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Rotational features of carbon–nitrogen bonds in *N*-aryl maleimides. Atroposelective reactions of *o-tert*-butylphenylmaleimides

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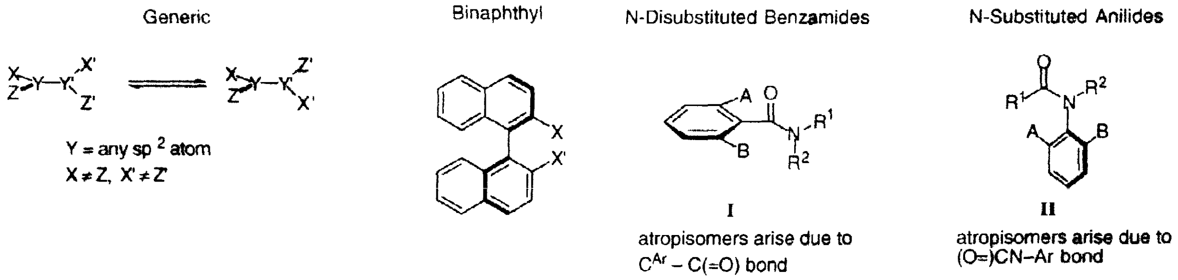
Summary: *Atroposelective addition and cycloaddition reactions of N-2-(tert-butylphenyl)- and N-2,5-(di-tert-butylphenyl)maleimide and a substituted derivative have been studied. Good to excellent stereoselectivities are generally observed, and high rotation barriers (about 29 kcal/mol) prevent the products from interconverting. Crystal structures of the precursors and products support a straightforward model where reactants attack trans to the o-tert-butyl group.*

Keywords: Axial chirality, rotation barrier, atroposelectivity, amides

Introduction

Stereoisomerism is a general property of molecules containing two sp^2 atoms connected by a single bond provided that the substituents of these atoms are not identical and that they are sufficiently large to favor twisted over planar conformations (Figure 1).[1] This type of stereoisomerism is often called axial (or helical) chirality, and stereoisomers resulting from slow rotation about an sp^2-sp^2 single bond (or more generally, slow rotation about any single bond) are called atropisomers. The rotational features of axially chiral biaryl atropisomers have be extensively studied, and the reactions of such biaryls (especially binaphthyl analogs) are of central importance in modern asymmetric synthesis.[2]

Figure 1. Atropisomers from sp^2–sp^2 Bonds



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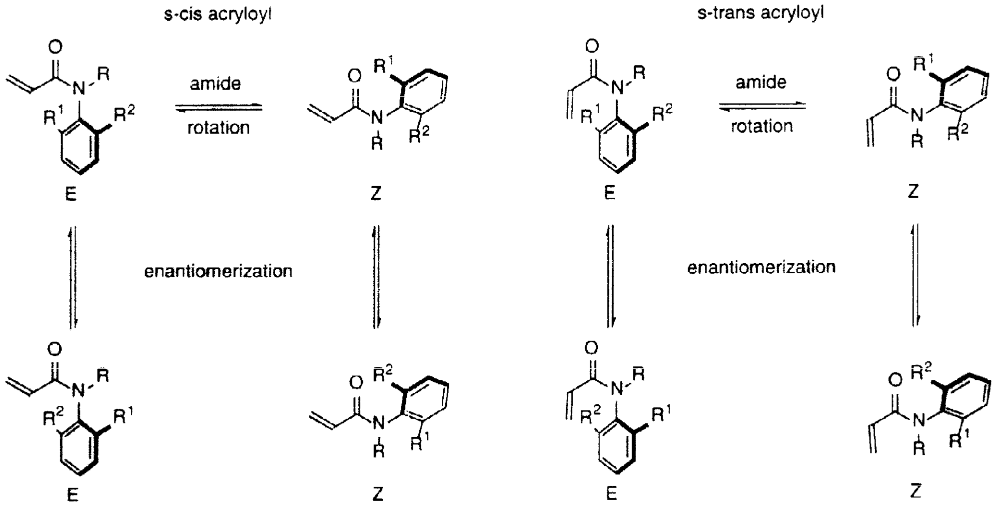
Amides contain sp^2 atoms that are disubstituted and are connected by a single bond, so atropisomers arise with suitable substitution.[3,4,5] For example, *N*,*N*-disubstituted benzamides such as I and *N*-substituted anilides such as II[6] can generally be resolved into stable (at room temperature) atropisomers when both "A" and "B" are larger than hydrogen. In the benzamide class, a carbon-carbon single bond causes the isomerism while a carbon-nitrogen bond is responsible in the anilide class. Although the rotational features of these types molecules have been known for some time, their use in stereocontrolled reactions has only recently come under study.[7] The neglect of the chemistry of these classes of molecules might be due to the tendency—instilled in organic chemists by resonance theory—to view such molecules as planar. However, there is overwhelming crystallographic evidence that these molecules prefer twisted geometries,[8] even when "A" and "B" are hydrogen (albeit with a smaller degree of twist and a lower rotation barrier than the non-hydrogen analogs).

We have been interested in asymmetric reactions induced by axial chirality about C–N bonds, and in 1994 we reported the first examples of atroposelective reactions of such amides and imides.[9] Extensions and full details of the work on anilides have recently been reported,[10] and herein we detail the complementary studies on the maleimide class. This work, taken together with that in other labs,[7] suggests broad potential for deployment of chiral amides and imides in synthesis.

Some of the possible rotational isomers of *N*-aryl substituted acrylamides are shown in Figure 2. These compounds are subject to atroposelective reactions (for example, cycloadditions) at the C–C double bond, and their isomer features are similar to other intermediates of interest for stereoselective synthesis such as enolates and radicals.[11] Eight rotational isomers are shown, grouped into two classes according to the geometry of the acryloyl unit (*s-cis* or *s-trans*). For acryloyl compounds, interconversions of *s-cis* and *s-trans* isomers will be rapid. In addition, aryl amides have E/Z rotational isomers about the carbonyl carbon-to-nitrogen bond (standard amide rotation) and rotation about the twisted N–Ar bond. This last rotation, depicted in top-to-bottom pairs in Figure 2, interconverts enantiomers, while the other two rotations provide conformational isomers of one enantiomer or the other.

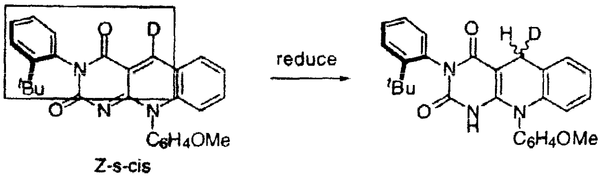
Figure 2. Rotational Features of N-Aryl Substituted Acrylamides



Which shapes are favored and indeed whether or not some of the indicated rotamers are even minima are determined by the substituents on the amide and the presence of rings. For example, *N*-alkylanilides (R = alkyl) tend to favor the *s-cis* acrylate rotamer and the E-amide geometry (far left pair). The Z-amide geometry is accessible but higher in energy, and all the ***s-trans*** rotamers are probably not minima due to A-strain. Therefore, reactions of acyclic systems can often be interpreted through the E, *s-cis* conformer.[12]

A number of the shapes represented in Figure 2 can be readily and selectively accessed by building rings. For example, Yoneda and coworkers have studied asymmetric reductions of flavin models (Figure 3).[13] These take on a shape analogous to Z, *s-cis* conformational isomer in Figure 2, and a number of such molecules have been resolved and their reactions studied. While certain chelation-controlled reductions give very high levels of stereoselection, simple reductions with reagents like sodium borohydride show little or no stereoselection. Based on previous results with amides,[11] this is not surprising; in the *s-cis* geometry, the β-carbon undergoing reaction is far removed from the face shielding group.

Figure 3. Some Reactions of Axially Chiral Flavins

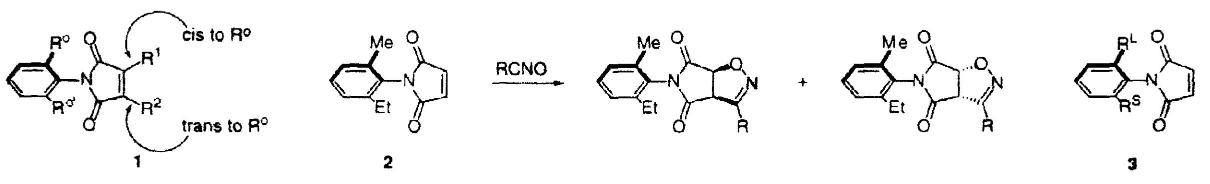


- $NaBH_4$, no selectivity
- 1-benzyl-1,4-dihydronicotinamide/ $MgClO_4$, H delivered trans to ^{t}Bu

Results and Discussion

We were interested in studying the general shape Z, *s-trans* (Figure 2, far right), which will be adopted by a large number of heterocycles that bear amide functional groups in conjugation with endocyclic double bonds. We choose *N*-aryl maleimides **1** (Figure 4) as representative of this class because they are readily prepared and because the study of their atroposelective reactions is simplified by symmetry; the alkene carbons are each α to one carbonyl group and β to the other. Indeed, when the α and β-substituents of the succinimide (R^1 and R^2) are identical, the molecule has a plane of symmetry and is achiral. Nonetheless, atroposelectivity is still readily studied since reactions can occur either cis or trans to the substituent R^o in **1**.

Figure 4. *ortho*-Substituted *N*-Aryl Maleimides



achiral if $R^1 = R^2$
chiral if $R^1 \neq R^2$

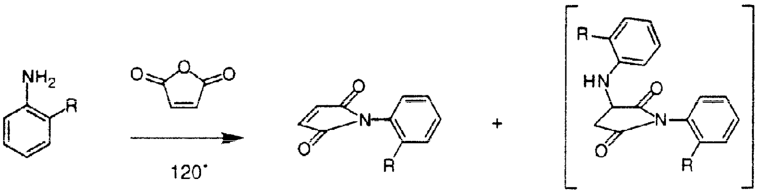
high rotation barrier
low stereoselectivity

Literature precedent[3-5] shows that the placement of two medium size substituents in the ortho positions of an *N*-aryl maleinide will lead to a molecule with a healthy barrier to N–Ar bond rotation.

However, in the absence of some type of directed reaction, such molecules are not expected to be generally useful for atroposelective reactions. Indeed, Konopikova and coworkers prepared maleimides such as **2** and studied their nitrile oxide cycloadditions.[14] Stereoselectivities were negligible, but the atropisomeric products did not interconvert at room temperature and could sometimes be separated and individually characterized. Our goal was to replace the two medium-sized substituents (see **2**) with one large substituent and one small one (see **3**) and then to study the effect on the rotation barrier—which we expected to be lower than **2**—and the stereoselectivity—which we expected to be higher than **2**. The small substituent is hydrogen in all cases, while the large substituent was varied. The simple prediction is that larger groups should both increase the barrier to rotation and increase the stereoselection. The rotation barrier is not easily measured in the achiral succinimide precursors, but it is readily obtained by measuring rates of diastereomer interconversion in the products.

To initiate the work, a series of *N*-arylmaleimides **4** bearing increasingly bulky ortho-substituents was synthesized, as shown in eq. 1. The appropriate aniline was combined neat with maleic anhydride in a sealed tube and heated at 120°C overnight. It was necessary to use a threefold excess of maleic anhydride to prevent the formation of the double aniline adduct **5**. The product imides **7** were isolated by dissolving the crude reaction mixture in ethyl acetate and filtering through a short column to remove excess maleic anhydride and baseline impurities, prior to column chromatography. All of these compounds were white solids.

Eq. 1



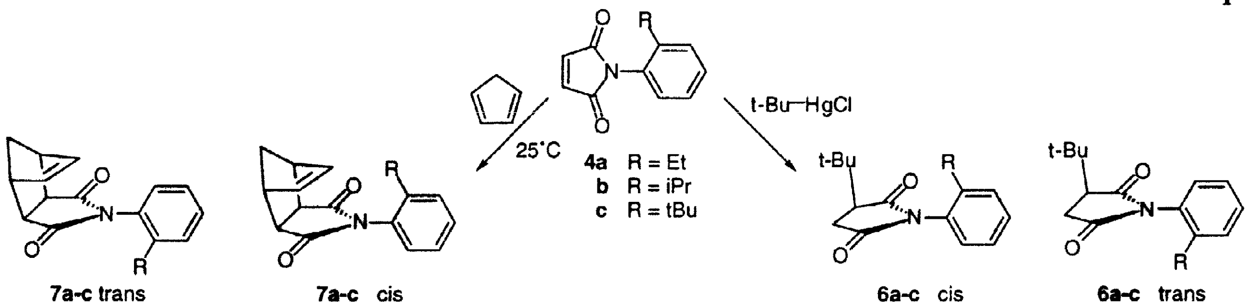
4a R = Et
b R = i-Pr
c R = t-Bu

5

The facial selectivity of each of the maleimide derivatives was tested by radical addition with *tert*-butyl mercuric chloride and by Diels-Alder addition of cyclopentadiene (Eq. 2). Reaction products were then equilibrated at a suitable temperature to assess their stability. The results of these experiments are shown in Table 1. Addition of t-butyl radical[16] to *o*-*tert*-butylmaleimide **4c** (Table 1, entry 1) at room temperature occurred with a 12.5/1 selectivity (as measured by ^{1}H NMR). This ratio did not change when the sample was left at room temperature overnight, but was reduced to a ratio of 2.5/1 by heating the product mixture at 120°C for 16 h. Heating that mixture for an additional 24 h did not change the 2.5/1 ratio, so we assume that this is the thermodynamic ratio.

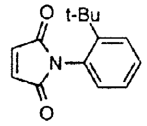
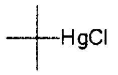
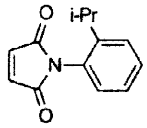
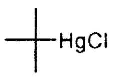
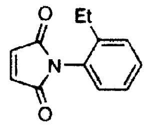
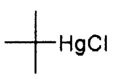
The isopropyl substrate **4b** showed a selectivity of 8.7/1 in the radical addition (Table 1, entry 3). Because the isomers **6b-trans/cis** equilibrated to the thermodynamic ratio of 1.8 to 1.0 simply on standing overnight, precautions were taken in attempting to measure the room temperature kinetic ratio. The reaction was allowed to proceed in $CDCl_3$ only until gas evolution ceased (< 1 min), before the mixture was filtered into an NMR tube and placed in a dry ice and acetone bath prior to brief warming to record the spectrum.

Eq. 2



The selectivity observed in the ^{t}BuHgCl addition to the ethyl substrate **4a** (Table 1, entry 5) was only 1.2/1; essentially identical to the thermodynamic ratio (1.1/1), raising the possiblity that the barrier to rotation in this series is very low. Indeed, the time scale of interconversion of **6a-trans/cis** was within the NMR regime. When a sample of this product was heated in a sealed NMR tube, the resonances of the ring *tert*-butyl groups, which are separated by 6.6 Hz, were observed to coalesce between 375 and 380 °K. These values indicate that the barrier to rotation could not be more than 21 kcal/mol.[15] This means that a sample kinetically enriched in one isomer would reach equilibrium with a half-life on the order of minutes at 25°C. It is therefore unlikely that the sample would show a remnant of the kinetic ratio of isomers by the time the reaction was complete and analyzed.

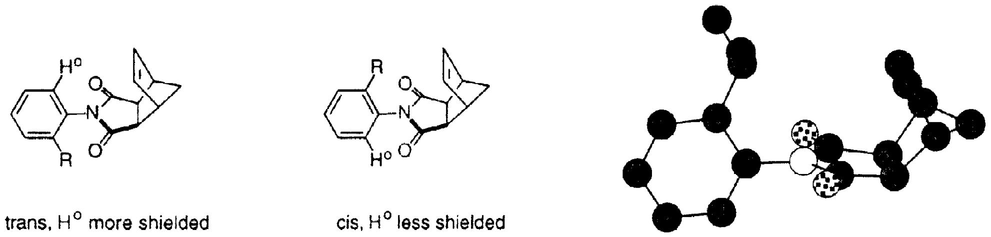
Table 1. Radical and Diels-Alder Reactions of 7a-c

Entry	Substrate	Reagent	Facial Selectivity at 25°	Ratio After Equilibration
1			**6c-trans/cis** 12.5/1	2.5/1.0
2	**4c**		only **7c-trans**	no second product observed after heating for 7 days at 140°C
3			**6b-trans/cis** 8.7/1	1.8/1.0
4	**4b**		**7b-trans/cis** 6.1/1	1.4/1.0
5		 h	**6a-trans/cis** 1.2/1.0	1.1/1.0
6	**4a**		**7a-trans/cis** 4.6 : 1.0	1.1/1.0

The Diels-Alder reaction with substrate **4c** showed only a single isomer **7c-trans** and we were unable to generate the atropisomer (**7c-cis**) of this compound even after heating the product in a sealed tube for 7 days at 140° C (Table 1, entry 1). In contrast, the Diels-Alder products were isolated as mixtures from **4b** (6.1/1) and **4a** (4.6/1) and these mixtures were equilibrated within a single day at 25°C (Table 1, entries 4 and 6). Reactions with **4a** and **4b** were allowed to run for only 2 min before cooling to –78°. Even so, the "kinetic" ratio of the isopropyl products **7b-trans/cis** was reduced from 6.1/1 to 1.4/1 in only 30 min at 25°C. The ratio of the ethyl product dropped from 4.6/1 to 2.6/1 in only 10 min, and after 30 min it had equilibrated to the thermodynamic ratio of 1.1/1. That ratio did not change when the sample was allowed to stand at room temperature for one week.

The gross structures of the products in Table 1 were evident from standard spectroscopic analysis. Atropisomers were assigned by a reliable trend in the ^{1}H NMR spectrum: H^o on the N-aryl ring is shielded in the trans (major) isomer relative to the cis (minor) isomer.[16] This assignment was confirmed in the case of **7b** (Table 2, entry 4) by x-ray crystallography. Interestingly, crystallization of the equilibrium mixture of isomers from ether provided exclusively the minor atropisomer **7b-cis**. Redissolution of this pure isomer in $CDCl_3$ resulted in a gradual return to the equilibrium mixture over 3 h at ambient temperature. The crystal structure of **7b-cis** was solved and it is shown in Figure 5. As expected, the isopropyl group is on the same side as the ethylene bridge derived from the cyclopentadiene. The crystal structure also confirms the standard endo approach in the Diels-Alder reaction. In this structure, the torsional angle of the N–Ar bond is 87°, and the nitrogen atom is essentially planar.

Figure 5. Assignment of Atropisomers by ^{1}H NMR Trends and Crystal Structure of 7b-cis



trans, H° more shielded

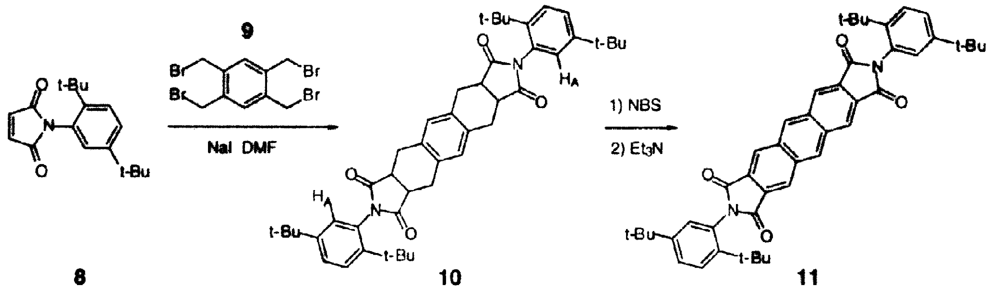
cis, H° less shielded

These preliminary experiments teach us that radical and Diels-Alder adducts of *N-o*-ethylphenyl-, and *N-o*-isopropylphenylmaleimides have substantial barriers to interconversion of atropisomers (20-25 kcal/mol) but these barriers are still too low for most practical synthetic applications. Kinetic stereoselectivities can be approached in the *N-o*-isopropyl system by working quickly. In the ethyl system, some selectivity is observed but the products equilibrate on the time scale of the reaction and analysis. In contrast, the reactions of *N-o*-tert-butylphenyl maleimide **4c** show good to excellent stereoselectivity and provide products that are separable and resist interconversion at room temperature. This suggests that useful synthetic application in this or related series can be developed.

Prior to expanding these studies, we decided to replace the *N*-(2-*tert*-butylphenyl)maleimide with *N*-(2,5-*di-tert*-butylphenyl)maleimide **8** for two reasons. First, the mono-*tert*-butyl analog is not readily available in large quantities. In contrast, the 2,5-*di-tert*-butyl aniline is readily prepared by a standard nitration/reduction sequence (see below). Second, there was one prior report of a Diels-Alder reaction with **1** that we wished to study in more detail.

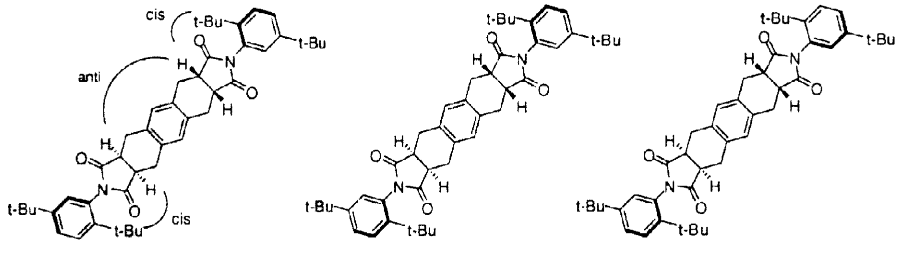
In 1990, Miller and coworkers reported the double Diels-Alder reaction of **8** with **9** en route to the preparation of **11** (Figure 2).[17] Miller and coworkers described intermediate product **10** as a single "trans-bis-endo" isomer. In was not entirely clear to us what this designation meant; there are several possible "trans" relationships and "bis-endo" products are indistinguishable from "bis-exo" products (although these are different from "exo-endo"). This stereochemical feature was not relevant to Miller's work, but the outcome was important to us so we decided to repeat the experiment.

Figure 6. Miller's Diels-Alder Reaction

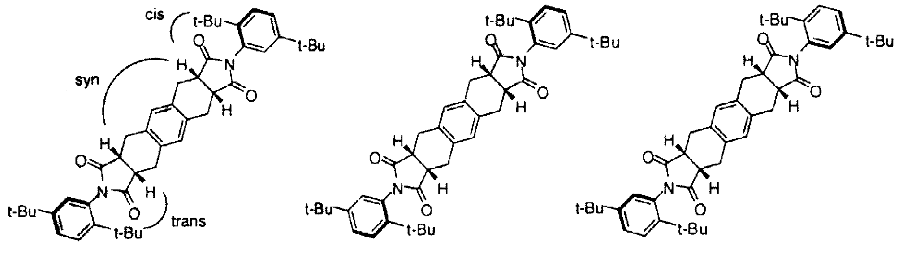


Assuming the usual cis-addition in Diels-Alder reactions, six isomeric forms of **10** can be created; these are distinguishable by whether each of the *ortho-tert*-butyl groups is cis or trans to the hydrogens on the bridge of the 5-6 ring fusion (atropisomers), and whether those bridgehead hydrogens are syn or anti to each other (configurational isomers). These are shown in Figure 7. With this backdrop, the synthesis of **1** and the repetition of the experiment in Figure 6 became the initial goals.

Figure 7. Isomers in the Double Diels-Alder Reaction of 1



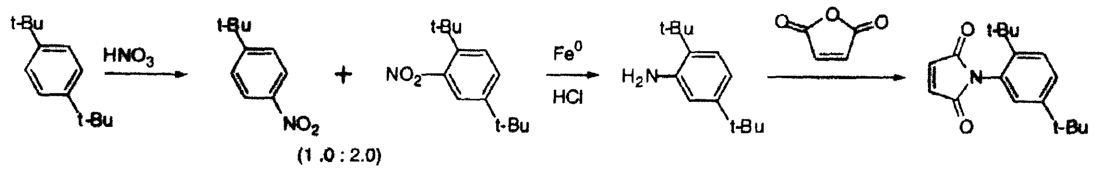
cis-anti-cis trans-anti-cis trans-anti-trans



trans-syn-cis cis-syn-cis trans-syn-trans

The synthesis of maleimide **8** is shown in Eq. 3. Inexpensive 1,4-di-*tert*-butylbenzene **12** was treated with nitric acid to give a separable 2:1 mixture of 1,4-di-*tert*-butyl-2-nitrobenzene **13** and 1-*tert*-butyl-4-nitrobenzene **14**.[19] 1,4-Di-*tert*-butyl-2-nitrobenzene **13** was then reduced to the corresponding amine **15** with iron and HCl in ethanol and water.[18] Subsequently, the amine **15** was melted with maleic anhydride at 120° C to produce *N*-(2,5-di-*tert*-butylphenyl)maleimide **8**, which was crystallized from diethyl ether.

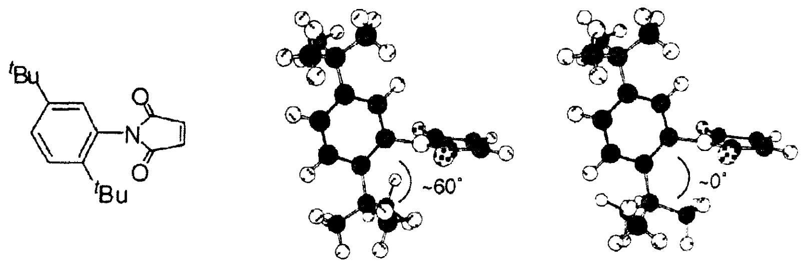
Eq. 3



12 **14** **13** 62% **15** 79% **8** 54%

X-Ray analysis of crystalline product **8** showed that two separate conformers were present in the unit cell (Figure 4). The only difference between the two structures is the rotational orientation of the ortho *tert*-butyl group over the maleimide plane. In one structure, a methyl group of the *tert*-butyl group eclipses the maleimide C–N bond with the other two methyl groups staggering the plane of the benzene ring. In the other structure, two methyl groups are staggered over the maleimide C–N bond with the third eclipsing the plane of the benzene ring. These are simply conformational isomers about a single bond, and we presume that this observation is not relevant to solution, where this bond rotation should be rapid. The maleimide and aromatic rings are exactly perpendicular and the pyrimidalization of the nitrogen is negligible.

Figure 8. Two Rotamers Observed in Crystal Structure of 1

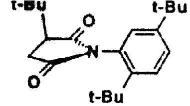
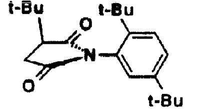
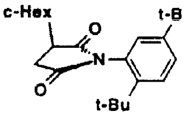
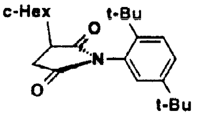
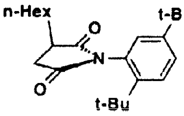
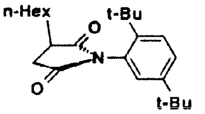
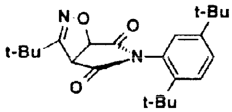
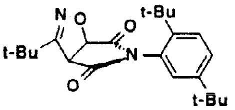
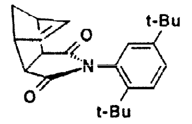
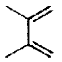
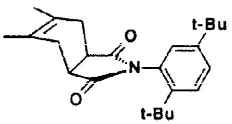
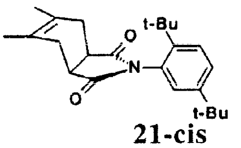


We repeated Miller's experiment in Figure 7 and indeed the ^{1}H NMR spectrum recorded in $CDCl_3$ appeared to be that of a single product **10**. However, when the spectrum was recorded in C_6D_6, two isomers were clearly evident in a ratio of about 1.4/1. Based on the subsequent results (see below) we assign these as the **10** cis-anti-cis and **10** cis-syn-cis structures, although it is not clear which is which. These products presumably come about by the bis-endo Diels-Alder transition state suggested by Miller. However, the ends of the molecule are so distant from each other that there is only slight facial selectivity in the second Diels-Alder addition and in chloroform it was not even possible to distinguish these two isomers. We can also conclude that the oxidation of **10** must have produced two atropisomers of **11**: one with the *o*-*t*-butyl groups cis and the other with them trans.

These observations indicate that the atroposelectivity of the Diels-Alder reaction (Figure 7) is complete—only one atropisomeric transition state occurs in each of the Diels-Alder additions, resulting in only two of the six possible products (Figure 9).

We next exposed the substrate **8** to a variety of bond forming reactions at various temperatures. Table 2 summarizes the results of these experiments. The kinetic ratios of product isomers are reported, as are the ratios of isomers after equilibration accomplished by heating product samples for about 1 day at 140°C. In this series, resonances of the ortho hydrogen on the aromatic ring provided both atroisomer ratios and assigments. In two cases (**17**, **21**), stereochemical assignments were confirmed by x-ray structures. Products were isolated by flash chromatography in good to excellent yields. Atropisomeric products did not interconvert readily at room temperature and they could sometimes be separated (see below and Experimental).

Table 2. Atroposelective Reactions of 8

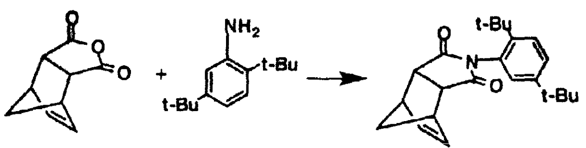
Entry	Reaction	Products (favored)	(disfavored)	Temp (°C)	Kinetic Ratio *[equilibrated]*
1 2	Giese Reaction with t-BuHgCl	 **16-trans**	 **16-cis**	25 0	12.5/1.0 11.2/1.0 *[2.5 /1.0]*
3 4	Giese Reaction with c-HexHgCl	 **17-trans**	 **17-cis**	25 0	3.4/1.0 3.3/1.0 *[1.7 /1.0]*
5	Giese Reaction with n-HexHgCl	 **18-trans**	 **18-cis**	0	1.7/1.0 *[1.1/1.0]*
6 7 8 9	Addition of t-Bu Nitrile Oxide	 **19-trans**	 **19-cis**	60 25 −35 −78	1.6/1.0 3.0/1.0 4.0/1.0 11.4/1.0 *[1.4 /1.0]*
10	Diels-Alder Reaction with 	 **20-trans**		25	only one isomer observed*[a]
11 12 13	Diels-Alder Reaction with 	 **21-trans**	 **21-cis**	120 80 25	2.1/1.0/0.0*[b] 14 /1.0/2.6*[b] 1.0/0/4.1*[b] *[1.8/1.0]*

(a) This sample was subsequently heated at 140° degrees for 7 days, but still showed only a single isomer by ^{1}H NMR. (b) The third quantity represents unreacted starting material after 24 h.

Selectivity in Diels-Alder reactions was high (Table 2, entries 10-13). The reaction of **8** with 2,3-dimethylbutadiene showed only a single isomer formed on reaction at room temperature for 24 h (entry 13), but only 20% of the substrate was consumed. Conducting the reaction at 80° C resulted in 85% conversion over 24 h, the selectivity was reduced to 14/1 (entry 12). When the reaction was conducted at 120° C for 24 h, the selectivity was reduced to 2.1/1.0, but the starting material was completely consumed (entry 11). Partial product equilibration probably occurs at this temperature (see below). Heating the mixture of isomers **21-trans/cis** at 140° C for seven days in a sealed tube reduced the ratio of isomers to 1.8/1.0—presumably the thermodynamic ratio. Consistent with observations reported for **4c**, Diels-Alder reaction of **8** with cyclopentadiene at room temperature consumed all of the starting material and produced only a single isomer **20-trans** (entry 10). Heating that sample for seven days at 140° C in a sealed tube did not result in the appearance of a second isomer.

From these results, it is uncertain whether the absence of a second isomer in the cyclopentadiene reaction means it was greatly disfavored in the equilibrium, or whether its absence is due to high stereoselectivity in the bond forming reaction coupled with a high barrier to rotation in the product. To determine which, we melted the preformed Diels-Alder product of cyclopentadiene and maleic anhydride with di-*tert*-butylphenyl amine (Eq. 4). This again produced **20-trans** with a small contaminent (<5%) whose identity could not be ascertained. Based on these experiments, it is probable the **20-trans** is highly favored at equilibrium and it is also favored kinetically in the Diels-Alder reaction.

Eq. 4



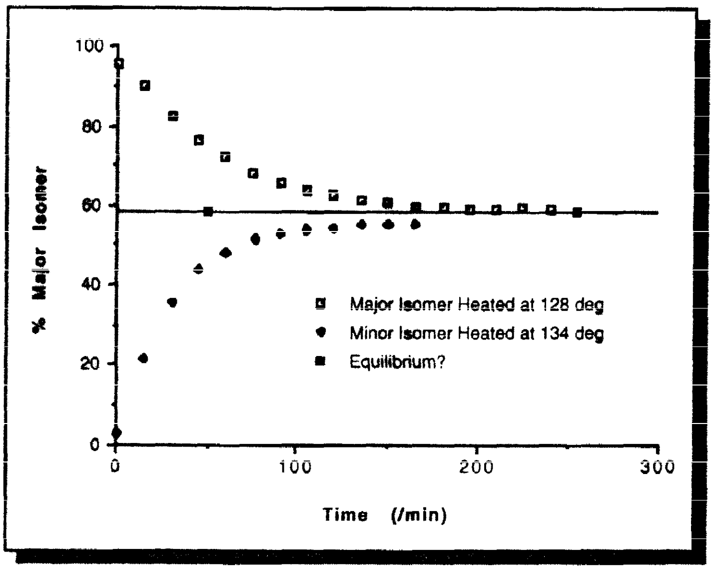
20-trans

Giese reactions of **8** with various alkyl mercuric chlorides were conducted at 25°C and 0°C, but the temperature effects were small (Table 2, entries 1-5). The requirement for water to initiate this reaction detered us from conducting reactions at lower temperatures. Selectivities varied widely with the size of the attacking radical: *tert*-butyl radical gives good selectivity (12.5/1, entry 1), cyclohexyl radical gives intermediate selectivity (3.5/1, entry 3) and hexyl radical gives poor selectivity (1.7/1, entry 5). Thermodynamic ratios (in brackets) were much lower, but followed the same trend. A wider range of selectivities as a function of temperature were observed with nitrile oxide reactions (Table 2, entries 6-9). The modest 3/1 selectivity in favor of **19-trans** at 25°C increased to 11.4/1 at –78°C, although this reaction was very slow.

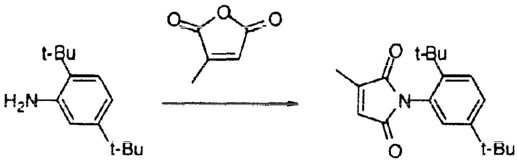
The nitrile oxide products **19-trans/cis** were further examined to provide information on the barrier to interconversion of the products. The individual isomers were separated by preparative HPLC with 20% ethyl acetate in hexanes. Samples of the major isomer **19-trans** and the minor isomer **19-cis** in *tert*-butyl benzene were heated at 128-134°C and the rate of interconversion was followed by analytical HPLC. The isomers slowly come to an equilibrium ratio of 58/42 (Figure 9). The major isomer at equilibrium is the same as that favored kinetically. From this data, we calculated the rate constants of epimerization of both the favored and disfavored isomers, the barriers to rotation from each isomer, and the difference in energy of the two atropisomers. Standard treatment of these data gave an average (forward and reverse) rotation barrier, $\Delta G^{\ddagger} \approx 27.5$ kcal/mol. This value compares favorably with the value of 28.5 kcal/mol reported by Kishikawa and coworkers for related compounds.[19]

A chiral (racemic) analog of **8** was then prepared by condensing citraconic anhydride with 2,5-di-*tert*-butyl aniline (Eq. 5). Unlike the maleic anhydride, citraconic anhydride is a liquid. Mixing the solid aniline with a threefold excess citraconic anhydride at room temperature resulted in an exothermic reaction, and a solid began to appear within minutes. But it was still necessary to heat the reaction at 120°C to achieve complete conversion to **22**.

Figure 9. Thermal Equilibration of 19-trans/cis (major/minor)



Eq. 5

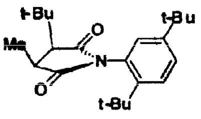
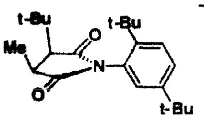
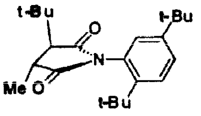
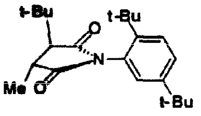
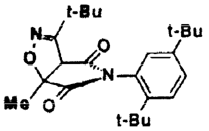
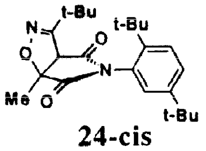
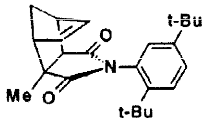
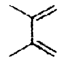
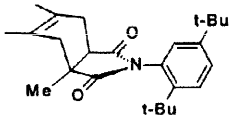
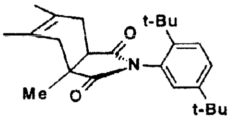


8 **22**, 22%

We then conducted a sampling of radical and cycloaddition reactions with **22** that paralleled the reactions of **8** and the results of this sampling are shown in Table 3. Once again, a single (racemic) product, **25-trans**, was observed in the Diels-Alder reaction with cyclopentadiene (entry 3). At room temperature, moderate selectivity was observed in the nitrile oxide cycloaddition: **24-trans/cis**, 2.8/1 (entry 2). The Diels-Alder reaction of **22** with 2,3-dimethylbutadiene did not occur at 45°C, but provided a 3.0/1 ratio of **26-trans/cis** at 120°C (entry 4). At this temperature, partial equilibration may occur, so this is probably not the true kinetic ratio.

The addition of *t*-butyl radical (entry 1 and Eq. 6) provides an interesting case study. Four isomers are possible: two from the initial addition of the *t*-butyl radical and an additional two from the ensuing hydrogen transfer step. The outcome of the first step is clear based on the prior results; the *t*-butyl radical will largely add trans to the *o*-*t*-butyl group on the aryl ring. But the outcome of the hydrogen transfer reaction is, a priori, unclear since 1,2-asymmetric induction from the newly introduced *t*-butyl group opposes the face shielding by the *o*-*t*-butyl group. When the reaction with *t*-BuHgCl was conducted at 25°C, four isomers formed in a kinetic ratio of **23a-d** of 20.5/17.0/3.6/1. When the mixture was heated at 140°C, these isomers then equilibrated in pairs, **23a** with **23b** and **23c** with **23d**, to a final ratio of 9.8/3.9/1.6/1. The two cis isomers (**23a,c**) and the two trans isomers (**23c,d**) are readily identified by their coupling constants ($J_{1,2cis}$ = 8 Hz, $J_{1,2trans}$ = 4 Hz). This information, coupled with the reasonable assumption that the major product must result from trans attack of the *t*-butyl radical, then provides a complete structural assignment.

Table 3. Atroposelective Reactions of 22

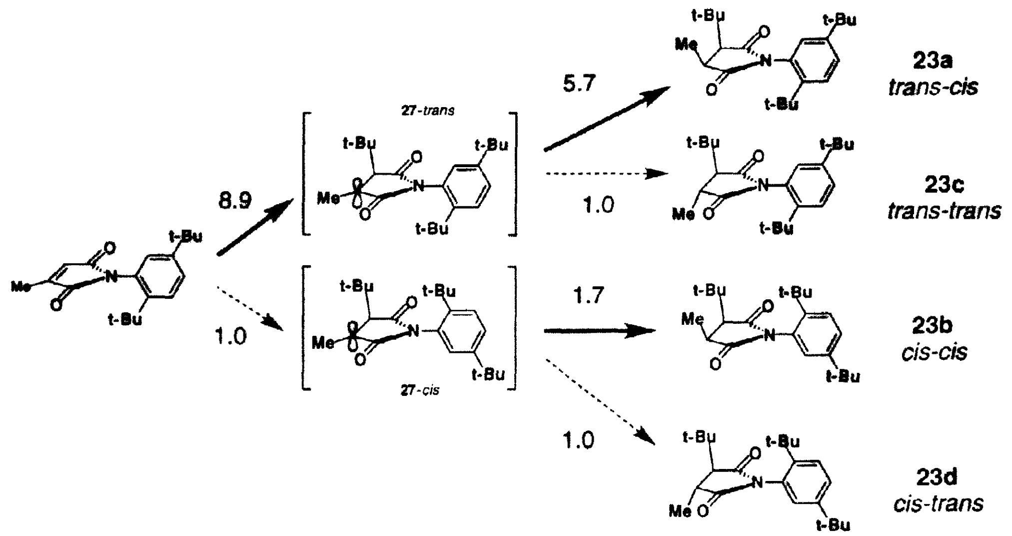
Entry	Reaction	Products (favored)	(disfavored)	Temp (/°C)	Kinetic Ratio *[equilibrated]*
1	Giese Reaction with t-BuHgCl	 **23a**	 **23b**	25	20.5/17 [*9.8/3.9*]
		 **23c**	 **23d**		3.6/1.0 [*1.6/1.0*]
2	Addition of t-Bu Nitrile Oxide	 **24-trans**	 **24-cis**	25	2.8/1.0
3	Diels-Alder Reaction with 	 **25-trans**		25	only one isomer observed[a]
4	Diels-Alder Reaction with 	 **26-trans**	 **26-cis**	120 45	3.0 : 1.0 : 3.0[b] no reaction

(a) This sample was subsequently heated at 140°C for 7 days, but still showed only a single isomer by ^1H NMR. (b) The third quantity represents unreacted starting material after 24h

The complete analysis of this reaction is shown in Eq. 6. The major product **23c**, which accounts for about 80% of the total, results from radical addition trans to the *o*-*t*-butyl group followed by hydrogen transfer cis to that group. The selectivity in the hydrogen transfer step of **27-trans** to give **23c/23d**) is about 5.7/1 with 1,2-induction dominating.[11] This is not surprising since Giese has shown that high 1,2-induction results when the *t*-butyl radical is added to citraconic anhydride[20] and based on the results in this paper we would expect a relatively low level of control by the *o*-*t*-butyl group in a radical hydrogen transfer from mercuric hydride (a small reagent). The ratio of **23c,d/23a,b** is about 8.9/1 and this reflects the selectivity in the radical addition in the first step. The only problem in this analysis is that there would appear to be too much **23d**. Since atroposelectivity and 1,2-induction are matched in the reaction of **27-cis**, we expected a very high selectivity in this case. But a rather low selectivity was observed. However, this is the ratio of two minor products, so we cannot be completely confident that the analysis is accurate.

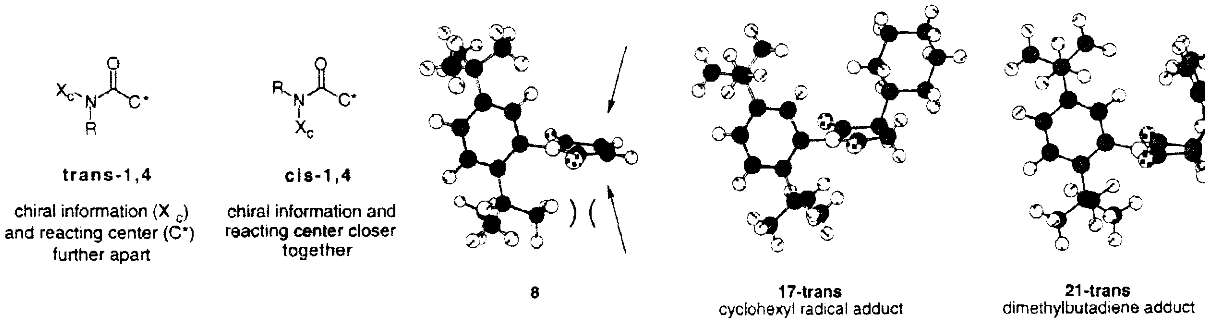
All the reactions reported in Table 3 were conducted with racemic **23**; however, very recently Kitagawa and coworkers[21] have reported a synthesis of one of the enantiomers of **23** from malic acid, so these adducts and others can now be made in enantiopure form.

Eq. 6



X-Ray crystal structures were solved for two of the major adducts, **17-trans** and **21-trans**, and these are shown in Figure 10 alongside a crystal structure of the starting maleimide **8**. Coupled with the results, these structures provide a number of insights into the chemistry of this class of molecules. First, the additional *m*-*t*-butyl group that was added in going from **4c** to **8** appears to be essentially inconsequential. The crystal structures show that it is remote from the site of stereoselection, as expected, and selectivities with **8** are very similar to that of **4c**.[1]

Figure 10. Crystal Strucutres and Transition State Models



8

17-trans cyclohexyl radical adduct

21-trans dimethylbutadiene adduct

Second, the simple model of reagents adding trans to the *o*-*t*-butyl group is well supported. The face shielding that is observed is significant, especially considering that most asymmetric reactions of amides and imides bear the chiral information (X_C) and the reacting center in a "cis-1,4" relationship (Figure 10). The "trans-1,4" relationship in **8** and **22** holds these two features further away, so this is a demanding test of stereocontrol. Best selectivities are observed when the incoming reagent must place a substituent over the imide ring. The high selectivity in Diels-Alder reactions is observed because an endo TS with attack cis to the *o*-hydrogen is relatively unhindered, while there are serious interactions between the diene and the *o*-*t*-butyl group if attack occurs on the other face. This is especially true in the reaction with cyclopentadiene, where the interactions persist in the product and lead to a large thermodynamic preference as well as a kinetic one. The significantly improved selectivity in additions of tertiary-radicals of over secondary and primary can likewise be interpreted. Assuming that the forming bond is staggered,[22] the tertiary radical must place an alkyl substituent over the ring, while less substituted radicals can place only a hydrogen atom, thereby facilitating attack on the more hindered side. Likewise, nitrile oxide cycloadditions are roughly planar, and can minimize (but not eliminate) unfavorable interactions with the *o*-*t*-butyl group in attack on the more hindered face.

Conclusions

These results suggest good potential for asymmetric reactions of axially chiral *N*-phenyl imides bearing either an *o*-*tert*-butyl group or another substituent of comparable size. Selectivities are especially high when the reaction occurs with a substituent over the ring in close proximity with the *t*-butyl group. In principle, the approach should be generalizable to lactams and other heterocycles as well. Although some progress has recently been made,[15,19] improved, general methods for the synthesis of enantiomerically pure substrates are still needed. If the *N*-aryl groups are to be used as chiral auxiliaries, methods of removal are also needed. Spurring research in this area is the predictability of the reaction outcome. In the past, asymmetric induction involving cyclic, sp^2-hybridized nitrogen atoms has usually been accomplished by appending an sp^3 stereogenic center (Figure 6). While good selectivities have been identified, the free rotation about the amide-auxiliary bond makes predictions difficult. The "locked" nature of the sp^2-sp^2 attachment should allow reliable prediction of the major isomer.

Figure 11. Comparing sp^3 and sp^2 Induction

sp^3-sp^2 connection free rotation makes predictions difficult

sp^2-sp^2 connection locking makes predictions easy

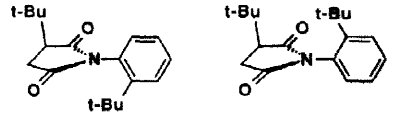
Experimental

***N*-(2-*tert*-Butylphenyl)maleimide (4c)**: 2-*tert*-Butyl aniline (1 mL, 6.4 mmol) and maleic anhydride (1.9 g, 19.2 mmol) were mixed in a high pressure vessel which was capped with a teflon screw. The mixture turned immediately red as the two reagents were mixed, and gave off heat. The vessel was submerged in a 120° C oil bath overnight. The next day, the mixture had become a white solid, and was dissolved in ethyl acetate, filtered through a short silica gel column and concentrated. The residue was purified by column chromatography (10% ethyl acetate in hexanes). *N*-(2-*tert*-butylphenyl) maleimide: mp 89-90° C; ^{1}H-NMR ($CDCl_3$) δ 7.96 (1 H, d, J = 7.9), 7.78 (1 H, t, J = 7.6), 7.65 (2 H, m), 7.29 (2 H, s), 1.67 (9 H, s); IR (NaCl) 3492, 1732, 1646, 945; HRMS calculated 229.1103, found 229.1103.

***N*-(2-*iso*-Propylphenyl)maleimide (4b)**: The above protocol used in the preparation of *N*-(2-*tert*-butylphenyl)maleimide. 2-*iso*-Propyl aniline (1 mL, 7.0 mmol) and maleic anhydride (2.1 g, 21.2 mmol) were combined to generate *N*-(2-*iso*-propylphenyl)maleimide (1.0 g, 66%): mp 85-86° C; R_f (20% EtOAc in Hexanes) 0.29; ^{1}H-NMR ($CDCl_3$) δ 7.81 (2 H, d, J = 4.2), 7.65 (1 H, m), 7.43 (1 H, d, J = 7.8), 7.24 (2 H, s), 3.08 (1 H, quint, J = 6.8), 1.56 (6 H, d, 6.8); ^{13}C-NMR ($CDCl_3$) δ 170 (2 C), 147, 134 (2 C), 130, 129, 128, 127, 29, 24 (2 C); IR (NaCl) 3004, 1738, 1509, 1460, 1422, 1183, 857, 718; MS *m/e* 215 (M, 100%), 200 (M - [CH_3], 32%), 186 (17%), 172 (M - [i-Pr], 60%), 154 (18%), 144 (16%), 132 (32%), 118 (22%), 103 (09%), 91 (16%), 77 (29%), 65 (09%); HRMS calculated 215.0946, found 215.0946.

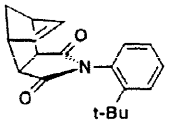
N-(2-Ethylphenyl)maleimide (4a): The above protocol used in the preparation of *N*-(2-*tert*-butylphenyl)maleimide. 2-Ethyl aniline (1 mL, 8.1 mmol) and maleic anhydride (2.4 g, 24.3 mmol) were combined to generate *N*-(2-ethylphenyl)maleimide: mp 51° C; R_f (20% EtOAc in Hexanes) 0.24; ^{1}H-NMR ($CDCl_3$) δ 7.35 (m, 3H), 7.1 (1 H, d, *J* = 8), 6.85 (2 H, s), 2.5 (2 H, q, *J* = 9), 1.2 (3 H, t, *J* = 9); ^{13}C-NMR ($CDCl_3$) δ 170.1 (2 C), 142.6, 134.5 (2 C), 129.9, 129.6, 129.5, 129.2, 127.0, 24.5, 24.4; IR (NaCl) 3471, 2974, 1716, 1396, 1149; MS *m/e* 201 (M, 100%), 186 (M – [CH_3], 12%), 183 (14%), 172 (M – [CH_3CH_2], 18%), 158 (27%), 144 (11%), 130 (25%), 118 (19%), 104 (23%), 91 (11%); HRMS calculated 201.0790, found 201.0788.

3-*tert*-Butyl-1-(2-*tert*-butylphenyl)-pyrrolidine-2,5-dione (6c, Table 1, entry 2).



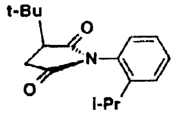
N-(2-*tert*-butylphenyl)maleimide **4c** (100 mg, 435 µmol), sodium borohydride (125 mg, 3.25 mmol) and *tert*-butyl mercuric chloride (150 mg, 525 µmol) were mixed before adding dichloromethane (5 mL) and setting the reaction vessel in a room temperature water bath. After flushing the vessel with argon, an exothermic reaction was initiated by injecting 150 µL of water (160 mg, 8.75 mmol) into the vessel. Significant gas evolution was observed for less than 2 min, before thin layer chromatography (20% ethyl acetate in hexanes) indicated complete consumption of starting material and formation of two products. The reaction mixture was filtered through a Florasil plug to remove excess water, elemental mercury and solid byproducts. The mixture was then concentrated, and subsequent ^{1}H NMR of the resulting 102 mg (68%) of white solid indicated the presence of only two atropisomers. The atropisomers were separated by column chromatography (10% ethyl acetate in hexanes). Major isomer (**6c-trans**): mp 86° C; ^{1}H-NMR ($CDCl_3$) δ 7.58 (1 H, dd, *J* = 1.1, 8.2), 7.39 (1 H, td, *J* = 1.3, 7.0), 7.27 (1 H, td, *J* = 1.4, 7.5), 6.79 (1 H, dd, *J* = 1.4, 7.7), 2.86 (1 H, qn, *J* = 7.7), 2.75 (2 H, m), 1.30 (9 H, s), 1.14 (9 H, s); ^{1}H-NMR (C_6H_6) δ 7.36 (1 H, dd, *J* = 1, 8.6), 7.09 (1 H, td, *J* = 1.3, 7.7), 6.97 (1 H, td, *J* = 1.1, 7.6), 6.77 (1 H, dd, *J* = 1.4, 7.7), 2.20 (1 H, dd, *J* = 2.0, 6.8), 2.10 (1 H, m), 1.29 (9 H, s), 0.83 (9 H, s); ^{13}C-NMR ($CDCl_3$) δ 178.6, 176.8, 147.9, 130.5, 130.3, 129.6, 128.9, 127.3, 49.9, 35.6, 33.8, 32.2, 31.5, 27.1. Minor isomer (**6c-cis**): ^{1}H-NMR ($CDCl_3$) δ 7.62 (1 H, d), 7.40 (1 H, m), 7.27 (1 H, m), 6.83 (1 H, d), 2.9 (1 H, m), 2.8 (2 H, m), 1.3 (9 H, s), 1.2 (9 H, s). Atropisomeric mixture: IR (NaCl) 2964, 1708, 1375, 1180, 758; ; MS *m/e* 287 (M, 45%), 272 (M – [CH_3], 100%), 230 (47%), 216 (19%), 198 (11%), 175 (35%); HRMS calculated 287.1885, found 287.1876.

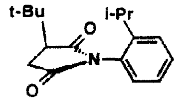
4-(2-*tert*-Butylphenyl)-4-aza-tricyclo [5.2.1.0.2.6] dec-8-ene-2,5-dione (7c, Table 1, entry 2).



N-(2-*tert*-Butylphenyl)maleimide **4c** (40 mg, 175 µmol) was dissolved in dichloromethane (2.0 mL) before adding cyclopentadiene (72 µL, 870 µmol). The solution was stirred for 2 h and then concentrated. After 1 h under high vacuum, the white solid product was purified by column chromatography (20% ethyl acetate in hexanes) to yield 44 mg (85%) of a single atropisomer **6c-trans**: ^{1}H-NMR ($CDCl_3$) δ 7.52 (1 H, dd), 7.34 (1 H, td), 7.20 (1 H, td), 6.66 (1 H, dd), 6.31 (2 H, t), 3.45 (4 H, m), 1.78 (1 H, dt), 1.59 (1 H, d), 1.28 (9 H, s); ^{13}C-NMR ($CDCl_3$) δ 178.4 (2 C), 148.2, 135.2 (2 C), 131.0, 130.8, 129.8, 128.7, 127.4, 52.5, 46.2 (2 C), 45.4 (2 C), 35.7, 31.8 (3 C); IR (NaCl) 2966, 1714, 1492, 1440, 1373, 1190, 767; MS *m/e* 295 (M, 27%), 280 (M – [CH_3], 10 %), 277 (13%), 238 (M – [C_3H_9], 21%), 229 (M – [C_5H_6], 4%), 226 (5%), 214 (100%), 196 (11%), 172 (45%); HRMS calculated 295.1572, found 295.1584.

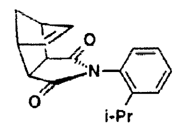
3-*tert*-Butyl-1-(2-*iso*-Propylphenyl)-pyrrolidine-2,5-dione (6b, Table 1, entry 3).

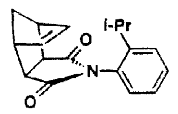




The procedure for the preparation of 3-*tert*-butyl-1-(2-*tert*-butylphenyl)-pyrrolidine-2,5-dione **6c** was repeated with *N*-(2-*iso*-propylphenyl)maleimide **4b** (40 mg, 185 µmol), sodium borohydride (55 mg, 1.3 mmol), *tert*-butyl mercury chloride (65 mg, 225 µmol) and water (75 µL) in CDCl$_3$ (2 mL). TLC with 20% ethyl acetate in hexanes revealed two products (R_f = 0.27, 0.43). These isomers could be separated by rapid column chromatography (10% ethyl acetate in hexanes); however, the pure samples equilibrated to an atropisomeric mixture within minutes of separation. Therefore they were characterized as a mixture of atropisomers **6b-trans/cis**. Atropisomeric Mixture: ^{1}H-NMR (CDCl$_3$) δ 7.48 (4 H, d), 7.3 (2 H, m), 7.02 (1 H, d), 6.96 (1 H, d), 2.85 (8 H, m), 1.2 (30 H, m); ^{1}H-NMR (C$_6$D$_6$) δ 7.2 (8 H, m), 2.5 (4 H, m), 2.2 (4 H, m), 1.9 (2 H, d of t), 1.14 (6 H, q, *J* = 7.4), 0.93 (9 H, s), 0.91 (9 H, s); ^{13}C-NMR (CDCl$_3$) δ 177.9 (minor), 177.8 (major), 176.1 (minor), 176.0 (major), 146.2 (minor), 146.0 (major), 129.9 (minor), 129.8 (major), 128.14 (major), 128.07 (minor), 126.8, 126.7, 126.5, 50.2, 49.9, 33.8, 33.4, 32.0, 31.9, 28.6, 28.5, 27.2 (3 C), 27.1 (3 C), 23.8, 23.7, 23.6, 23.3; IR (NaCl) 2966, 1708, 1490, 1454, 1378, 1188; MS *m/e* 273 (M, 100%), 258 (M – [CH$_3$], 21%), 216 (M – [t-Bu], 83%), 202 (13%), 175 (29%); HRMS calculated 273.1729, found 273.1722.

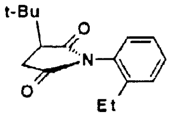
4-(2-*iso*-Propylphenyl)-4-aza-tricyclo [5.2.1.0.2.6]dec-8-ene-2,5-dione (7b, Table 1, entry 4).

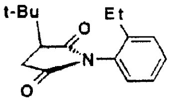




The protocol for the preparation of 4-(2-*tert*-butyl-phenyl)-4-aza-tricyclo [5.2.1.0.2.6]dec-8-ene-2,5-dione **4c** was repeated with *N*-(2-*iso*-propylphenyl) maleimide **4b** (40 mg, 185 µmol) and cyclopentadiene (77 µL, 0.92 mmol) in dichloromethane (2 mL). The isomers **6b-trans/cis** were inseparable by chromatography, but the minor isomer **6b-cis** was crystallized from the mixture in diethyl ether. The minor product returned to an equilibrium mixture of atropisomers on standing at room temperature solution for 3 h. Major: ^{1}H-NMR (CDCl$_3$) δ 7.39 (1 H, d, J = 3.9), 7.24 (1 H, m), 6.81 (1 H, d, J = 7.8), 6.30 (1 H, d, J = 5.5), 3.5 (3 H, m), 2.68 (2 H, qn, J = 6.8), 1.80 (1 H, d, J = 8.7), 1.61 (1 H, d, J = 8.0). Minor: ^{1}H-NMR (CDCl$_3$) δ 7.39 (1 H, d, J = 3.9), 7.24 (1 H, m), 6.92 (1 H, d, J = 7.7), 6.30 (1 H, d, J = 5.5), 3.5 (3 H, m), 2.71 (2 H, qn, J = 6.8), 1.82 (1 H, d, J = 8.6), 1.64 (1 H, d, J = 8.2). Atropisomeric mixture: ^{13}C-NMR (CDCl$_3$) δ 177.6, 177.3, 146.7, 146.4, 135.4, 134.8, 130.0, 128.6, 128.2, 127.0, 126.9, 126.8, 126.7, 53.1, 52.5, 47.0, 46.0, 45.6, 45.4, 28.7, 28.3, 23.8, 23.7; IR (NaCl) 2967, 2870, 1707, 1493, 1451, 1373, 1185; MS *m/e* 281 (M, 59%), 263 (10 %), 248 (6%), 215 (M ..– [C$_5$H$_6$], 200 (26%), 172 (32%); HRMS calculated 281.1416, found 281.1408.

3-*tert*-Butyl-1-(2-Ethyl-phenyl)pyrrolidine-2,5-dione (6a, Table 1, entry 5).

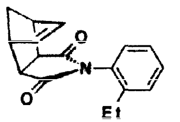


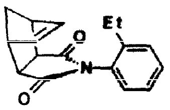


The procedure for the preparation of 3-*tert*-butyl-1-(2-*tert*-butyl-phenyl)-pyrrolidine-2,5-dione **6c** was repeated with *N*-(2-ethylphenyl) maleimide **4a** (40 mg, 200 µmol), sodium borohydride (55 mg, 1.2 mmol), *tert*-butyl mercury chloride and water (75 µL) in deuterated chloroform (2 mL). TLC (20% ethyl acetate in hexanes) indicated two products (R_f = 0.24, 0.34). It was not possible to separate these interconverting isomers. Major: ^{1}H-NMR (CDCl$_3$) δ 7.37 (2H, m), 7.29 (1 H, t, J = 6.9), 7.01, (1 H, d, J = 7.9), 2.85 (3 H, m), 2.42 (2 H, m), 1.17 (2 H, d, J = 7.7), 1.14 (9 H, s). Minor: ^{1}H-NMR (CDCl$_3$) δ 7.37 (2 H, m), 7.28 (1 H, t, J = 7.1), 6.97 (1 H, d, J = 8.6), 2.85 (3 H, m), 2.42 (2 H, m), 1.18 (2 H, d, J = 7.5), 1.13 (9 H, s). Atropisomeric mixture: ^{1}H-NMR (C$_6$D$_6$) δ 7.2 (8 H, m), 2.5 (4 H, m), 2.2 (4 H, m), 1.9 (2 H, d of t), 1.14 (6 H, q, *J* = 7.4), 0.93 (9 H, s), 0.91 (9 H, s); ^{13}C-NMR (CDCl$_3$) δ 177.8, 176.0 (major), 175.9 (minor), 141.4 (major), 141.3 (minor), 130.7, 129.8 (minor), 129.7 (major), 129.3, 128.2, 127.0, 50.3, 50.1, 33.9 (minor), 33.6 (major), 32.1 (minor), 32.0 (major), 27.3 (major), 27.1

(minor), 24.2, 24.1, 14.3, 14.1; IR (NaCl) 2964, 2256, 1706, 1380, 1195, 906, 728; MS *m/e* 267 (M, 68%), 201 (100 %); HRMS calculated 259.1572, found 259.1560.

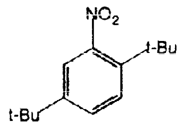
4-(2-Ethylphenyl)-4-aza-tricyclo [5.2.1.0.2.6]dec-8-ene-2,5-dione (7a, Table 1, entry 6).





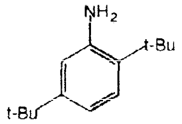
The protocol for the preparation of 4-(2-*tert*-butyl-phenyl)-4-aza-tricyclo [5.2.1.0.2.6]dec-8-ene-2,5-dione **6c** was repeated *N*-(2-ethylphenyl) maleimide **4a** (40 mg, 200 μmol) and cyclopentadiene (82 μL, 1.0 mmol) in dichloromethane (2 mL). Isomer separation was impractical. Major isomer: ^{1}H-NMR ($CDCl_3$) δ 7.38 (2 H, m), 7.26 (1 H, m), 6.85 (1 H, d, *J* = 8), 6.60 (1 H, m), 6.50 (1 H, m), 3.5 (2 H, m), 3.0 (2 H, m), 2.45 (2 H, m), 1.82 (1 H, d, *J* = 8), 1.68 (1 H, d, *J* = 8), 1.16 (3 H, t, *J* = 8). Minor isomer: ^{1}H-NMR ($CDCl_3$) δ 7.39 (2 H, m), 7.26 (1 H, m), 6.98 (1 H, d, *J* = 8), 6.60 (1 H, m), 6.50 (1 H, m), 3.5 (2 H, m), 3.0 (2 H, m), 2.45 (2 H, m), 1.88 (1 H, d, *J* = 8), 1.62 (1 H, d, *J* = 8), 1.14 (3 H, t, *J* = 8). Atropisomeric mixture: ^{13}C-NMR ($CDCl_3$) δ 177.4, 177.2, 141.8, 141.6, 135.4 (2 C), 134.8 (2 C), 130.8, 129.9, 129.6, 129.3, 128.7, 128.3, 127.1, 127.0, 53.1, 52.5, 47.0 (2 C), 46.0 (2 C), 45.7 (2C), 45.4, 24.7, 24.3, 15.0, 14.3; IR (NaCl) 2971, 2941, 1709, 1494, 1453, 1374, 1185; MS *m/e* 267 (M, 10%), 201 (M – [C_5H_6], 15%), 84 (100%); HRMS calculated 267.1259, found 267.1266.

1,4-Di-*tert*-butyl-2-nitrobenzene 13.



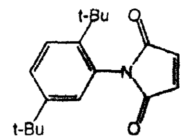
Nitric acid (200 mL) was added neat to 1,4-di-*tert*-butylbenzene (53 mmol, 10 g) at 0°C, and the reaction mixture was stirred for 8 h. The solution was diluted with water (100 mL) and extracted 4 times with portions of dichloromethane (200 mL). Each extract was washed with water (100 mL) and 50% saturated K_2CO_3 (100 mL), before combining, drying over magnesium sulfate, filtering, and concentrating the extracts. Column chromatography (10% ethyl acetate in hexanes) of the residue yielded two products, oily 1-*tert*-butyl-4-nitrobenzene and solid 1,4-di-*tert*-butyl-2-nitrobenzene **6** (33 mmol, 7.82 g, 62 %): mp 88-89° C; ^{1}H-NMR ($CDCl_3$) δ 7.48 (2 H, s), 7.28 (1 H, s), 1.40 (9 H, s), 1.32 (9 H, s); MS *m/e* 235 (M, 8.4%), 220 (M – [CH_3], 37%), 175 (4.8%), 160 (4.0%), 131 (9.5%), 127 (9.0%), 117 (13%), 91 (20%), 77 (15%), 69 (12%), 65 (8.9%), 57 (57%), 43 (69%), 41 (100%). 1-*tert*-butyl-4-nitrobenzene **7**: MS *m/e* 179 (M, 21%), 164 (M – [CH_3], 100%), 115 (18%), 106 (20%), 103 (12%), 91 (30%), 77 (23%), 63 (26%), 51 (24%), 46 (61%), 41 (39%).

2,5-Di-*tert*-butylaniline 15.[18]



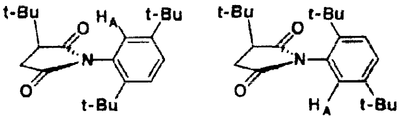
Iron powder (107 mmol, 6.0 g), 12N HCl (4.2 mmol, 360 μL), and 1,4-di-*tert*-butyl-2-nitrobenzene **6** (17 mmol, 4.0 g) were refluxed in 50% aqueous ethanol (100 mL) for 2 d. The mixture was cooled to room temperature and potassium hydroxide (8.4 mmol, 500 mg) in water (20 mL) was slowly added with stirring. The solution was filtered through celite, the celite was washed three times with portions of ethanol (100 mL). The ethanol portions were combined, concentrated, and the residue was taken up in dichloromethane. This solution was dried over magnesium sulfate, filtered, and concentrated. The solid residue was purified by flash column chromatography (10% ethyl acetate in hexanes) to yield 2,5-di-*tert*-butylaniline: mp 98-99° C; (13.4 mmol, 2.75 g, 79 %): ^{1}H-NMR ($CDCl_3$) δ 7.17 (1 H, d, *J* = 8.3), 6.77 (1 H, d of d, *J* = 2.1, 8.2), ~3.6 (2 H, very br s), 1.42 (9 H, s), 1.29 (9 H, s); MS *m/e* 205 (M, 13%), 190 (M – [CH_3], 24%), 175 (M – 2[CH_3], 3.4%), 162 (4.5%), 147 (M – [*tert*-butyl], 3.9%), 134 (8.4%), 115 (9.3%), 106 (9.3%), 91 (14%), 77 (11%), 69 (7.8%), 57 (30%), 41 (100%).

N-(2,5-Di-*tert*-butylphenyl) maleimide 8.



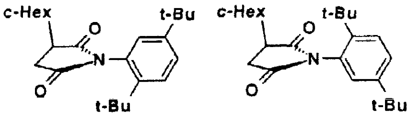
Maleic anhydride (25 mmol, 2.5 g) and 2,5-di-*tert*-butylaniline (4.9 mmol, 1.0 g) were melted together at 130° C. After 1 h, the liquid had solidified, and the red solid was cooled to room temperature before being dissolved in ethyl acetate. The solution was passed through a short silica gel column, before being concentrated to an oil and purified by flash column chromatography (10% ethyl acetate in hexanes) to isolate *N*-(2,5-di-*tert*-butylphenyl) maleimide **1** (2.65 mmol, 755 mg, 54%): mp 184-185° C; ^{1}H-NMR ($CDCl_3$) δ 7.51 (1 H, d, *J* = 8.4), 7.41 (1 H, d of d, *J* = 2.2, 8.6), 6.89 (2 H, s), 6.84 (1 H, d, *J* = 2.2), 6.84 (1 H, d, *J* = 2.2), 1.284 (9 H, s), 1.28 (9 H, s); ^{13}C-NMR ($CDCl_3$) δ 171.2 (2 C), 150.4, 146.3, 135.2 (2 C), 128.7, 128.5, 128.2, 127.3, 35.2, 34.4, 31.7 (3 C), 31.3 (3 C); IR (NaCl) 2962, 1716, 1411, 1369, 1147, 827, 752 692; MS *m/e* 285 (M, 34%), 270 (M - [CH_3], 100 %), 228 (M - [t-Bu], 40%), 196 (10%), 186 (11%), 172 (28%), 128 (12%), 115 (16%), 91 (12%), 77 (11%), 57 (60%), 41 (67%); HRMS calculated 285.1729, found 285.1721.

3-*tert*-Butyl-1-(2,5-di-*tert*-butylphenyl)-pyrrolidine-2,5-dione (16, Table 2, entry 1).



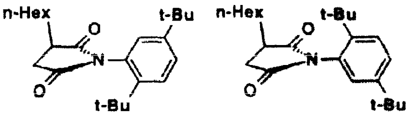
The procedure for the preparation of **7** (see below) was repeated with *N*-(2.5-di-*tert*-butylphenyl) maleimide **8** (100 mg, 0.33 mmol), *t*-butyl mercury chloride (120 mg, 0.40 mmol), sodium borohydride (100 mg, 2.50 mmol) and water (120 µL,, 6.68 mmol) in 5 mL dichloromethane (0.08 M). After 6 h, thin layer chromatography (20% ethyl acetate in hexanes) indicated complete consumption of starting material (R_f = 0.32), and formation of two products (R_f = 0.60, 0.45). ^{1}H-NMR spectroscopy of the residue showed two compounds with a ratio (based on intergration of H_A) of 12.5/1.0. The residue was dissolved in benzene, sealed in a tube, and heated at 120°C for 24 h. A ^{1}H-NMR spectrum then indicated a ratio of 2.5/1.0. The isomers were separated by column chromatography (10% ethyl acetate in hexanes eluent). Major isomer, **16-trans**: ^{1}H-NMR ($CDCl_3$) δ 7.47 (1 H, d, *J* = 8.4), 7.37 (1 H, d of d, *J* = 8.5, 2.1), 6.66 (1 H, d, *J* = 1.9), 2.8 (3 H, m), 1.26 (9 H, s), 1.25 (9 H, s), 1.13 (9 H, s); ^{1}H-NMR (C_6D_6) δ 7.39 (1 H, s, *J* = 8.6), 7.24 (1 H, dd, *J* = 8.5, 2.3), 6.97 (1 H, d, *J* = 2.3), 2.2 (3 H, m), 1.33 (9 H, s), 1.14 (9 H, s), 0.88 (9 H, s); ^{13}C-NMR ($CDCl_3$) δ 180.3, 177.1, 150.2, 144.6, 129.8, 128.4, 127.2, 126.9, 35.1, 34.8, 34.1, 31.6 (3 C), 31.12 (3 C), 31.06 (3 C), 29.0, 26.6. Minor isomer, **16-cis**: ^{1}H-NMR ($CDCl_3$) δ 7.50 (1 H, d, *J* = 8.5), 7.40 (1 H, dd, *J* = 8.4, 2.2), 6.73 (1 H, d, J = 2.2), 3.04 (2 H, d, J = 9.3), 2.95 (1 H, t, J = 9.0), 1.29 (9 H, s), 1.28 (9 H, s), 1.15 (9 H, s); ^{13}C-NMR ($CDCl_3$) δ 180.1, 177.15, 150.3, 144.7, 128.4, 127.4, 126.9, 31.6 (3 C), 31.5 (3 C), 31.1 (3 C), 35.3, 35.2, 34.2, 31.6, 31.1, 28.9, 27.4. Atropisomeric mixture: IR (NaCl) 2960, 2358, 1708, 1374, 1180, 758; MS *m/e* 343 (M, 10%), 286 (M - [*t*-Bu], 33%), 272 (100%), 230 (47%), 198 (11%), 175 (34%); HRMS calculated 343.2511, found 343.2460.

3-Cyclohexane-1-(2,5-di-*tert*-butylphenyl)pyrrolidine-2,5-dione (17, Table 2, entry 2).



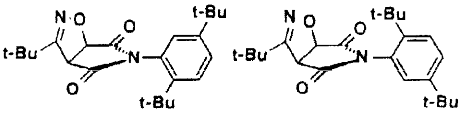
N-(2,5-Di-*tert*-butylphenyl) maleimide **8** (300 mg, 1.05 mmol), cyclohexyl mercury chloride (400 mg, 1.26 mmol) and sodium borohydride (300 mg, 7.88 mmol) were mixed and the flask was set in a room temperature water bath, before adding dry dichloromethane (13 mL, 0.08 M), under nitrogen. An exothermic reaction was initiated by adding water (120 µL, 6.68 mmol). After the effervescence ceased, thin layer chromatography (20% ethyl acetate in hexanes) indicated complete consumption of the starting material (R_f = 0.52) and the presense of two products (R_f = 0.63, 0.67). The reaction was filtered through Florasil to remove excess water, mercury, and solid byproducts. The crude reaction mixture was analyzed by ^{1}H NMR to determine the kinetic isomer ratio, before the sample was purified by column chromatography (10% ethyl acetate in hexanes eluent). The major isomer was isolated by crystalization from diethyl ether and pentane, and a crystal structure was solved. Trans isomer, **17-trans**: mp 191-192; ^{1}H-NMR (CDCl$_3$) δ 7.49 (1 H, d, *J* = 8.5), 7.39 (1 H, dd, *J* = 8.5, 2.1), 6.68 (1 H, d, *J* = 2.1), 2.95 (1 H, m), 2.82 (1 H, d, *J* = 9.4), 2.68 (1 H, dd, *J* = 9.4, 3.8), 2.12 (1 H, td), 1.70 (5 H, m), 1.59 (2 H, m), 1.28 (18 H, s), 1.21 (4 H, m); ^{13}C-NMR (CDCl$_3$) δ 179.9, 177.6, 150.4, 144.8, 130.1, 128.7, 127.4, 127.2, 46.9, 45.9, 35.4, 34.3, 31.8 (3C), 31.7, 31.3 (3C), 30.8, 27.7, 26.4, 26.2, 26.1. Cis isomer, **17-cis**: ^{1}H-NMR (CDCl$_3$) δ 7.50 (1 H, d, *J* = 8.5), 7.40 (1 H, dd, *J* = 8.5, 2.0), 6.73 (1 H, d, *J* = 2.0), 2.95 (1 H, m), 2.81 (1 H, d, *J* = 9.3), 2.68 (1 H, dd), 2.12 (1 H, m), 1.70 (5 H, m), 1.59 (2 H, m), 1.29 (18 H, s), 1.23 (4 H, m). Atropisomeric mixture: mp 190-193; IR (NaCl) 3022, 1711, 1213, 762, 667; MS *m/e* 259 (M, 66%), 244 (M - [CH$_3$], 20%), 203 (100%), 184 (12%) HRMS calculated 369.2668, found 369.2662.

3-Hexane-1-(2,5-di-*tert*-butylphenyl)-pyrrolidine-2,5-dione (18, Table 2, entry 5).



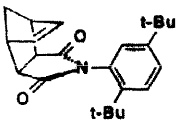
The above procedure was repeated with *N*-(2,5-di-*tert*-butylphenyl) maleimide **8** (100 mg, 0.35 mmol), *n*-hexyl mercury chloride (375 mg, 1.26 mmol), sodium borohydride (300 mg, 7.88 mmol), and water (375 μL, 20.9 mmol) in dichloromethane (2 mL). TLC (20% EtOAc in hexanes) indicated consumption of the starting material (R$_f$ = 0.47), and presence of two products (R$_f$ = 0.56, 0.60). The major isomer was isolated by column chromatography (5% EtOAc in hexanes). Major isomer, **18-trans**: ^{1}H-NMR (CDCl$_3$) δ 7.50 (1 H, d, J = 8.5), 7.39 (1 H, dd, J = 8.5, 2.2), 6.72 (1 H, d, J = 2.2), 3.05 (1 H, d, J = 9.3), 2.98 (1 H, d, J = 2.3), 2.58 (1 H, d, J = 2.3), 2.58 (1 H, dd, J = 17.5, 3.8), 2.05 (1 H, m), 1.65 (1 H, m), 1.4 (4 H, m), 1.33 (4 H, d, J = 5.5), 1.29 (9 H, s), 1.28 (9 H, s), 0.90 (3 H, t, J = 6.6): ^{13}C-NMR (CDCl$_3$) δ 180.6, 177.4, 150.5, 144.9, 130.2, 128.8, 127.6, 127.2, 40.6, 35.4, 35.1, 34.4, 31.9 (6 C), 31.5, 31.4, 29.3, 27.0, 22.8, 14.3. Minor isomer, **18-cis**: ^{1}H-NMR (CDCl$_3$) δ 7.52 (1 H, d, J = 8), 7.42 (1 H, d of d, J = 8, 2), 6.78 (1 H, d, J = 2), 3.05 (1 H, d, J = 9), 2.98 (1 H, m), 2.55 (1 H, dd), 2.05 (1 H, m), 1.85 (1 H, m), 1.4 (4 H, m), 1.3 (4 H, d), 1.29 (9 H, s), 1.28 (9 H, s), 0.92 (3 H, t). Atropisomeric mixture: IR (NaCl) 2958, 1710, 1410, 1357, 1178, 754; MS *m/e* 371 (M, 16%), 356 (M – [CH$_3$], 100%), 314 (10%), 300 (8%), 231 (9%), 186 (5%); HRMS calculated 371.2824, found 371.2850.

1-(3-*tert*-Butyl-4,5-dicarboximido[d] isoxazole)-2,5-di-*tert*-butyl benzene (19, Table 2, entry 7).



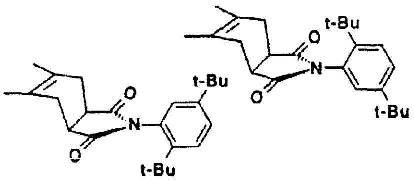
N-(2,5-Di-*tert*-butylphenyl) maleimide **8** (530 μmol, 150 mg) and *tert*-butyl hydroximoyl chloride (790 μmol, 110 mg) were dissolved in chloroform (5 mL, 100 mM in *N*-(2,5-di-*tert*-butylphenyl) maleimide) with TEA (950 μmol, 130 μL) and the mixture was refluxed for 2 h. The reaction mixture was concentrated, and the residue was taken up in diethyl ether, and filtered. The ether solution was concentrated and purified by column chromatography (10% EtOAc in hexanes). The two isomers of 1-(3-*tert*-butyl-4,5-dicarboximido[d]isoxazole)-2,5-di-*tert*-butyl benzene (390 μmol, 150 mg, 74 %) were separated by HPLC with a 10% EtOAc in hexanes eluent. To determine the barrier to atropisomerization, pure samples of the major and minor isomers of 1-(3-*tert*-butyl-4,5-dicarboximido[d]isoxazole)-2,5-di-*tert*-butyl benzene (6 mg) were dissolved in *tert*-butyl benzene (2 mL) and heated in an oil bath at the appropriate temperature (See Figure 9). At 15 minute intervals, 10 μL of solution was removed by syringe. The ratio of isomers in these samples were determined analytical HPLC (12% EtOAc in hexanes, 5 mL/min; UV 0.2 sensitivity, 254 nm). Major isomer, **19-trans**: mp 215-216° C; ^{1}H-NMR (CDCl$_3$) δ 7.51 (1 H, d, *J* = 8.6), 7.42 (1 H, dd, *J* = 8.4, 2.1), 6.63 (1 H, d, *J* = 2.13), 5.36 (1 H, d, *J* = 9.9), 4.41 (1 H, d, *J* = 10.3), 1.33 (9 H, s), 1.28 (9 H, s), 1.24 (9 H, s); ^{13}C-NMR (CDCl$_3$) 172.2, 171.56, 160.46, 150.63, 144.87, 129.18, 128.50, 127.25, 80.56, 77.42, 76.99, 76.55, 56.26, 35.24, 34.20, 33.84, 31.42, 31.03, 29.09. Minor isomer, **19-cis**: mp 216-217° C; ^{1}H-NMR (CDCl$_3$) δ 7.50 (1 H, d, *J* = 8.6), 7.42 (1 H, dd, *J* = 8.4, 2.1), 6.77 (1 H, d, *J* = 2.16), 5.49 (1 H, d, *J* = 9.7), 4.60 (1 H, d, *J* = 9.3), 1.36 (9 H, s), 1.29 (9 H, s), 1.24 (9 H, s); ^{13}C-NMR (CDCl$_3$) 173.27, 171.85, 161.40, 150.66, 144.61, 128.76, 127.40, 126.63, 79.72, 56.07, 35.27, 34.10, 34.04, 31.61, 30.93, 28.35. Atropisomeric mixture: IR (NaCl) 2962, 1716, 1402, 1359, 1193, 731; MS *m/e* 384 (M, 7%), 369 (M – [CH_3], 32 %), 270 (8 %), 216 (7%); HRMS calculated 384.2413 (M), 369.2178 (M – [CH_3], found 384.2418 (M), 369.2183 (M – [CH_3]).

1-(5-Norbornene-2,3-dicarboximido)-2,5-di-*tert*-butyl benzene (20, Table 2 entry 10).



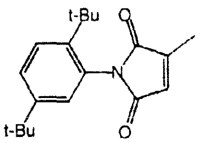
N-(2,5-Di-*tert*-butylphenyl) maleimide **8** (0.35 mmol, 100 mg) was dissolved in chloroform (7.5 mL) before adding cyclopentadiene (1.75 mmol, 145 µL). The solution was stirred for 2 h and then concentrated. After 1 h of drying under high vacuum, the white solid 1-(5-norbornene-2,3-dicarboximido)-2,5-di-*tert*-butyl benzene (0.31 mmol, 110 mg, 90 %) was purified by column chromatography (20% ethyl acetate in hexanes): mp 204-205° C; ¹H-NMR ($CDCl_3$) δ 7.44 (1 H, d, *J* = 8.5), 7.34 (1 H, dd, *J* = 2.2, 8.6), 6.62 (1 H, d, *J* = 2.2), 6.33 (2 H, t, *J* = 1.6), 3.52 (2 H, m), 3.44 (2 H, m), 1.8 (2 H, d, *J* = 8.9), 1.6 (2 H, d, *J* = 8.9), 1.45 (1 H, m), 1.30 (1 H, d, *J* = 2.2), 1.26 (18 H, s); MS *m/e* 351 (M), 336 (M – [CH_3]), 314, 294 (M – [*t*-Bu]), 270, 228, 214, 91, 66, 57. HRMS calculated 351.2198, found 351.2153.

2-(2,5-Di-*tert*-butylphenyl)-5,6-dimethyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione (21, Table 2, entry 11)



2,3-Dimethyl-1,3-butadiene (200 µl, 1.75 mmol) and *N*-(2,5-di-*tert*-butylphenyl) maleimide **8** (100 mg, 350 µmol) were dissolved in benzene (5 mL) and sealed with a magnetic stir rod in a glass tube. The sealed tube was heated to 120° C for 24 h (reactions at lower temperatures and shorter reaction times did not result in complete consumption of the starting material). The solution was concentrated and crude ¹H NMR analysis indicated complete consumption of starting material and two products in a 2.1/1.0 ratio. The isomeric ratio was reduced to 1.8/1.0 by heating the mixture at 140° for seven days. The products were separated by column chromatography (3% ethyl acetate in hexanes eluent) to 42.6 mg (33 %) of the major product and 16.2 mg (13 %) of the minor product. Major, **21-trans**: mp 154-155° C; ¹H-NMR ($CDCl_3$) δ 7.43 (1 H, d, *J* = 8.4), 7.33 (1 H, d of d, *J* = 8.5, 2.3), 6.42 (1 H, d, *J* = 2.2), 3.19 (2 H, m), 2.60 (2 H, d, *J* = 14.4), 2.27 (2 H, br d, *J* = 13.8), 2.00 (1 H, m), 1.75 (6 H, s), 1.25 (9 H, s), 1.23 (9 H, s), 0.87 (1 H, m); ¹³C-NMR ($CDCl_3$) δ 180.8 (2 C), 150.1, 144.7, 130.8, 128.1, 127.7 (2 C), 127.3, 126.7, 40.4 (2 C), 35.0, 34.0, 31.5 (3 C), 31.2 (2 C), 31.0 (3 C), 19.1 (2 C); IR (NaCl) 2967, 2253, 1707, 1408, 1192, 911, 739 cm⁻¹; MS *m/e* 367 (13%), 352 (34%), 311 (60%), 296 (21%), 255 (14%), 167 (08%), 149 (24%), 129 (78%), 57 (100%); HRMS found 367.2513, calculated 367.2511. Minor, **21-cis**: ¹H-NMR ($CDCl_3$) δ 7.43 (1 H, d, *J* = 8.6), 7.34 (1 H, d of d, *J* = 8.6, 2.2), 6.69 (1 H, d, *J* = 2.2), 3.22 (2 H, d, *J* = 15.5), 2.54 (2 H, d, *J* = 15.5), 2.34 (2 H, br d, *J* = 15.1), 1.68 (6 H, s), 1.25 (9 H, s), 1.19 (9 H, s); ¹³C-NMR ($CDCl_3$) δ 181.0 (2 C), 150.4, 145.4, 131.4, 127.9, 127.7, 127.5 (2 C), 126.8, 40.6 (2 C), 34.7, 34.3, 31.2 (6 C), 30.5 (2 C), 19.5 (2 C); IR (NaCl) 2963, 2253, 1703, 1402, 1360, 1188, 907, 733, 648

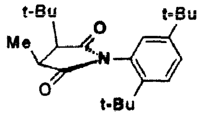
1-(2,5-Di-*tert*-butylphenyl)-3-methylpyrrole-2,5-dione (22).



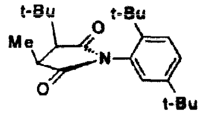
Citraconic anhydride (660 µL, 7.30 mmol) and 2,5-di-*tert*-butylaniline (500 mg, 2.43 mmol) were heated without solvent to 120° C, for 2 h. The resulting red oil was chromatographed (20% EtOAc in hexanes), and the product was recrystallized in minimal ethyl ether and hexane (0° C, 24 h). 1-

(2,5-Di-*tert*-butyl-phenyl)-3-methyl-pyrrole-2,5-dione (157 mg, 22% recovered yield) was used without further purification: mp 136-137° C; ^{1}H-NMR (CDCl$_3$) δ 7.47 (1 H, d, *J* = 8.6), 7.38 (1 H, d, *J* = 8.3, 2.2), 6.84 (1 H, d, *J* = 2.2), 6.50 (1 H, m), 2.17 (3 H, d, *J* = 1.7), 1.26 (9 H, s), 1.26 (9 H, s); ^{13}C-NMR (CDCl$_3$) δ 172.0, 171.1, 150.1, 146.6, 146.1, 129.1, 128.2, 128.1, 128.0, 126.8, 34.9, 34.1, 31.5 (3 C), 31.1 (3 C), 11.3; IR (NaCl) 3461 (br), 2969, 2255, 1711, 1646, 1416, 909, 735; MS *m/e* 299, 284, 242, 228, 210, 186, 57; HRMS calc: 299.1885, found: 299.1875.

3-*tert*-Butyl-4-methyl-1-(2,5-di-*tert*-butylphenyl)pyrrolidine-2,5-dione (23, Table 3, entry 1).



Major cis



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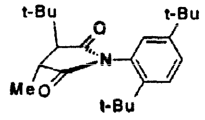
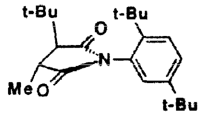


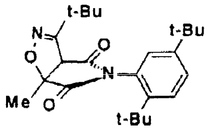
Major trans

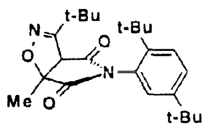


Minor trans

The above Giese reaction procedure was repeated with 1-(2,5-di-*tert*-butyl-phenyl)-3-methyl-pyrrole-2,5-dione **22** (100 mg, 0.33 mmol), *t*-butyl mercury chloride (120 mg, 0.40 mmol), sodium borohydride (100 mg, 2.50 mmol) and water (120 μL, 6.68 mmol) in dichloromethane (5 mL, 0.08 M). The filtered (Florasil) solution was concentrated to a residue (113 mg, 96 %) and ^{1}H NMR showed four compounds (based on integration of the hydrogen alpha to the *t*-butyl group on the imide ring at δ 2.94, 2.80, 2.3, 2.1). To equilibrate, the residue was dissolved in benzene, and heated in a sealed tube at 120° for 24 h. (at δ 2.95, 2.7, 2.3, 2.1). Major cis isomer: ^{1}H-NMR (CDCl$_3$) δ 7.46 (1 H, d, *J* = 8.6), 7.36 (1 H, d of d, *J* = 8.5, 2.3), 6.69 (1 H, d, *J* = 2.2), 3.13 (1 H, m), 2.80 (1 H, d, *J* = 8.2), 1.54 (1 H, d, *J* = 7.5), 1.27 (9 H, s), 1.27 (9 H, s), 1.26 (9 H, s). Minor cis isomer: ^{1}H-NMR (CDCl$_3$) δ 7.45 (1 H, d, *J* = 8.6), 7.35 (1 H, d of d, *J* = 8.5, 2.2), 6.69 (1 H, d, *J* = 2.2), 3.15 (1 H, m), 2.94 (1 H, d, *J* = 8.3), 1.58 (3 H, d, *J* = 7.6), 1.28 (9 H, s), 1.26 (18 H, s);

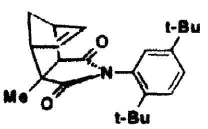
1-(3-*tert*-Butyl-4,5-dicarboximido [d]isoxazole-5a-methyl)-2,5-di-*tert*-butyl benzene (27, Table 3, entry 2).





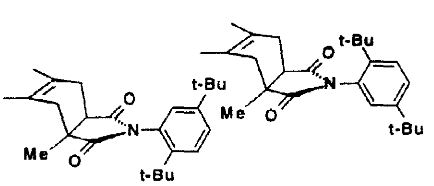
1-(2,5-Di-*tert*-butyl-phenyl)-3-methyl-pyrrole-2,5-dione **22** (100 mg, 335 μmol) was dissolved in 3.5 mL of Et$_2$O with *tert*-butyl hydroximoyl chloride (75 mg, 500 μmol). Triethyl amine was added (100 μL, 600 μmol) and an immediate white precipitate was observed. The solution was stirred for 2 d, and then filtered through celite, concentrated and left under high vacuum for 2 h. The atropisomers (53 mg and 20 mg, 54% combined yield) were isolated by column chromatography (10% ethyl acetate in hexanes). Major isomer, **24-trans**: mp 180-181°C; ^{1}H-NMR (CDCl$_3$) δ 7.48 (1 H, d, *J* = 8.5), 7.43 (1 H, dd, *J* = 8.5, 1.8), 6.71 (1 H, d, *J* = 1.9), 4.18 (1 H, s), 1.72 (3 H, s), 1.33 (9 H, s), 1.27 (9 H, s), 1.22 (9 H, s); ^{13}C-NMR (CDCl$_3$) δ 175.4, 171.9, 162.0, 151.0, 144.9, 129.2, 129.0, 127.6, 127.1, 87.7, 76.8, 61.1, 35.6, 34.4, 31.8 (3 C), 31.2 (3 C), 28.8 (3 C), 19.1. Minor isomer, **27-cis**: ^{1}H-NMR (CDCl$_3$) δ 7.48 (1 H, d, *J* = 8.5), 7.39 (1 H, d of d, *J* = 8.6, 2.2), 6.63 (1 H, d, *J* = 2.1), 4.18 (1 H, s), 1.77 (3 H, s), 1.34 (9 H, s), 1.27 (9 H, s), 1.23 (9 H, s). Atropisomeric Mixture: IR (NaCl) 3022, 2972, 1722, 1213, 758, 667; MS *m/e* 398 (M, 17%), 383 (M – [CH$_3$], 100%), 284 (17%), 257 (8%), 216 (12%); HRMS calculated 398.2569, found 398.2576.

4-(2,5-Di-*tert*-butylphenyl)-2-methyl-4-aza-tricyclo[5.2.1.0 2,6] dec-8-ene-3,5-dione (25, Table 3, entry 3).



The procedure for preparation of 1-(5-norbornene-2,3-dicarboximido)-2,5-di-*tert*-butyl benzene **20-trans** was repeated with 1-(2,5-di-*tert*-butyl-phenyl)-3-methyl-pyrrole-2,5-dione **22** (200 mg, 0.67 mmol) and 275 μL of cyclopentadiene (275 μL, 3.3 mmol) in 5 mL of CH_2Cl_2 to yield 210 mg (85%) of a white solid (R_f = 0.38, 20% EtOAc in hexanes). ^{1}H-NMR ($CDCl_3$) δ 7.44 (1 H, d, J = 8.6), 7.34 (1 H, d of d, J = 8.4, 2.2), 6.66 (1 H, d, J = 6.4), 6.39 (1 H, d of d, J = 5.6, 2.9), 6.30 (1 H, d of d, J = 5.6, 2.8), 3.47 (1 H, d, J = 1.2), 3.05 (1 H, s), 2.97 (1 H, d, J = 4.5), 1.83 (2 H, t, J = 1.7), 1.6 (3H, s), 1.27 (9 H, s), 1.26 (9 H, s); ^{13}C-NMR ($CDCl_3$) δ 181.6, 144.8, 137.0, 134.9, 128.3, 127.4, 126.9, 53.3, 51.7, 51.3, 50.5, 46.2, 35.3, 31.8, 31.3, 21.5; IR (NaCl) 2968, 1708, 1404, 1355, 1209, 754; MS *m/e* 365 (M, 23%), 350 (M - $[CH_3]$, 25%), 299 (11%), 284 (M - $[C_5H_6]$, 100%), 242 (19%), 228 (8%), 186 (8%); HRMS calculated 365.2355, found 365.2364.

2-(2,5-Di-*tert*-butylphenyl)-4-methyl-5,6-dimethyl-3a,7,7a-trihydro3isoindole-1,3-dione (26, Table 3, entry 4).



Benzene (5 mL), 1-(2,5-di-*tert*-butyl-phenyl)-3-methyl-pyrrole-2,5-dione **22** (100 mg, 0.33 mmol), and 2,3-dimethyl-1,3-butadiene (190 μL, 1.67 mmol) were mixed in a sealed tube and heated to 120° for 48 h. The solution was then concentrated, left under high vacuum for 3 h and a ^{1}H NMR of the residue was taken. Some starting material and two isomeric (3 : 1 ratio by ortho aryl proton) products were observed. The residue was subjected to column chromatography (eluent 5% ethyl acetate in hexanes), and the major (53 mg, 42%) and minor (24 mg, 19%) isomers were recovered. Major: mp 86° C; ^{1}H-NMR ($CDCl_3$) δ 7.42 (1 H, d, *J* = 8.5), 7.33 (1 H, d of d, *J* = 8.6, 2.2), 6.41 (1 H, d, *J* = 2.2), 2.77 (2 H, d of d, *J* = 6.0, 2.2), 2.60 (1 H, d of d, *J* = 14.5, 2.2), 2.52 (1 H, d, 14.2), 1.74 (3 H, s), 1.73 (3 H, s), 1.40 (3 H, s), 1.26 (9 H, s), 1.23 (9 H, s); IR (NaCl) 2963, 1711, 1406, 1358, 469 (br). Minor: ^{1}H-NMR ($CDCl_3$) δ 7.48 (1 H, d), 7.38 (1 H, m), 6.50 (1 H, d, *J* = 2), 2.78 (2 H, d of d), 2.55 (2 H, m), 1.65 (3 H, s br), 1.4 (3 H, s), 1.22 (9 H, s), 1.2 (9 H, s).

Acknowledgments. We thank the National Science Foundation for funding of this work.

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