 125.4 mg (1.12 mmol) of 3-hydroxy-2-pyrone (Aldrich Chemical Co., 2,3-dihydroxypyridine) and dissolved in 3 mL of CH_2Cl_2 under argon. To this was added 0.16 mL (1.3 mmol, 1.2 equiv) of 2,6-lutidine followed by 0.31 mL (1.3 mmol, 1.2 equiv) of TBDMS-OTf. This was stirred for 1 h, and then the solvent was removed. Purification by silica gel chromatography (10% EtOAc/hexane) gave 170.2 mg (0.75 mmol, 67%) of the silyl ether as a volatile light yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.17 (dd, J = 5.1, 1.8 Hz, 1 H), 6.61 (dd, J = 7.0, 1.8 Hz, 1 H), 6.10 (dd, J = 7.0, 5.1 Hz, 1 H), 0.97 (s, 9 H), 0.24 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 160.9, 144.0, 142.4, 122.2, 106.0, 25.5, 18.4, -4.6; IR ($CHCl_3$) 1759, 1709 cm^{-1}; HRMS m/e (M^+ - t-Bu) calcd for $C_{24}H_{34}O_5SSi$ 405.1192, found 405.1186.

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Registry No. **1**, 98061-54-2; *endo*-**2**, 141510-29-4; *exo*-**2**, 141553-87-9; *endo*-**3**, 141510-30-7; *exo*-**3**, 141553-88-0; *endo*-**4**, 141510-31-8; *exo*-**4**, 141553-89-1; *endo*-**5**, 141510-32-9; *exo*-**5**, 141553-90-4; *endo*-**6**, 141510-33-0; *exo*-**6**, 141553-91-5; *endo*-**7**, 141510-34-1; *exo*-**7**, 141553-92-6; *endo*-**8**, 141510-35-2; *exo*-**8**, 141553-93-7; *endo*-**9**, 141510-36-3; *exo*-**9**, 141553-94-8; *endo*-**10**, 141526-86-5; *exo*-**10**, 141610-01-7; **11**, 141510-37-4; **12**, 141510-38-5; **13**, 141510-39-6; Ph_2SO_2, 127-63-9; $PhCO_2Me$, 93-58-3; PhBr, 108-86-1; Ph_2S, 139-66-2; $PhOSi(Me)_3$, 1529-17-5; PhOH, 108-95-2; dihydro-3-methylene-2(3*H*)-furanone, 547-65-9; 3-(*tert*-butyldimethylsiloxy)-2-pyrone, 141510-40-9; 3-hydroxy-2-pyrone, 496-64-0; nitroethylene, 3638-64-0; acrylonitrile, 107-13-1; acrolein, 107-02-8; methacrolein, 78-85-3; methyl vinyl ketone, 78-94-4; methyl acrylate, 96-33-3; benzyl acrylate, 2495-35-4; methyl methacrylate, 80-62-6; 3-(*p*-toluenesulfonyl)-2-pyrone, 99268-87-8; 3-carbomethoxy-2-pyrone, 25991-27-9; 3-bromo-2-pyrone, 19978-32-6; 2-pyrone, 504-31-4; benzene, 71-43-2.

Supplementary Material Available: Characterization of new compounds by NMR (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Diels–Alder Cycloadditions Using Nucleophilic 2-Pyridones. Regiocontrolled and Stereocontrolled Synthesis of Unsaturated, Bridged, Bicyclic Lactams

Gary H. Posner,* Victoria Vinader, and Kamyar Afarinkia

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

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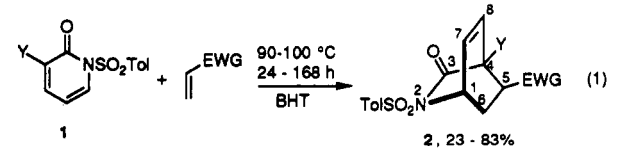
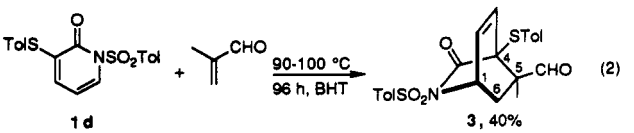
Captodative 3-oxy- and 3-(tolylthio)-1-tosyl-2-pyridones **1a–1d** are shown to be reactive as nucleophilic dienes undergoing 2 + 4-cycloadditions with various electrophilic alkenes under sufficiently *mild thermal conditions* (90–100 °C) that the initial bicylic lactam adducts can be isolated on gram scale in fair to very good yields (23–83%) *without loss of an isocyanate* from the heteroatom bridge. These bicyclic adducts are formed with complete regiocontrol and stereocontrol. For pyridone sulfide **1d**, these Diels–Alder cycloadditions are the first examples of a captodative unsaturated sulfide acting as an enophile. NMR data (^{13}C) are presented correlating the electron density in the pyridone diene systems with their Diels–Alder reactivity, and some transformations of the bicyclic lactam adducts are shown to illustrate the value and versatility of these richly functionalized synthetic intermediates.

Introduction

A few years ago this laboratory reported the first examples of efficient 2 + 4-cycloadditions of electron-poor 1,3-disulfonyl-2-pyridones with electron-rich dienophiles such as vinylic ethers.[1] To complement such *inverse*-electron-demand Diels–Alder reactions, we now report *normal*-electron-demand 2 + 4-cycloadditions of captodative 1,3-disubstituted 2-pyridones under thermal (i.e., not high-pressure) conditions with electron-poor dienophiles such as CH_2=C(R)EWG, in which the R group is hydrogen or methyl and the electron-withdrawing-group (EWG) is nitro, aldehyde, ester, or ketone (eqs 1 and 2). These successful cycloadditions, stopping at the initial bicyclic lactam stage without extrusion of an isocyanate from the heteroatom bridge,[2] are *among the few examples*



Y	EWG
a, MeO	g, NO_2
b, $PhCH_2O$	h, CHO
c, t-$BuMe_2SiO$	i, CO_2Me
d, TolS	j, COMe



in which normally highly aromatic 2-pyridones (more aromatic than 2-pyrones)[3] *have entered as enophiles into*

(1) Posner, G. H.; Switzer, C. *J. Org. Chem.* **1987**, *52*, 1644 and references therein to 2 + 4-cycloadditions of 2-pyridones.

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