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Computational and Experimental Investigation of the Diels−Alder Cycloadditions of 4-Chloro-2(*H*)-pyran-2-one†

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4-Chloro-2(*H*)-pyran-2-one undergoes thermal Diels−Alder cycloaddition with electron-deficient dienophiles to afford, without any significant selectivity, 6-endo- and 5-endo-substituted bicyclic lactone cycloadducts. In contrast to 3- and 5-bromo-2(*H*)-pyran-2-one, 4-chloro-2(*H*)-pyran-2-one does not undergo thermal cycloadditions with electron-rich dienophiles. The regio- and stereochemical preferences of the cycloadditions of 4-chloro-2(*H*)-pyran-2-one and other related 2(*H*)-pyran-2-ones are investigated computationally. Calculations were carried out on the transition states leading to the four possible regio- and stereoisomeric cycloadducts using density functional theory (B3LYP/6-31G*). These studies allow prediction of the regio- and stereoselectivity in these reactions which are in line with experimental observations.

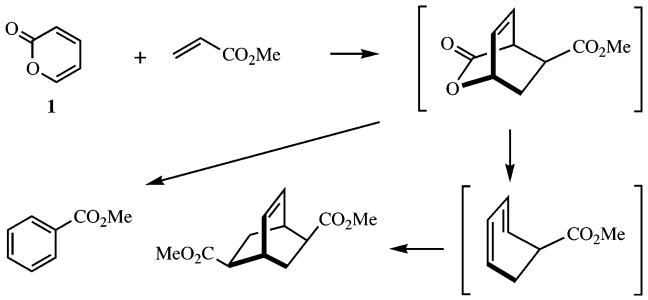
Introduction

2(*H*)-Pyran-2-one **1** undergoes Diels−Alder cycloaddition with dienophiles to afford, in the first instance, bridged bicyclic lactones which usually cannot be isolated but readily undergo loss of CO_2 to afford a cyclohexadiene intermediate. This is usually followed by further cycloaddition to afford barrelenes or, more commonly, aromatization to afford benzenes (Scheme 1).[1] Substituted 2(*H*)-pyran-2-ones also undergo this reaction, and indeed, this has proven to be a useful route for the synthesis of benzenes.[1,2]

However, it has been recognized for some time that the initially produced bridged bicyclic lactone cycloadducts are also valuable starting materials for synthesis. They are functionally rich and, as Diels−Alder products, are expected to be obtained with regio- and stereoselectivity. Therefore, various strategies have been devised for arresting the second step of this process so that bridged lactone cycloadducts can be isolated and further manipulated for the preparation of complex molecules. These include the use of Lewis acids[3] to selectively lower the activation energy for cycloaddition or application of medium high pressure (14−20 kbar) to disfavor the loss of CO_2.[4]

By far, the most synthetically useful strategy for obtaining the bridged bicyclic lactone cycloadduct is matching the electronic demand of the dienophile with that of the pyrone, by means of ring substitution. This is not only an excellent method for arresting the cycloreversion (loss of CO_2) in this reaction but also has the advantage of adding to the diversity of substituents on the cycloadducts.[1,2]

SCHEME 1



For example, Posner has demonstrated that 3-phenylsulfenyl-2(*H*)-pyran-2-one **2**[5,6] and 3-phenylsulfonyl-2(*H*)-pyran-2-one **3** react with electron-deficient and electron-rich dienophiles, respectively, to afford isolable bridged bicyclic lactone cycloadducts (Scheme 2).[7−10] The synthetic value of these cycloadducts have been shown

† Dedicated to Prof. Gary H. Posner on the occasion of his 60th birthday.

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(7) Posner, G. H.; Wettlaufer, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 7373.
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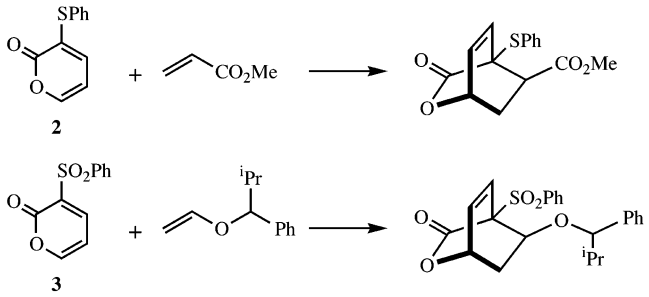
SCHEME 2



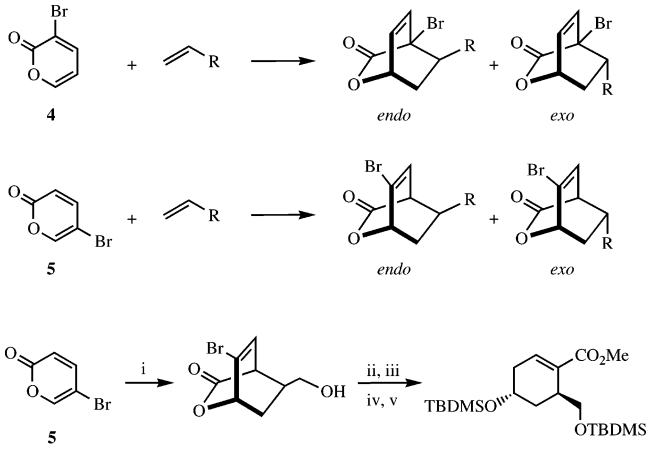
through a number of syntheses of natural products and medicinally important targets by Posner[7−10] and others.[11−13]

The study of the role and scope of ring substituents on the Diels−Alder cycloaddition of 2(*H*)-pyran-2-ones has therefore become an important prerequisite for the development of the methodologies that use this cycloaddition for the synthesis of complex molecules.

Qualitative prediction of the electron demand of most substituted 2(*H*)-pyran-2-one, and hence the regio- and stereochemical outcome of the cycloadditions, is sometimes straightforward. In general, the role of a substituent on influencing the electron demand of 2(*H*)-pyran-2-ones directly corresponds to the role it plays on activation and deactivation of the benzene ring toward aromatic electrophilic substitution. Activating groups, such as sulfide, encourage the pyrone to undergo normal electron-demand cycloadditions. In contrast, deactivating groups, such as sulfone, encourage the pyrone to undergo inverse-electron-demand cycloadditions. Attempts at quantification of this effect have also been carried out. Posner has used NMR to show a correlation between the ^{13}C chemical shift of the C-6 of the 3-substituted 2(*H*)-pyran-2-ones with their electronic demand,[4] although this can only be used when comparing 2-pyrones with similar patterns of substitution. Nevertheless, prediction of the electronic demand of 2(*H*)-pyran-2-ones is haphazard. In particular, one cannot in a straightforward manner predict the reactivity of 2-pyrones substituted with groups which are weakly inductive or indeed halo-substituted pyrones such as 3- and 5-bromo-2(*H*)-pyran-2-ones. The latter is a significant problem with this methodology since cycloadditions of 3- and 5-bromo-2(*H*)-pyran-2-ones are some of the most interesting, unique, and useful features of the pyrone cycloaddition methodology.

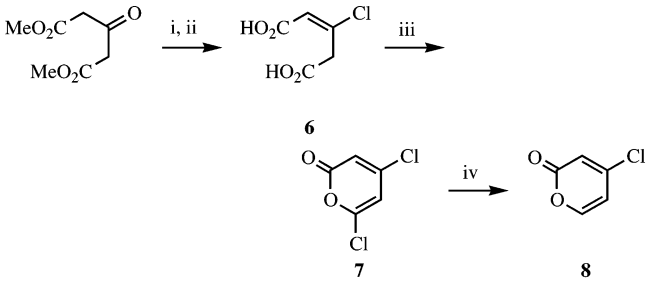
3-Bromo-2(*H*)-pyran-2-one **4** and 5-bromo-2(*H*)-pyran-2-one **5** (Scheme 3) are ambident dienes reacting with both electron-rich (when R is an electron-donating group), electron-poor (when R is an electron-withdrawing group), and electron-neutral (when R is an alkyl or aryl group) dienophiles with good regio- and stereoselectivity.[14−17] More recently, it has been shown that 3,5-dibromo-2(*H*)-pyran-2-one is also an ambident diene.[18,19] Since 2(*H*)-

SCHEME 3[a]



[a] Key: (i) acrolein, 25 °C, 4 day, then $NaBH_4$, MeOH; (ii) camphorsulfonic acid, MeOH, 25 °C, 15 h; (iii) TBDMSOTf, Et_3N; (iv) DBU, ether; (v) Bu_3SnH, AIBN, AIBN, benzene, reflux, 2 h (45% overall).

SCHEME 4[a]



[a] Key: (i) PCl_5, 50 °C, 30 min; (ii) 20% hydrochloric acid, reflux, 2.5 h (62%); (iii) PCl_5, 100 °C, 15 min (68%); (iv) Zn/AcOH (51%).

pyran-2-one itself is prone to polymerization, difficult to handle and not selective in its cycloaddition, these easily prepared[15,17] bromopyrones can be considered synthetic equivalents of 2(*H*)-pyran-2-one. After the cycloaddition of a bromopyrone, the bromine atom can be replaced by hydrogen affording the same products as those which would have been obtained from the cycloaddition of 2(*H*)-pyran-2-one itself (Scheme 3). The regio- and stereoselectivity of the cycloadditions and the ambident nature of the bromopyrones are valuable bonuses since the unsubstituted 2(*H*)-pyran-2-one only reacts with electron-deficient dienophiles and the cycloadditions are not selective. Thus, by using one of these bromopyrones as a synthetic equivalent of 2(*H*)-pyran-2-one, a wider range of bridged bicyclic lactone cycloadducts can be obtained. The bromine atom in the cycloadducts can be replaced by other groups (e.g., by Stille coupling),[11] hence expanding the diversity of molecules obtained by this methodology even further.

Although their unique ambident nature makes these two bromopyrone dienes synthetically very powerful, little is known about the reasons for this unusual nature and in particular the role of other halogens in the

(11) Jung, M. E.; Head, D. B. *Bull. Soc. Chim. Fr.* **1990**, *127*, 830.
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(13) Afarinkia, K.; Mahmood, F. *Tetrahedron* **1999**, *55*, 3129.
(14) Posner, G. H.; Afarinkia, K.; Dai, H. *Org. Synth.* **1995**, *73*, 231.
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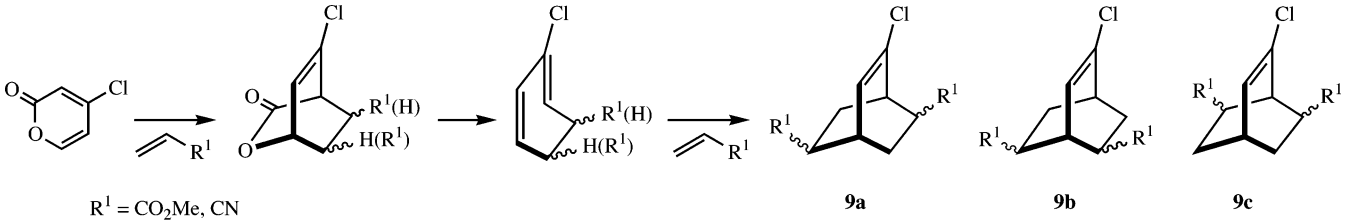
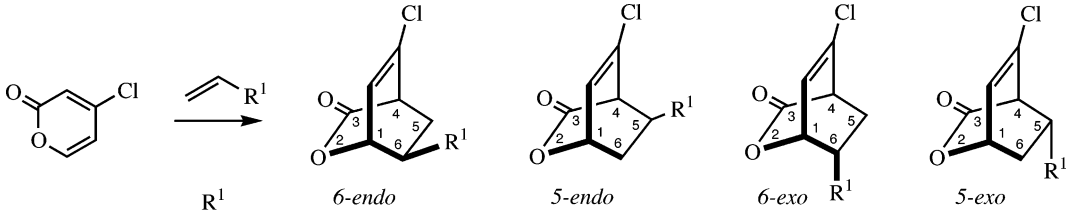
SCHEME 5



SCHEME 6



R^1	6-endo	5-endo	6-exo	5-exo
CO_2Me	**10a**	**10b**	**10c**	**10d**
CN	**11a**	**11b**	**11c**	**11d**

activation of the pyrone ring. In particular, it is not known if the role of the bromo substituent can be mirrored by other halogen substituents or whether the position of the halogen substituent is important on the reactivity of the pyrone. The resolution of both issues would not only lead to a better understanding of the factors that influence the electronic demand of pyrones in general but also can further expand the synthetic utility of the pyrone cycloaddition methodology. This is particularly pertinent since in recent years some attempts at the total synthesis of natural products using the cycloadditions of 4-substituted 2-pyrones have been unsuccessful,[21] highlighting the shortcomings of a methodology which does not have a universal model for predicting the outcome of reactions.

As part of our ongoing interest in the cycloadditions chemistry of 2(*H*)-pyran-2-ones, we wish to report our computational and experimental investigation of the Diels−Alder reactions of 4-chloro-2(*H*)-pyran-2-one, **8**. We will demonstrate that the results of density functional theory (DFT) calculations agree with the experimental observations of the regio and stereochemical preferences of the cycloadditions of 4-chloro-2(*H*)-pyran-2-one and 2(*H*)-pyran-2-one. DFT (B3LYP/6-31G*) calculations therefore appear to be a reliable tool for predicting the regio and stereochemical preferences of these pyrone cycloadditions.

Experimental Results and Discussion

4-Chloro-2(*H*)-pyran-2-one **8** was prepared by a previously published procedure[21−23] and was obtained as a light yellow solid (Scheme 4). We initially carried out the reactions of 4-chloro-2(*H*)-pyran-2-one and methyl acrylate at 100 °C. At this temperature, both 3-bromo- and 5-bromo-2(*H*)-pyran-2-ones undergo efficient regio- and steroselective cycloadditions with a wide range of activated and unactivated alkenes to afford the expected cylcoadducts.[15−17] However, the expected bridged lactone cycloadducts were not obtained under these conditions. Instead, the reaction resulted in a complex mixture from which individual pure compounds could not be isolated. However, after partial purification by chromatography, we were able to confirm the presence of at least eight regio and stereoisomeric bicyclo[2.2.2]octenes (barrelenes), **9**, in the reaction mixture in 85% combined yield (Scheme 5). The presence of these barrelenes was not unexpected since similar "double" cycloadducts had been previously observed in the cycloadditions of substituted and unsubstituted 2(*H*)-pyran-2-one.[24] They are presumed to have been formed by the loss of the bridging CO_2 from the initial cycloadduct and the subsequent cycloaddition of the resulting dihydrobenzene with excess dienophile (Scheme 5).

However, when the cycloaddition of 4-chloro-2(*H*)-pyran-2-one with methyl acrylate and acrylonitrile was carried out at 70 °C, analysis of the crude reaction mixture revealed that it contained cycloadducts **10a**−**d** and **11a**−**d** with only small traces of the "double" cycloadducts **9a**−**c**. Hence, it was possible to isolate the cycloadducts **10a**−**d** and **11a**−**d** in a combined isolated yield of 70% and 41% respectively (Scheme 6, Table 1). The regio- and stereochemical assignment of the cycloadducts was based on earlier empirical rules set out by Posner[1] and us[16,17] using the size of the proton coupling between H-4/H-5 and H-1/H-6 (Scheme 7).

The major product of both cycloadditions, **10a** and **11a**, are the 6-endo cycloadducts followed by the corresponding 5-endo cyloadducts **10b** and **11b**. This contrasts with the regio- and stereoselective formation of the 5-endo cycloadduct in the corresponding cycloaddition of 3-bromo-2(*H*)-pyran-2-one[15] and 5-bromo-2(*H*)-pyran-2-one.[16,17,25]

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(21) Kvita, V.; Sauter, H. *Helv. Chim. Acta* **1990**, *73*, 883−889.
(22) Bryson, T. A.; Dolak, T. M. *Org. Synth.* **1977**, *57*, 62.
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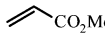
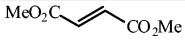
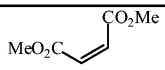
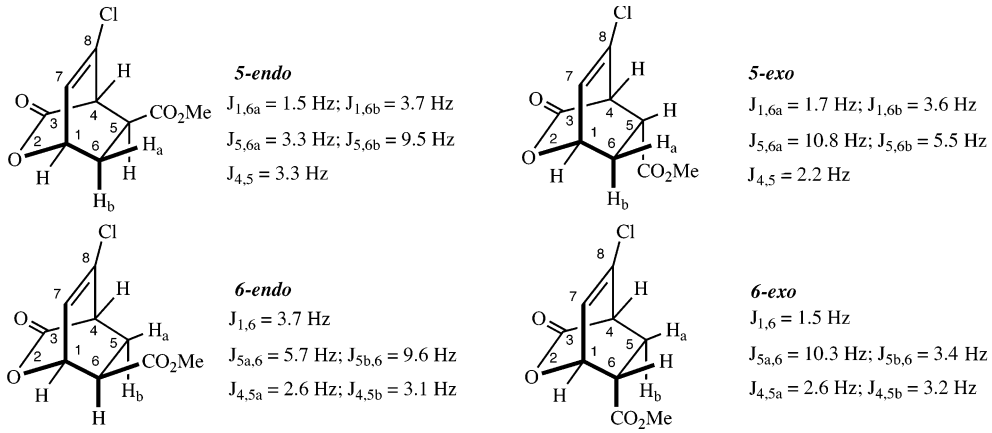
(24) Diels, O.; Alder, K. *Justus Liebigs Ann. Chem.* **1931**, *490*, 257. Shimo, T.; Kataoka, K.; Maeda, A.; Somekawa, K. *J. Heterocycl. Chem.* **1992**, *29*, 811. De Lucchi, O.; Modena, G. *Tetrahedron* **1984**, *40*, 2585. Zimmermann, H. E.; Grunewald, G. L.; Paufler, R. M.; Sherwin, M. A. *J. Am. Chem. Soc.* **1969**, *91*, 2330.
(25) However, it should be noted that cycloaddition of 5-bromo-2(*H*)-pyran-2-one with methylvinyl ketone affords a 9:1 mixture of 5-endo and 6-endo cycloadducts. See ref 9.

TABLE 1.

Dienophile	Conditions	Combined Yield (%)	Cycloadduct (ratio)			
			6-endo	5-endo	6-exo	5-exo
	80 °C, 5 days	26[a]	**10a** (57)	**10b** (29)	**10c** (14)	**10d** (0)
	70 °C, 4 days	59	**10a** (47)	**10b** (41)	**10c** (9)	**10d** (2)
	70 °C, 14 days	70	**10a** (47)	**10b** (41)	**10c** (9)	**10d** (2)
	70 °C, 14 days	76[b]	**10a** (58)	**10b** (29)	**10c** (7)	**10d** (6)
	70 °C, 26 days	41	**11a** (58)	**11b** (25)	**11c** (17)	**11d** (0)
	70 °C, 14 days	18	**12a** (25)	**12b** (75)		
	70 °C, 14 days	20	**13a** (55)	**13b** (45)		
	70 °C, 15 days	24	**14**			

[a] Significant quantities of the "double" cycloadducts were also obtained. [b] Performed on 2.6 g of 4-chloro-2(*H*)-pyran-2-one.

SCHEME 7



It is difficult to gauge the tendency of 2(*H*)-pyran-2-one to afford 6-endo cycloadducts under thermal conditions, since as was discussed above they tend to undergo "double-cycloadditions" which results in the loss of regiochemical information. However, high-pressure promoted Diels–Alder reactions of 2(*H*)-pyran-2-one with acrolyl chloride[26] and methyl acrylate[4] is reported to afford a 1:1 and 2.5:1 ratio of the two major 5-endo and the 6-endo cycloadducts, respectively. These observation further demonstrate that the pattern of the reactivity of 4-chloro-2(*H*)-pyran-2-one is significantly different from those of bromopyrones but similar to that of unsubstituted 2(*H*)-pyran-2-one.

Cycloaddition reactions with a range of other electron-deficient dienophiles were similarly inefficient. For example, methyl methacrylate afforded a combined isolated yield of 18% of the 5-endo and 6-endo cycloadducts **12a** and **12b** in a 25:75 ratio. However, there was no significant reaction with the more sterically demanding methyl crotonate. While dimethyl fumarate afforded a near equal ratio of the 5-exo-6-endo and 5-endo-6-exo cycloadducts **13a** and **13b** in a combined yield of 24%, dimethyl maleate afforded only the 5-endo-6-endo isomer **14** in 20% yield. (Table 1).

One of the key differences between 2(*H*)-pyran-2-one and its 3- and 5-bromo derivatives is that the former only undergoes cycloadditions to electron-rich alkenes under Lewis acid catalyzed conditions.[3] Therefore, a key feature of the role of the 4-chloro substituent is whether it undergoes cycloaddition with electron-rich dienophiles. However, we obtained no reaction between 4-chloro-2(*H*)-pyran-2-one and electron neutral, e.g., styrene and hexene, and highly electron-rich dienophiles, e.g., butyl vinyl ether. Indeed, even on prolonged heating and at higher temperature no significant cycloaddition was observed from analysis of the crude reaction mixture by NMR. However, trace quantities of cycloadducts were observed in the reaction between 4-chloro-2(*H*)-pyran-2-one and poorly electron-rich dienophiles, e.g., vinylene carbonate, vinyl acetate, and *N*-vinylphthalimide.

Each of these experimental observations confirm that a 4-chloro substitution on the pyrone nucleous does not

(26) Pfaff, E.; Plieninger, H. *Chem. Ber.* **1982**, *115*, 1967

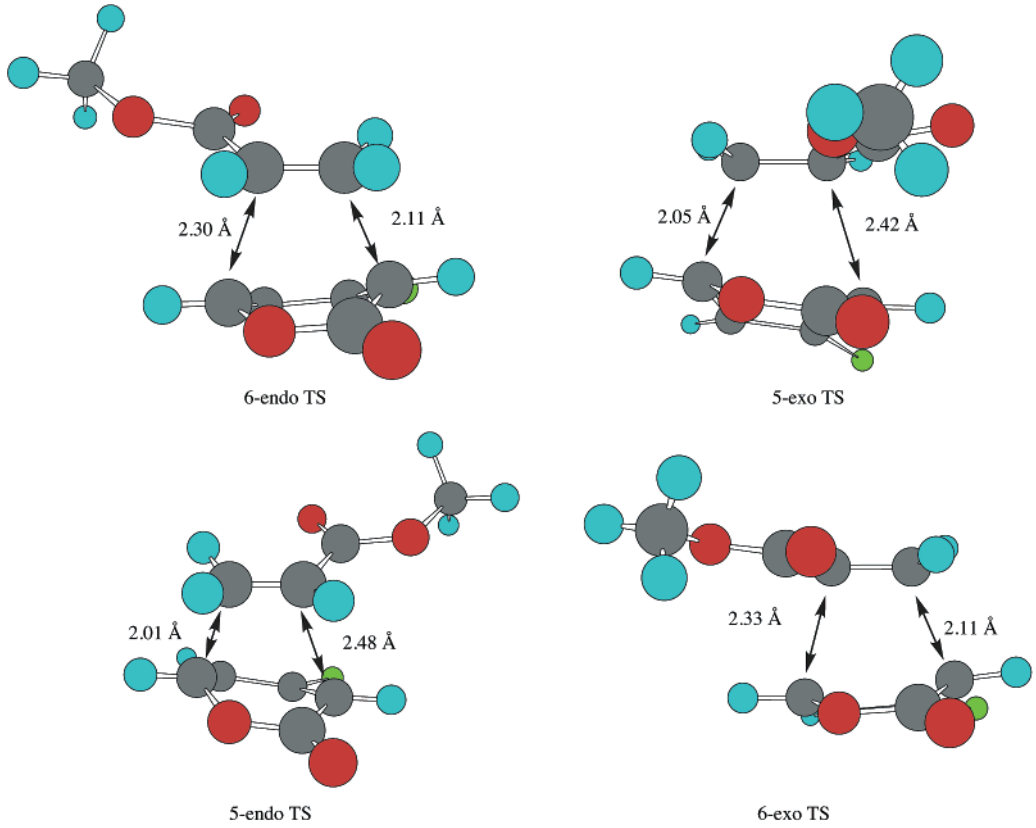


FIGURE 1. Computed transition structures for transition states leading to the cycloadducts of 4-chloro-2(*H*)-pyran-2-one **8** with methyl acrylate.

significantly alter the ring's electronic nature for Diels–Alder cycloadditions. This contrasts with Posner's observation that both 3- and 5-bromo substitution on the pyrone nucleus significantly influence its electronic nature. Therefore, we decide to examine the differences of these pyrones, and a number of related pyrones for which experimental data is available, by theory.

Computational Results and Discussion

To understand and predict the regio- and stereoselectivity of the pyrone cycloadditions, we carried out a range of calculations on the four transition states (TS) leading to the four possible stereoisomers in the cycloadditions of 4-chloro-2(*H*)-pyran-2-one **8** with acrylonitrile and methyl acrylate. These are namely the 6-endo, the 5-endo, the 6-exo, and the 5-exo cycloadducts. Calculations were performed using Gaussian.[27] All transition structures were initially optimized with AM1[28,29] and then reoptimized using B3LYP/6-31G*.[30] This DFT method (model chemistry) has been previously shown by Houk to be a reliable method for predicting the regio- and stereoselectivity of the cycloaddition of Danishefski's diene with acrylonitrile.[31]

The computed transition structures for all four possible transition states leading to the 5-endo, 5-exo, 6-endo, and 6-exo cycloadducts of 4-chloro-2(*H*)-pyran-2-one **8** with methyl acrylate (i.e., transition states leading to compounds **10a**–**d**) and acrylonitrile (i.e., transition states leading to compounds **11a**–**d**) are shown in Figures 1 and 2, respectively. The calculated relative energies of transition states leading to the four possible cycloadducts from the reaction of 4-chloro-2(*H*)-pyran-2-one **8** with acrylonitrile and methyl acrylate are shown in Table 2 along with the yields of each cycloadduct obtained experimentally. As can be seen, it is possible to correlate the calculated energy of the four transition states to the final yield of the four cycloadducts. Calculated values of the four transition states confirm that the one with the lowest energy, and hence the one likely to be the most abundant, is the 6-endo isomer in both cases. The 5-exo isomer in both cases has the highest relative energy and is expected to be the most disfavored cycloadduct and indeed it is observed only in trace amounts. The 5-endo transition state for the cycloaddition of 4-chloro-2(*H*)-

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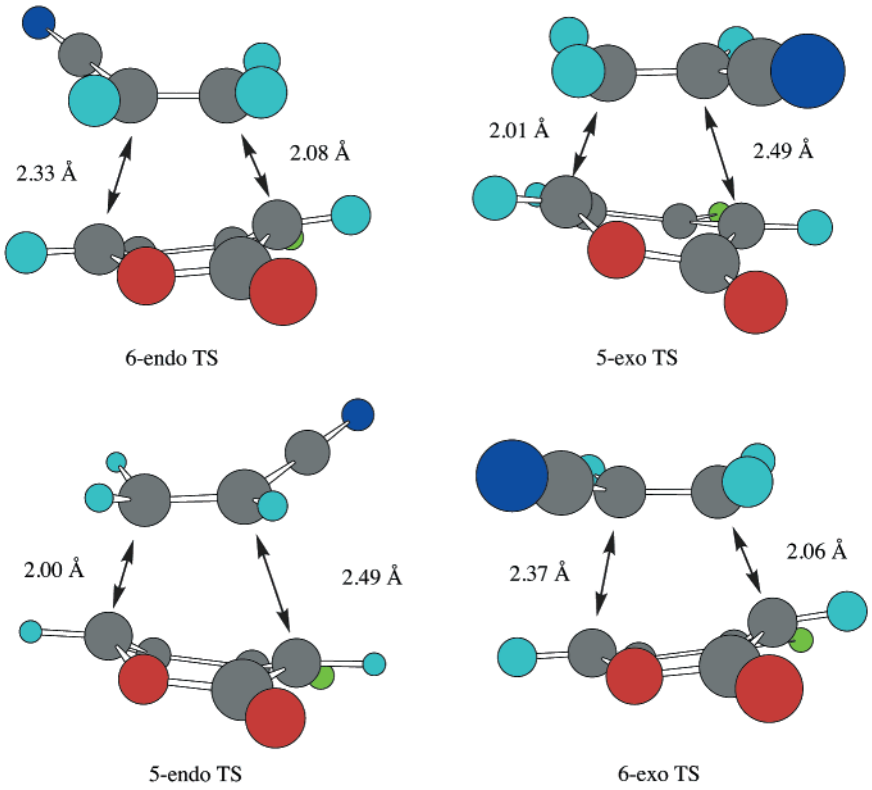

FIGURE 2. Computed transition structures for transition states leading to the cycloadducts of 4-chloro-2(*H*)-pyran-2-one **8** with acrylonitrile.

SCHEME 8

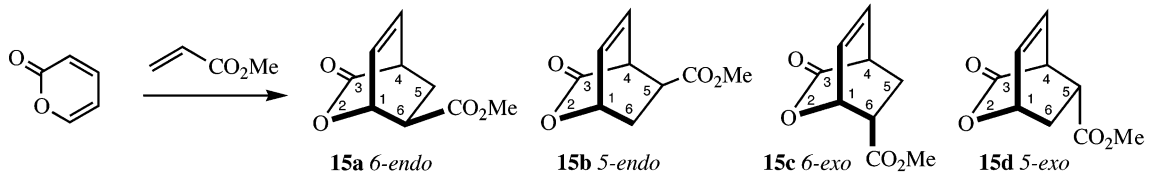

TABLE 2.

cycloadduct	configuration	ΔH_f[a] (kcal/mol)	yield (%)
10a	6-endo	0.000	48 (58)[b]
10b	5-endo	0.537	43 (29)
10c	6-exo	1.947	9 (7)
10d	5-exo	2.536	0 (6)
11a	6-endo	0.000	58
11b	5-endo	1.744	25
11c	6-exo	1.747	17
11d	5-exo	3.085	0

[a] The difference in the calculated barrier heights, with 6-endo taken as the energy zero. [b] Yields from large-scale preparation in parentheses.

pyran-2-one with methyl acrylate is only slightly higher in energy than that of the 6-endo transition state which reflects near equal proportion of the two cycloadducts.

Since the method used for the calculation of the energies of the transition states proved reliable for predicting both the preferred regio and stereoisomer of the cycloadditions of 4-chloro-2(*H*)-pyran-2-one, we decided to test the usefulness of this method for predicting the outcome of the cycloadditions of other 2(*H*)-pyran-2-ones. Luckily, there are already a large number of experimentally derived yields of the cycloadducts in the literature by us, Posner and others. Therefore, it is possible to gauge the reliability of the theoretical method for the prediction of the selectivities with the actual experimentally derived figures.

We next considered the cycloaddition of 2(*H*)-pyran-2-one with methyl acrylate (Scheme 8). As was discussed already, this reaction does not lead to expected bicyclic lactone cycloadducts under thermal conditions. However, Marko has demonstrated that under medium high-pressure conditions, it is possible to obtain bicyclic lactone cycloadducts.[4] The computed transition structures for all four possible transition states leading to the 5-endo, 5-exo, 6-endo, and 6-exo cycloadducts of 2(*H*)-pyran-2-one **8** with methyl acrylate (i.e., transition states leading to compounds **15a**−**d**) are shown in Figure 3. The calculated relative energies of transition states leading to the four possible cycloadducts from the reaction of 2(*H*)-pyran-2-one **1** with methyl acrylate are shown in Table 3 along with the yields of each cycloadducts obtained experimentally. Although the energetics of the pressure-induced and thermally promoted cycloadditions may be different, it is nevertheless possible to correctly predict the major isomer of the cycloaddition and the prediction is closely mirrored in the observed yields of

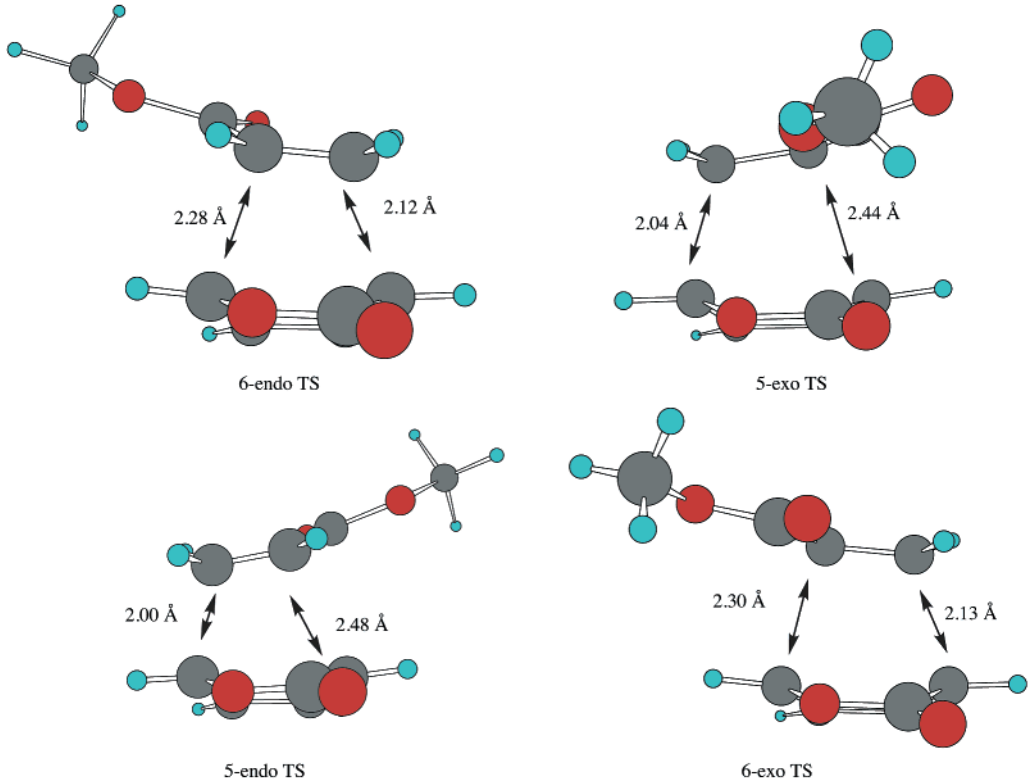

FIGURE 3.

TABLE 3.

cycloadduct	configuration	ΔH_f[a] (kcal/mol)	yield[4] (%)
15a	6-endo	0.171	25
15b	5-endo	0.000	60
15c	6-exo	2.992	5
15d	5-exo	2.737	10

[a] The difference in the calculated barrier heights, with 6-endo taken as the energy zero.

the cycloadducts. Interestingly, the major cycloadduct in this example is predicted and found experimentally to be the 5-endo one which contrasts with the observation that the major product in the cycloaddition of 4-chloro-2(*H*)-pyran-2-one is predicted and found experimentally to be the 6-endo one.

In conclusion, we have demonstrated that 4-chloro-2(*H*)-pyran-2-one undergoes thermal Diels−Alder cycloaddition with electron-deficient dienophiles to afford, without any significant selectivity, 6-endo- and 5-endo-substituted bicyclic lactone cycloadducts. However, 4-chloro-2(*H*)-pyran-2-one, in contrast to 3- and 5-bromo-2(*H*)-pyran-2-one, does not undergo significant cycloaddition to electron rich or electron neutral dienophiles. Furthermore, the regio and stereo preferences of the cycloadditions of 4-chloro-2(*H*)-pyran-2-one can be predicted computationally using DFT (B3LYP/6-31G*).

Experimental Section

3-Chloropent-2-enedioic Acid 6. A three-necked round-bottomed flask, fitted with a magnetic stirrer bar, a condenser connected to a gas bubbler, a gas-inlet adapter attached to an argon source, and an addition funnel, was charged with dimethyl acetone-1,3-dicarboxylate (25.02 g, 0.144 mol). A flow of argon was passed through the solution during portionwise addition of phosphorus pentachloride (30.80 g, 0.148 mol, 1.03 equiv) and continued until the end of the reaction. After addition, the reaction mixture was heated at 50 °C for 30 min, cooled by placing the reaction flask in ice, and then poured on ice (150 g). The reaction vessel was rinsed with water−dichloromethane (1:1, 150 mL), and the mixture was added to the ice. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were stripped of solvent by rotary evaporation to give a red oil, which was dried on high vacuum and used in the next reaction without further purification. Aqueous hydrochloric acid (20%, 150 mL) was added to this oil, and the mixture was refluxed for 2.5 h. The solution was evaporated to dryness on rotary evaporator. The solid was dissolved in diethyl ether (150 mL), and the resulting solution was dried over calcium chloride, filtered, and stripped of solvent by evaporation. The resulting solid was dried on high vacuum and kept over phosphorus pentaoxide in vacuo, 14.72 g (62%): mp 112−115 °C (lit.[32] mp 110−115 °C); ^{1}H NMR (acetone-d_6) δ 7.94 (br s, 2H, 2 × CO_2H), 6.39 and 6.30 (s, 1H, H-2), 4.14 (s, 2H, CH_2); IR 3425, 1702, 1640, 1396, 1291, 1207, 1059, 868 cm^{-1}.

4,6-Dichloropyrone 7. A round-bottomed flask was placed in an ice bath and was charged with phosphorus pentachloride (29.66 g, 0.142 mol). Acid **6** (11.72 g, 0.071 mol) was added in one portion, and the mixture was maintained at 0 °C while swirling until solid mixture liquefied. The resulting red solution was stirred at room temperature for 1 h, heated at 100 °C for 15 min, and then cooled to room temperature. The residue was taken up with dichloromethane (250 mL) and extracted with water (2 × 125 mL). The combined organic layers were filtered on Celite, and the dark red solution was neutralized to pH 7 by slow addition of saturated aqueous sodium bicarbonate (400 mL) with vigorous stirring,. The organic phase was separated and dried over sodium sulfate. After evaporation of the solvent, the residue was purified by

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chromatography (silica gel, dichloromethane) to give 4,6-dichloropyrone (8.0 g, 68%) as a solid: mp 43−44 °C (lit.[13] mp 43−45 °C); ^{1}H NMR ($CDCl_3$) δ 6.32 (s, 2H); IR 3052, 1702, 1638, 1422, 1396, 1265, 1208, 1045, 897, 738, 675 cm^{-1}.

4-Chloro-2(*H*)-pyran-2-one 8. To a solution of 4,6-dichloropyrone **7** (5.06 g, 0.031 mol) in acetic acid (30 mL) was added zinc powder (2.4 g, 0.037 mol, 1.2 equiv), in one portion. The reaction mixture was stirred at room temperature for 42 h. The solid was filtered off, and acetic acid was removed by evaporation. The residue was taken up in dichloromethane−water (150:50 mL) and neutralized to pH 7 by addition of solid potassium hydrogen carbonate. The organic layer was separated and the aqueous layer extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over sodium sulfate, and the solvent was removed by evaporation. The residue was chromatographed (silica gel, dichloromethane to give 4-chloropyrone (2.0 g, 51%) as an off-white solid: mp 59 °C (lit.[13] mp 56−58 °C); ^{1}H NMR ($CDCl_3$) 7.45 (dd, 1 H, J = 0.8 Hz, 5.6 Hz, H-6), 6.41 (dd, 1H, J = 0.8 Hz, 2.0 Hz, H-3), 6.29 (dd, 1H, J = 2.0 Hz, 5.6 Hz, H-5); ^{13}C NMR ($CDCl_3$) 160.1 (C-2), 151.3 (C-6), 150.8 (C-4), 114.8 (C-3), 108.9 (C-5); IR 3078, 2922, 1740, 1612, 1538, 1412, 1240, 1169, 1039, 864, 824, 780 cm^{-1}.

Cycloaddition of 4-Chloro-2(*H*)-pyran-2-one and Methyl Acrylate. A sealed pressure tube (purchased from Aldrich Chemical Co. Cat No Z18,109-9) was charged with 4-chloro-2(*H*)-pyran-2-one **8** (88 mg, 0.68 mmol), methyl acrylate (0.6 mL, 6.66 mmol, 10 equiv), a few crystals of 2,6-di-*tert*-butyl-4-methylphenol (acting as an anti-polymerization agent), and a small magnetic stirrer bar. The pressure tube was sealed and then immersed in an oil bath maintained at 70 °C. After 14 days, the tube was cooled and the contents were stripped of volatile materials. NMR analysis of the crude product indicated the presence of three isomers of cycloadducts (48:43:9) and a trace of another isomer as well as unreacted starting material (ca 8%). Pure samples of the isomers were obtained by a combination of silica gel chromatography, using 20% v/v ethyl acetate in petroleum ether, and recrystallization from diethyl ether. Combined isolated yield of cycloadducts was 102 mg, 70%.

Methyl 8-chloro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-6-*endo*-carboxylate 10a: ^{1}H NMR ($CDCl_3$) 6.40 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.5 Hz, H-7), 5.49 (dd, 1H, $J_{1,6}$ = 3.7 Hz, $J_{1,7}$ = 5.5 Hz, H-1), 3.73 (s, 3H, CO_2CH_3), 3.60 (m, 1H, H-4), 3.37 (ddd, 1H, $J_{6,1}$ = 3.7 Hz, $J_{6,5endo}$ = 5.7 Hz, $J_{6,5exo}$ = 9.6 Hz, H-6), 2.30 (ddd, 1H, $J_{5exo,4}$ = 3.1 Hz, $J_{5exo,6}$ = 9.6 Hz, $J_{5exo,5endo}$ = 13.3 Hz, H-5$_{exo}$), 2.18 (ddd, 1H, $J_{5endo,4}$ = 2.6 Hz, $J_{5endo,6}$ = 5.7 Hz, $J_{5endo,5exo}$ = 13.3 Hz, H-5$_{endo}$); ^{13}C NMR ($CDCl_3$) 171.1 (CO_2Me), 171.0 (C-3), 136.8 (C-8), 125.4 (C-7), 74.7 (C-1), 53.1 (CO_2CH_3), 49.0 (C-4), 43.7 (C-6), 24.65 (C-5); IR 3515, 3094, 2956, 1770, 1732, 1623, 1437, 1358, 1327, 1303, 1203, 1141, 1089, 1058, 1031, 998, 974, 955, 895, 849, 831, 809, 785, 766, 718 cm^{-1}; *m*/*z* 216 (5, M$^+$), 172 (34, M$^+$ − CO_2), 130 (13), 115 (33), 114 (21), 113 (100), 112 (43), 102 (11), 76 (16, 113-HCl); HRMS calcd for C_9H_9ClO 216.0189, found 216.0199. Anal. Calcd for $C_9H_9ClO_4$: C, 49.90; H, 4.19. Found: C, 50.11; H, 3.94.

Methyl 8-chloro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*endo*-carboxylate 10b: mp 90 °C; ^{1}H NMR ($CDCl_3$) 6.48 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.5 Hz, H-7), 5.29 (ddd, 1H, $J_{1,6endo}$ = 1.5 Hz, $J_{1,6exo}$ = 3.7 Hz, $J_{1,7}$ = 5.5 Hz, H-1), 3.98 (m, 1H, H-4), 3.76 (s, 3H, CO_2CH_3), 3.14 (dt, 1H, $J_{5,4}$ = $J_{5,6endo}$ = 3.3 Hz, $J_{5,6exo}$ = 9.5 Hz, H-5), 2.47 (ddd, 1H, $J_{6exo,1}$ = 3.7 Hz, $J_{6exo,5}$ = 9.5 Hz, $J_{6exo,6endo}$ = 13.8 Hz, H-6$_{exo}$), 2.21 (ddd, 1H, $J_{6endo,1}$ = 1.5 Hz, $J_{6endo,5}$ = 3.3 Hz, $J_{6exo,6endo}$ = 13.8 Hz, H-6$_{endo}$); ^{13}C NMR ($CDCl_3$) 171.35 (CO_2CH_3), 170.5 (C-3), 133.5 (C-8), 128.0 (C-7), 74.6 (C-1), 53.2 (CO_2CH_3), 51.5 (C-4), 37.1 (C-5), 30.0 (C-6); IR 2922, 2851, 1768,1738, 1621, 1437, 1359, 1320, 1174, 1052, 990, 948, 844, 767 cm^{-1}; *m*/*z* 216 (2.5, M$^+$), 185 (5.5), 172 (32, M$^+$ − CO_2), 130 (6), 115 (33), 114 (16), 113 (100), 112 (24), 102 (8), 76 (27, 113-HCl), 49 (6); HRMS calcd for $C_9H_9ClO_4$ 216.0189, found 216.0216.

Methyl 8-chloro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-6-*exo*-carboxylate 10c: ^{1}H NMR ($CDCl_3$) 6.44 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.3 Hz, H-7), 5.54 (dd, 1H, $J_{1,6}$ = 1.5 Hz, $J_{1,7}$ = 5.3 Hz, H-1), 3.79 (s, 3H, CO_2CH_3), 3.60 (m, 1H, H-4), 2.87 (ddd, 1H, $J_{6,1}$ = 1.5 Hz, $J_{6,5exo}$ = 3.4 Hz, $J_{6,5endo}$ = 10.3 Hz, H-6), 2.58 (ddd, 1H, $J_{5exo,4}$ = 3.2 Hz, $J_{5exo,6}$ = 3.4 Hz, $J_{5exo,5endo}$ = 13.3 Hz, H-6$_{exo}$), 2.04 (ddd, 1H, $J_{5endo,4}$ = 2.6 Hz, $J_{5endo,6}$ = 10.3 Hz, $J_{5exo,5endo}$ = 13.4 Hz, H-5$_{endo}$); ^{13}C NMR ($CDCl_3$) 170.95 (CO_2CH_3), 170.9 (C-3), 137.3 (C-8), 126.3 (C-7), 76.3 (C-1), 53.3 (CO_2CH_3), 49.1 (C-4), 43.9 (C-6), 23.3 (C-5).

Methyl 8-chloro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*exo*-carboxylate 10d: ^{1}H NMR ($CDCl_3$) 6.47 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.5 Hz, H-7), 5.29 (ddd, 1H, $J_{1,6endo}$ = 1.7 Hz, $J_{1,6exo}$ = 3.6 Hz, $J_{1,7}$ = 5.5 Hz, H-1), 3.81 (m, 1H, H-4), 3.77 (s, 3H, CO_2CH_3), 2.96 (ddd, 1H, $J_{5,4}$ = 2.2 Hz, $J_{5,6exo}$ = 5.5 Hz, $J_{5,6endo}$ = 10.8 Hz, H-5), 2.53 (ddd, 1H, $J_{6exo,1}$ = 3.6 Hz, $J_{6exo,5}$ = 5.5 Hz, $J_{6exo,6endo}$ = 13.8 Hz, H-6$_{exo}$), 2.06 (ddd, 1H, $J_{6endo,1}$ = 1.7 Hz, $J_{6endo,5}$ = 10.8 Hz, $J_{6exo,6endo}$ = 13.8 Hz, H-6$_{endo}$). ^{13}C NMR ($CDCl_3$) 172.1 (CO_2CH_3), 169.4 (C-3), 135.3 (C-8), 128.35 (C-7), 74.2 (C-1), 53.3 (CO_2CH_3), 51.7 (C-4), 39.2 (C-5), 30.5 (C-6); IR 3521, 3091, 2956, 1766, 1727, 1623, 1356, 1325, 1287, 1238,1207, 1135, 1057, 1036, 996, 957, 906, 857, 814, 748, 717 cm^{-1}; *m*/*z* 172 (11, M$^+$ − CO_2), 130 (10), 115 (34), 114 (15), 113 (100), 112 (24), 102 (11), 84 (14), 77 (12), 76 (27, 113-HCl); HRMS calcd for $C_9H_9ClO_4Na$ 239.0087, found 239.0078.

Cycloaddition of 4-Chloro-2(*H*)-pyran-2-one and Acrylonitrile. A sealed pressure tube (purchased from Aldrich Chemical Co. Cat No Z18,109-9) was charged with 4-chloropyrone **8** (100 mg, 0.77 mmol), acrylonitrile (0.6 mL, 9.11 mmol, 12 equiv), a few crystals of 2,6-di-*tert*-butyl-4-methylphenol (acting as anti-polymerization agent), and a small magnetic stirrer bar. The pressure tube was sealed and then immersed in an oil bath maintained at 70 °C. After 26 days, the tube was cooled to room temperature, and the contents were stripped of volatile materials. NMR analysis of the crude residue indicated the presence of three cycloadducts (58:25:17) and unreacted starting material (ca 20%). Pure samples of the isomers were obtained by combination of silica gel chromatography, using 25% v/v ethyl acetate in petroleum ether, and recrystallization from diethyl ether. Combined isolated yield of cycloadducts was 58.5 mg, 41%.

8-Chloro-6-*endo*-cyano-2-oxabicyclo[2.2.2]oct-7-en-3-one 11a: mp 94 °C; ^{1}H NMR ($CDCl_3$) 6.56 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.5 Hz, H-7), 5.43 (dd, 1H, $J_{1,6}$ = 3.5 Hz, $J_{1,7}$ = 5.5 Hz, H-1), 3.69 (m, 1H, H-4), 3.41 (ddd, 1H, $J_{6,1}$ = 3.6 Hz, $J_{6,5endo}$ = 5.4 Hz, $J_{6,5exo}$ = 9.7 Hz, H-6), 2.51 (ddd, 1H, $J_{5exo,4}$ = 2.9 Hz, $J_{5exo,6}$ = 9.7 Hz, $J_{5exo,5endo}$ = 13.4 Hz, H-5$_{exo}$), 2.10 (ddd, 1H, $J_{5endo,4}$ = 2.9 Hz, $J_{5endo,6}$ = 5.4 Hz, $J_{5endo,5exo}$ = 13.4 Hz, H-5$_{endo}$); ^{13}C NMR ($CDCl_3$) 169.0 (C-3), 138.0 (C-8), 124.9 (C-7), 118.3 (CN), 73.4 (C-1), 48.3 (C-4), 29.0 (C-6), 26.5 (C-5); IR 3468, 3092, 2958, 2246, 1771, 16222, 1456, 1361, 1320, 1246, 1208, 1143, 1070, 1027,1017, 1000, 963, 927, 841, 812, 715 cm^{-1}; *m*/*z* 185 (5), 183 (7, M$^+$), 139 (29, M$^+$ − CO_2),132 (20), 130 (59), 112(6), 104 (100), 102 (65), 85 (27), 83 (45), 77 (8), 76 (30), 74 (10), 67 (14), 51 (25), 50 (12), 49 (60), 47 (11), 39 (15).

8-Chloro-5-*endo*-cyano-2-oxabicyclo[2.2.2]oct-7-en-3-one 11b: mp 114 °C; ^{1}H NMR ($CDCl_3$) 6.65 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.7 Hz, H-7), 5.36 (ddd, 1H, $J_{1,6endo}$ = 1.6 Hz, $J_{1,6exo}$ = 3.6 Hz, $J_{1,7}$ = 5.7 Hz, H-1), 3.89 (m, 1H, H-4), 3.28 (dt, 1H, $J_{5,4}$ = $J_{5,6endo}$ = 3.2 Hz, $J_{5,6exo}$ = 9.5 Hz, H-5), 2.69 (ddd, 1H, $J_{6exo,1}$ = 3.6 Hz, $J_{6exo,5}$ = 9.5 Hz, $J_{6exo,6endo}$ = 14 Hz, H-6$_{exo}$), 2.06 (ddd, 1H, $J_{6endo,1}$ = 1.6 Hz, $J_{6endo,5}$ = 3.2 Hz, $J_{6exo,6endo}$ = 14 Hz, H-6$_{endo}$); ^{13}C NMR ($CDCl_3$) 167.5 (C-3), 133.4 (C-8), 128.0 (C-7), 117.9 (CN), 73.3 (C-1), 50.6 (C-4), 31.9 (C-6), 22.95(C-5); IR (film) 3361, 2923, 2853, 2248, 1755, 1622, 1449, 1357, 1267, 1164, 1061, 1030, 976, 898, 844, 817, 724 cm^{-1}; *m*/*z* 185 (4), 183 (8, M$^+$), 139 (20, M$^+$ − CO_2), 132 (5), 130 (9), 112(5), 105 (11), 104 (100), 102 (23), 85 (27), 77 (7), 76 (25), 51 (14), 50 (10), 44 (14), 39 (12); HRMS calcd for $C_8H_6ClNO_2$ 183.0087, found 183.0083.

8-Chloro-6-*exo*-cyano-2-oxabicyclo[2.2.2]oct-7-ene-3-one 11c: ^{1}H NMR ($CDCl_3$) 6.43 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.7 Hz, H-7), 5.43 (dd, 1H, $J_{1,6}$ = 1.2 Hz, $J_{1,7}$ = 5.6 Hz, H-1), 3.69 (m, 1H, H-4), 2.98 (ddd, 1H, $J_{6,1}$ = 1.2 Hz, $J_{6,5exo}$ = 5.4 Hz, $J_{6,5endo}$ = 9.5 Hz, H-6), 2.30 (m, 2H, H-5$_{exo}$ and H-5$_{endo}$); ^{13}C NMR ($CDCl_3$) 168.7 (C-3), 137.0 (C-8), 125.2 (C-7), 118.1 (CN), 73.8 (C-1), 47.9 (C-4), 28.9 (C-6), 25.0 (C-5).

Cycloaddition of 4-Chloro-2(*H*)-pyran-2-one and Methyl Metacrylate. A sealed pressure tube (purchased from Aldrich Chemical Co. Cat No Z18,109-9) was charged with 4-chloropyrone **8** (113 mg, 0.87 mmol), methyl metacrylate (0.5 mL, 4.69 mmol, 5.4 equiv), a few crystals of 2,6-di-*tert*-butyl-4-methylphenol (acting as anti-polymerization agent), and a small magnetic stirrer bar. The pressure tube was sealed and then immersed in an oil bath maintained at 70 °C. After 14 days, the tube was cooled to room temperature and the contents were stripped of volatile materials. NMR analysis of the crude residue indicated the presence of two cycloadducts (75:25) and unreacted starting material (ca 44%). Pure samples of the isomers were obtained by silica gel chromatography, using 20% v/v ethyl acetate in petroleum ether. Combined isolated yield of cycloadducts was 36 mg, 18%.

Methyl 8-chloro-5-*exo*-methyl-3-oxo-2-oxabicyclo-[2.2.2]oct-7-ene-5-*endo*-carboxylate 12b: ^{1}H NMR ($CDCl_3$) 6.43 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.6 Hz, H-7), 5.22 (dd, 1H, $J_{1,6endo}$ = 1.8 Hz, $J_{1,6exo}$ = 3.6 Hz, $J_{1,7}$ = 5.6 Hz, H-1), 3.78 (d, 1H, $J_{7,4}$ = 2.6 Hz, H-4), 3.76 (s, 3H, CO_2CH_3), 2.65 (dd, 1H, $J_{6endo,1}$ = 1.8 Hz, $J_{6exo,6endo}$ = 14 Hz, H-6$_{endo}$), 1.78 (dd, 1H, $J_{6exo,1}$ = 3.6 Hz, $J_{6exo,6endo}$ = 14 Hz, H-6$_{exo}$), 1.47 [s, 3H, C(CH_3)]; ^{13}C NMR ($CDCl_3$) 173.8 (CO_2CH_3), 169.9 (C-3), 134.8 (C-8), 127.5 (C-7), 74.5 (C-1), 57.4 (CO_2CH_3), 52.8 (C-4), 44.2 (C-5), 37.8 (C-6), 25.6 [C(CH_3)]; IR 2954, 1760, 1735, 1622, 1435, 1355, 1304, 1263, 1227, 1207, 1174, 1136,1115, 1045, 1006, 983, 940, 876, 843, 811, 768, 714 cm^{-1}; *m*/*z* 230 (4, M$^+$), 186 (10, M$^+$ − CO_2), 148 (15), 130 (13), 129 (35), 128 (13, 127 (99), 126 (13), 102 (13), 90 (10), 91 (74), 85 (52), 83 (84), 65 (11), 51 (33), 49 (100,), 47 (12), 44 (10), 39 (11); HRMS calcd for $C_{10}H_{11}ClO_4$ 230.0342, found 230.0348. Anal. Calcd for $C_{10}H_{11}ClO_4$: C, 52.08; H, 4.81. Found: C, 52.26; H, 5.15.

Methyl 8-chloro-6-(*exo*)-methyl-3-oxo-2-oxabicyclo-[2.2.2]oct-7-ene-6-(endo)-carboxylate 12a. ^{1}H NMR ($CDCl_3$) 6.44 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.6 Hz, C-7), 5.15 (d, 1H, $J_{1,7}$ = 5.6 Hz, H-1), 3.73 (s, 3H, CO_2CH_3), 3.52 (m, 1H, H-4), 2.61 (dd, 1H, $J_{5exo,4}$ = 2.8 Hz, $J_{5endo,5exo}$ = 13.5 Hz, H-5$_{exo}$), 1.74 (dd, 1H, $J_{5endo,4}$ = 2.7 Hz, $J_{5exo,5endo}$ = 13.5 Hz, H-5$_{endo}$), 1.49 [s, 3H, C(CH_3)].

Cycloaddition of 4-Chloro-2(*H*)-pyran-2-one and Dimethyl Fumarate. A sealed pressure tube (purchased from Aldrich Chemical Co. Cat No Z18,109-9) was charged with 4-chloropyrone **8** (80 mg, 0.61 mmol), dimethyl fumarate (250 mg, 1.85 mmol, 3 equiv), dichloromethane (1 mL), a few crystals of 2,6-di-*tert*-butyl-4-methylphenol (acting as anti-polymerization agent), and a small magnetic stirrer bar. The pressure tube was sealed and then immersed in an oil bath maintained at 70 °C. After 15 days, the tube was cooled to room temperature and the contents were stripped of volatile materials. NMR analysis of the crude residue indicated the presence of two cycloadducts (55:45) and unreacted starting material (ca 14%). Cycloadducts were separated from unreacted materials by silica gel chromatography, using 30% v/v ethyl acetate in petroleum ether. Combined isolated yield of unseparable cycloadducts was 34 mg, 20%.

Dimethyl 8-chloro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*exo*,6-*endo*-dicarboxylate 13a: ^{1}H NMR ($CDCl_3$) 6.45 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.4 Hz, H-7), 5.52 (dd, 1H, $J_{1,6}$ = 3.8 Hz, $J_{1,7}$ = 5.4 Hz, H-1), 3.87 (t, 1H, $J_{4,5}$ = 2.2 Hz, $J_{4,7}$ = 2.2 Hz, H-4), 3.80 (s, 3H, CO_2CH_3), 3.76 (s, 3H, CO_2CH_3), 3.79 (m, 1H, H-6$_{exo}$), 3.38 (m, 1H, H-5$_{endo}$).

Dimethyl 8-chloro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*endo*,6-*exo*-dicarboxylate 13b: ^{1}H NMR ($CDCl_3$) 6.51 (dd, 1H, $J_{7,4}$ = 2.2 Hz, $J_{7,1}$ = 5.7 Hz, H-7), 5.59 (dd, 1H, $J_{1,6}$ = 1.3 Hz, $J_{1,7}$ = 5.7 Hz, H-1), 4.02 (t, 1H, $J_{4,5}$ = 2.2 Hz, $J_{4,7}$ = 2.2 Hz, H-4), 3.81 (s, 3H, CO_2CH_3), 3.78 (s, 3H, CO_2CH_3), 3.79 (m, 1H, H-5$_{exo}$), 3.38 (m, 1H, H-6$_{endo}$); IR 2957, 2924, 2852, 1775, 1738, 1622, 1437, 1356, 1303, 1276, 1245, 1208, 1135, 1059, 1027, 992 cm^{-1}; *m*/*z* 274 (4, M$^+$), 243 (5), 230 (7, M$^+$ − CO_2), 197 (31), 171 (100), 173 (41), 172 (27), 170 (36), 149 (21), 148 (73), 140 (19), 119 (33), 103 (10), 89 (54), 74 (80), 66 (94).

Cycloaddition of 4-Chloro-2(*H*)-pyran-2-one and Dimethyl Maleate. A sealed pressure tube (purchased from Aldrich Chemical Co. Cat No Z18,109-9) was charged with 4-chloropyrone **8** (82 mg, 0.63 mmol), dimethyl maleate (0.5 mL, 4.0 mmol, 6.3 equiv), a few crystals of 2,6-di-*tert*-butyl-4-methylphenol (acting as anti-polymerization agent), and a small magnetic stirrer bar. The pressure tube was sealed and then immersed in an oil bath maintained at 70 °C. After 15 days, the tube was cooled to room temperature and the contents were stripped of volatile materials. NMR analysis of the crude residue indicated the presence of single cycloadduct and unreacted starting material. Pure sample was obtained silica gel chromatography, using 30% v/v ethyl acetate in petroleum ether. Isolated yield of cycloadduct was 41 mg, 24%.

Dimethyl 8-chloro-3-oxo-2-oxabicyclo[2.2.2]oct-7-ene-5-*endo*,6-*endo*-dicarboxylate 14: ^{1}H NMR ($CDCl_3$) 6.62 (dd, 1H, $J_{7,4}$ = 2.3 Hz, $J_{7,1}$ = 5.6 Hz, H-7), 5.43 (dd, 1H, $J_{1,6}$ = 3.0 Hz, $J_{1,7}$ = 5.7 Hz, H-1), 3.84 (t, 1H, $J_{5,4}$ = $J_{4,7}$ = 2.3 Hz, H-4), 3.73 (s, 3H, CO_2CH_3), 3.69 (s, 3H, CO_2CH_3), 3.60 (dd, 1H, $J_{6,1}$ = 3.0 Hz, $J_{6,5}$ = 10.2 Hz, H-6), 3.54 (dd, 1H, $J_{5,4}$ = 2.3 Hz, $J_{5,6}$ = 10.2 Hz, H-5); ^{13}C NMR ($CDCl_3$) 169.1 (2 × CO_2CH_3), 169.0 (C-3), 133.5 (C-8), 126.7 (C-7), 74.0 (C-1), 52.8 (CO_2CH_3), 52.52 (CO_2CH_3), 51.4 (C-4), 47.2 (C-5), 41.3 (C-6); IR 2956, 2921, 1772, 1743, 1625, 1437, 1356, 1210, 1173, 1026, 986 cm^{-1}; *m*/*z* 274 (14, M$^+$), 243 (20), 197 (12), 171 (22), 148 (13), 139 (16), 130 (18), 129 (15), 127 (39), 114 (13), 113 (100), 112 (18), 105 (12), 102 (18), 91 (45), 76 (58), 73 (27), 69 (14), 59 (96), 57 (16), 55 (11), 44 (13), 43 (14), 41 (11); HRMS calcd for $C_{11}H_{11}ClO_4$ 274.0240, found 274.0282.

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Supporting Information Available: Coordinates of all transition states in pdb format. Absolute energies of all transition states. This material is available free of charge via the Internet at http://pubs.acs.org.

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