Pergamon

Tetrahedron Vol. 51, No. 14, pp. 3979-3996, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00140-9

Stereoselective Synthesis, NMR Conformational Study and Diels-Alder Reaction of β-Functionalized 1-Acetylvinyl arenecarboxylates

Javier Peralta, Joseph P. Bullock,§ Roderick W. Bates,§ Simon Bott,§
Gerardo Zepeda, and Joaquín Tamariz*

Department of Organic Chemistry, Escuela Nacional de Ciencias Biológicas, IPN. Prol. Carpio y Plan de Ayala, 11340 México, D.F. § Department of Chemistry, University of North Texas, Denton, TX 76203-5068

Abstract: A stereoselective synthesis of novel β-substituted 1-acetylvinyl arenecarboxylates **2a-2h**, via the bromo derivative **4a**, is described. Isomer *Z* was the only product formed. Low temperature NMR experiments showed an *s-cis/s-trans* (20:80) conformeric equilibrium, and also a restricted rotational C-N barrier in **2a**. X-ray diffraction of the latter revealed a planar *s-trans* conformation. Alkene **4a** proved to be more reactive than **2a-2h** towards cyclopentadiene (**6**) and isoprene (**11**) in Diels-Alder additions, giving the corresponding adducts **10** and **14** in high stereo- and regioselectivity.

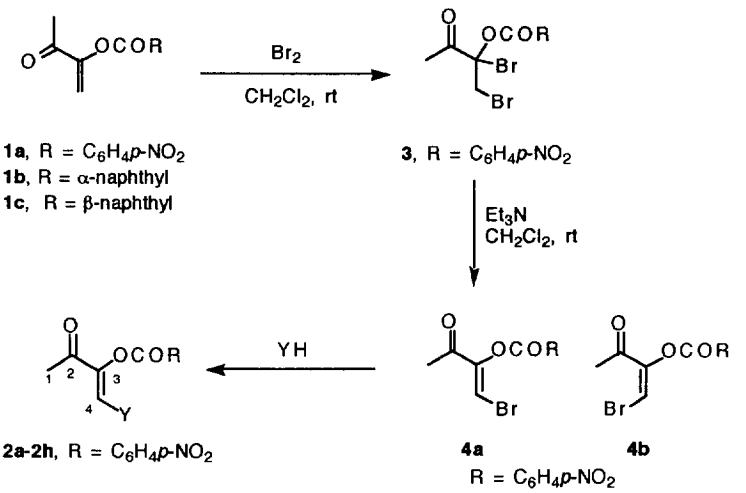
The stereoselective synthesis of α,β-difunctionalized enones, acrylic esters and acroleins has attracted significant attention since they have proved to be interesting synthetic targets,[1] efficient dienophiles[2] and heterodienes[3] in Diels-Alder cycloadditions. Recently, we reported that captodative 1-acetylvinyl arenecarboxylates, **1**, showed highly selective Diels-Alder[4] and 1,3-dipolar[5] cycloadditions. Besides, they were useful synthons in natural terpenoid synthesis.[6]

As a part of our efforts to prepare α,β-disubstituted enones from **1**, in order to evaluate their reactivity and selectivity as dienophiles and dienes in Diels-Alder reactions and as versatile intermediates in organic synthesis, we now report a stereoselective synthesis of novel β-functionalized 1-acetylvinyl arenecarboxylates **2**. Furthermore, we describe a low temperature NMR analysis of *s-cis/s-trans* conformations of vinilogous dimethylamide **2a**, as well as, the determination of the activation energies of their C-C and C-N rotation barriers.

RESULTS AND DISCUSSION

Olefins **2** were prepared by a three-step synthetic route from compound **1a**[6a,7] as starting material (Scheme 1). When **1a** was brominated, the dibromo compound **3** was afforded in 92% yield. This was treated with triethylamine under smooth conditions to give bromo derivative **4a** in 72% yield. The ^{1}H NMR spectrum of the crude showed only one series of signals, confirming the presence of a single stereoisomer. The assignment of the *Z* configuration of the double bond was established by single crystal X-ray diffraction (Figure

1). This exhibits two molecules in the asymmetric unit, both of them maintaining the planar *s-trans* conformation and the *Z* configuration. Hence, the dehydrobromination reaction was highly stereoselective.



Scheme 1. Preparation of olefins **2a-2h**.

This selectivity could be explained by comparison of the stability of **4a** with respect to *E* isomer **4b**. Considering a similar *s-trans* or *s-cis* planar conformation of the enone system of **4b**, as shown in the structure of **4a** (Figure 1), it appears that repulsive interactions present in **4b** between the π-planar acetyl group and the bromine atom would destabilize the elimination process.[8]

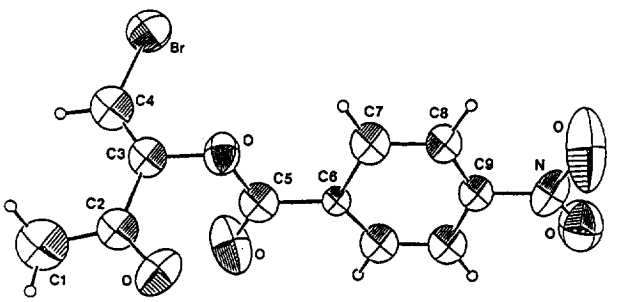


Figure 1. Perspective view of the X-ray crystal structure of **4a**.

The addition of nucleophiles (YH) such as amines, anilines and thiols to **4a** provided the desired β-substituted olefins **2a-h** in fair yields (Table 1). Secondary amines were added rapidly under gentle conditions giving derivatives **2a-d**. Anilines activated by electron-releasing groups were also added, but they required the presence of triethylamine as catalyst and longer reaction times. The increase of temperature led to lower yields. In the case of anilines, in contrast with secondary amines, it was necessary to use a more polar solvent.

Inactivated anilines, e.g. nitroanilines, even aniline itself, were not reactive enough to undergo addition toward **4a**.

Table 1. Reaction Conditions for the Preparation of Olefins **2** by Addition of Nucleophiles (YH) to **4a.**

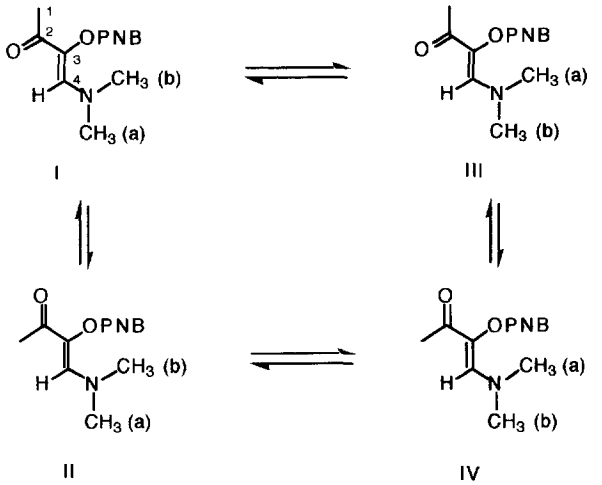
Method[a]	Y	Product	mp (°C)	Yield (%)[b]
A	NMe_2	**2a**	153-154	84
A	NEt_2	**2b**	155-156	84
A	$Ni\text{-}Pr_2$	**2c**	159-160	51
A	$N(CH_2)_4$	**2d**	163-164	16
B	$NHC_6H_4p\text{-}Me$	**2e**	172-173	56
B	$NHC_6H_4p\text{-}OMe$	**2f**	168-169	41
C	$Sn\text{-}Pr$	**2g**	119-120	93
C	SPh	**2h**	63-64	85

[a] A: CH_2Cl_2, rt, 1 h; B: Et_3N, DMF, rt, 24 h; C: Et_3N, DMF, rt, 1 h. [b] After recrystallization.

Similar conditions were used with the thiols: *n*-propyl mercaptan and thiophenol, to yield olefins **2g** and **2h**, respectively. The reactivity of these nucleophiles was higher, because the conversion of starting materials was completed in only 1 h, and the yields were better. On the other hand, the introduction of an oxygenated functionality, by addition of alcohols and phenols to the brominated compound **4a**, was unsuccessful. Transesterification of the *p*-nitrobenzoyl (PNB) group took place rapidly.

The new compounds **2a-2h** were thoroughly characterized by spectroscopy and elemental analysis. The configuration of the double bond was established by ^1H NMR using NOE experiments. A correlation between vinyl proton H-4 and the acetyl group was observed, proving to be a *Z* configuration as for **4a**.

The proton spectra for the amino derivatives **2a-2d** appear as broad signals in both $CDCl_3$ and C_6D_6. An equilibrium between the *s-cis* and *s-trans* rotamers I and II (Scheme 2) has been previously proposed for analogous enamino carbonyl compounds.[9] Indeed, when we determined low temperature ^1H NMR spectra for **2a** in $CDCl_3$, the ensemble of the broad singlets for the *N,N*-dimethyl, acetyl and PNB groups and the olefinic proton became narrow and a second series of signals was distinguished in *ca.* 80 : 20 ratio (Figures 2a and b) with a coalescence temperature of *ca.* 18°C. The smaller vinylic proton signal was shifted to low field (7.23 ppm), which suggests a *s-cis* conformer attribution.[10] Moreover, when the solution was cooled to -32.5°C (Figure 2c) a second coalescence temperature was reached for the *N,N*-dimethyl groups (2.87 ppm) and at -61°C (Figure 2d) four signals were completely separated. This is interpreted in terms of the existence of two pairs of rotamers I/III and II/IV, respectively, owing to restricted rotation around the C_4-N bond and leading to differentiation of the two methyl groups.



Scheme 2. Equilibria between pairs of rotamers *s-cis* I/III and *s-trans* II/IV of olefin **2a**.

In contrast with enamino aldehydes and ketones,[10a,11] these results showed: (a) the preponderance of the *s-trans* rotamer II (*ca.* 80%) over the *s-cis* isomer I (*ca.* 20%), which agrees with polarized enamides;[10b] (b) the rotation around the C_2-C_3 bond was slower than the C_4-N rotation. These equilibria and the higher thermodynamic stability of the involved rotamers depend on several factors. The steric interactions between the olefin substituents located in a *cis* or *geminal* positions would tend to diminish the mesomerism of the nitrogen lone-pair with the π-enone system, and consequently, the rotational barriers of the single bonds would then be reduced. While the mesomerism increases the stability of the planar conformers, the steric hindrance could destabilize them. Activation energies ($\Delta G_c^{\neq}$) for rotation around C_4-NMe_2 in unsubstituted enaminones have been calculated at the coalescence temperature (T_c) to be *ca.* 13.5 Kcal/mol.[10a,12] Using equation 1[13] and considering the T_c for each equilibrium for olefin **2a**, the $\Delta G_c^{\neq}$ were estimated. For the C_4-N restricted rotation, barriers of 11.8 Kcal/mol and 11.6 Kcal/mol were calculated for the isomers *s-trans* and *s-cis*, respectively. These are approximate values, because no distinction was possible between the coalescence temperatures (-32.5°C) of the two isomers, since their signals overlapped. These energies are similar to those calculated (*ca.* 11.0 Kcal/mol) for 4-methyl-4-dimethylamino substituted butenone[10a] and α-cyanoacrylates;[14] but they are higher than the barrier energy for 4-dimethylamino-3-methyl-3-buten-2-one, structurally closely related to **2a**, in which case the NMe_2 group signal was not split, even decreasing the temperature down to -120°C.[10a] This suggests that the PNB group on C_3 does not have a strong effect in inhibiting the enaminone mesomerism in **2a**, but it could play a role in favoring the *s-trans* form.[15] We calculated an activation energy for the *s-cis*/*s-trans* equilibrium and the value for **2a** amounts to $\Delta G_c^{\neq}$ = 14.0 Kcal/mol, which is somewhat higher than the value obtained (*ca.* 11.0 Kcal/mol) for the unsubstituted enaminone 4-dimethylamino-3-buten-2-one,[9] and less than the polarized enamines (*ca.* 17.0 Kcal/mol).[16]

$$\Delta G_c^{\neq} = 2.3\ RT_c\ (10.32 + \log T_c/k_c) \qquad [1]$$

where $k_c = 2.22\ \Delta\nu$ and $\Delta\nu = \delta_{rot\ I} - \delta_{rot\ II}$ (Hz)

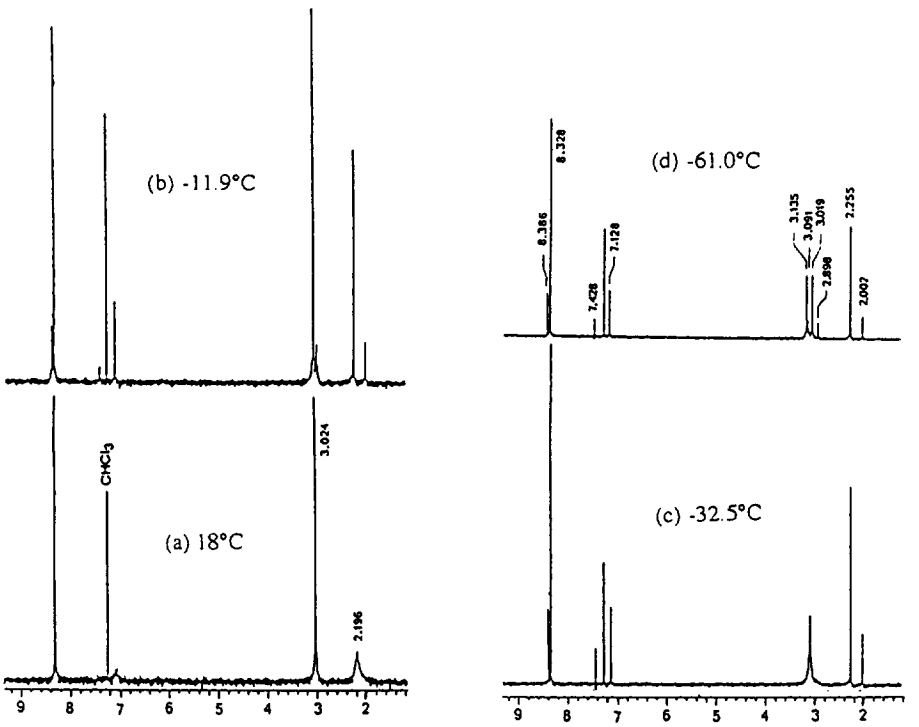
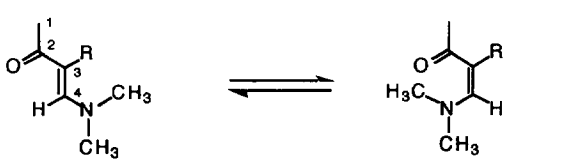


Figure 2. Low temperature ^1H NMR spectra of **2a** in $CDCl_3$.

Dabrowski and Kozerski[17] estimated that the C_4-N barrier of compound **5a** was too low to be observed and there was free rotation around the C_2-C_3 bond. Therefore, they attributed the experimentally determined value of $\Delta G_c^{\neq}$ = 13.8 Kcal/mol to the C_3=C_4 barrier. They argued a less effective conjugation of the nitrogen lone electron pair due to steric interactions between $N(CH_3)_2$ and the acetoxy group on C_3. A similar explanation was followed for compound **5b**, with values amounting to $\Delta G_c^{\neq}$ = 11.0 and 11.2 Kcal/mol, corresponding to C_4-N and C_3=C_4 barriers, respectively.

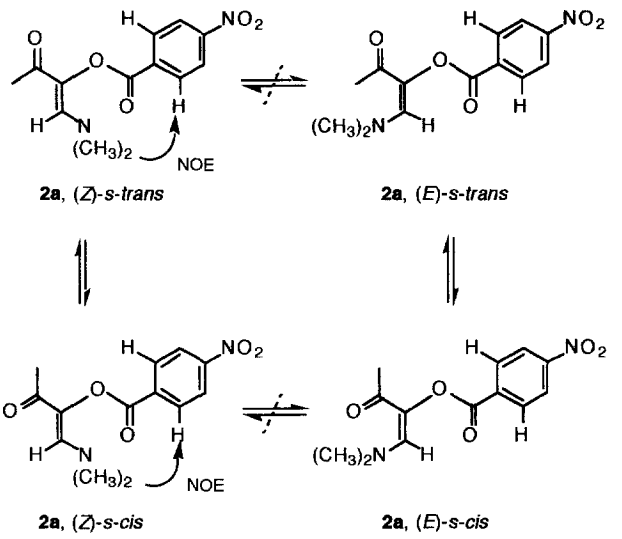


(Z)-s-cis + *(Z)-s-trans* ⇌ *(E)-s-cis* + *(E)-s-trans*

5a, R = $OCOCH_3$
5b, R = Br

Considering the structural analogy between **5a** and **2a**, and that the C_3=C_4 barrier of **5a** was comparable to *s-cis/s-trans* equilibrium of **2a**, we assessed the possibility that the latter was rather an *E/Z* isomerization (Scheme 3). Low temperature (-18.4°C) NOE experiments with selected irradiation on both isomeric $N(CH_3)_2$ signals [3.05 ppm (major isomer) and 2.98 ppm (minor isomer) (Figure 2b)], exhibited enhancements in both singlets of the PNB protons, attributed to the split signals of the two isomers [8.36 ppm (minor isomer) and 8.31 ppm (major isomer) (Figure 2b)]. This agrees with a *Z* geometric configuration in both isomers, since no NOE effect should be expected for the (*E*)-isomer. Therefore, the first equilibrium detected at T_c = 18°C (Figure 2) corresponded to the C_2-C_3 rotation: *(Z)-s-trans/(Z)-s-cis*.

Likewise, the C_3=C_4 barrier was estimated to be relatively high, since only a normal slight enlargement of the signals was observed by ^{1}H NMR (300 MHz), and the shape of the original spectrum was recovered after cooling to room temperature, when a sample of **2a** in DMSO-d_6 was gradually heated up to 150°C. No additional signals were formed, which would provide an evidence of the isomer *E* formation. Attemps to isomerize **2f** by acidic treatment (*p*-TsOH, $CDCl_3$) were unsuccesful. Only side-product signals were gradually detected by ^{1}H NMR up to 60°C. This appears to support the higher stability of the *Z* isomer with respect to the *E* isomer.[1h,1m,18]



2a, *(Z)-s-trans* **2a**, *(E)-s-trans*

2a, *(Z)-s-cis* **2a**, *(E)-s-cis*

Scheme 3. Low temperature (-18.4°C) NOE experiments of **2a** showed only the presence of isomers *(Z)-s-trans* and *(Z)-s-cis*.

In fact, a strong electronic delocalization through the coplanar π-orbitals of the vinylogous amide should be reflected in a shortness of C_4-N and C_2-C_3 bonds. Indeed, the single crystal X-ray structure of **2a** (Figure 3) shows these bond distances (Table 2) to be shorter than those expected for non-delocalized enone and enamine groups.[19] Moreover, the bond distance for N-CH_3 is rather close to an N_{sp2} hybridation. The dihedral angles (Table 3) revealed that the enone was planar with a sp^2 hybridation of the nitrogen atom, allowing an extensive

conjugation of all the enamino carbonyl π-orbitals. As regards the conformation of **2a**, the *s-trans* was the preferred one, at least in the crystalline form, as well as for that of compound **4a** (Figure 1).

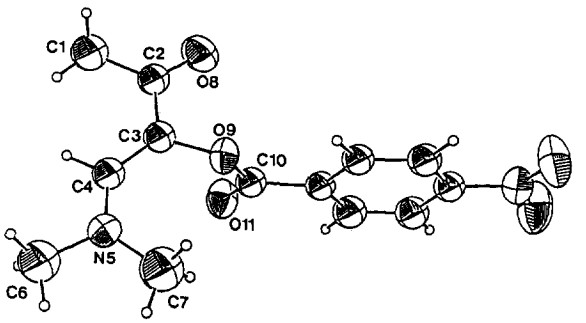


Figure 3. Perspective view of the X-ray crystal structure of **2a**.

Table 2. Comparison of X-ray Selected Bond Distances (Å) (estimated standard deviations) of Crystal Structure of **2a** with the Average Lenghts of Bonds of Enone and Enamine Systems.[19]

Bond	X-ray	Average Length[19]
C(1)-C(2)	1.501 (9)	1.511
C(2)-O(8)	1.231 (7)	1.222
C(2)-C(3)	1.41 (1)	1.462
C(3)-C(4)	1.366 (9)	1.340
C(4)-N(5)	1.32 (1)	1.358 (Nsp^2); 1.418 (Nsp^3)
N(5)-C(6)	1.447 (8)	1.451(Nsp^2)
N(5)-C(7)	1.45 (1)	1.468 (Nsp^3)
C(3)-O(9)	1.423 (7)	1.353
O(9)-C(10)	1.354 (6)	1.359

Table 3. Selected Bond Angles (deg) and Torsion Angles (deg) (estimated standard deviations) of Crystal Structure of **2a**.

Bond Angles (deg)		Torsion Angles (deg)	
C(1)-C(2)-O(8)	119.1 (7)	C(4)-C(3)-O(9)-C(10)	99.42 (0.66)
C(1)-C(2)-C(3)	120.6 (6)	C(2)-C(3)-O(9)-C(10)	(-) 83.55 (0.64)
C(3)-C(2)-O(8)	120.3 (6)	C(6)-N(5)-C(4)-C(3)	(-) 178.68 (0.66)
C(2)-C(3)-O(9)	114.2 (5)	C(7)-N(5)-C(4)-C(3)	4.15 (1.09)
C(4)-C(3)-O(9)	120.8 (7)	N(5)-C(4)-C(3)-O(9)	(-) 1.16 (1.04)
C(3)-C(4)-N(5)	133.0 (6)	N(5)-C(4)-C(3)-C(2)	(-) 177.86 (0.63)
C(4)-N(5)-C(6)	120.6 (6)	O(9)-C(3)-C(2)-O(8)	5.87 (0.81)
C(4)-N(5)-C(7)	125.2 (5)	O(9)-C(3)-C(2)-C(1)	(-) 174.84 (0.51)
C(6)-N(5)-C(7)	114.2 (7)	C(4)-C(3)-C(2)-O(8)	(-) 177.24 (0.58)
C(3)-O(9)-C(10)	115.3 (4)	C(4)-C(3)-C(2)-C(1)	2.05 (0.93)

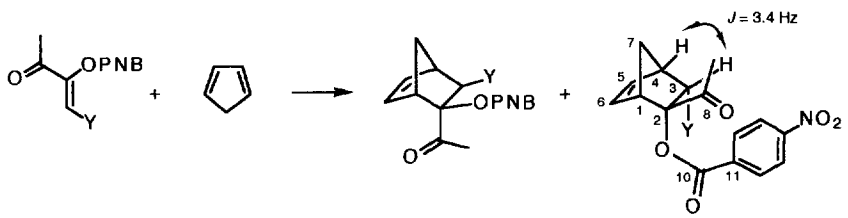
A computational optimization of the molecular structure and conformational study of **2a**, using the AM1 algorithm of MOPAC V-6.0, showed that the minor rotamer *s-cis* had a lower enthalpy of formation than the *s-*

trans. This is contrary to X-ray and NMR analyses, and it could be attributed to solvent and crystalline lattice effects, not accounted for in MOPAC calculations.

Analogous low-temperature ^1H NMR experiments were undertaken with the thiol compounds **2g** and **2h**. In contrast with **2a**, when the solution was cooling down to -90°C, a coalescence temperature was unobserved, showing that the *s-cis/s-trans* conformational barrier is very low. This suggests that the electronic interaction of the sulfur onto the enone system is less significant than that provided by the amino group.

In addition to the evidence given by the low temperature ^1H NMR experiments for the *s-trans* conformational preference of **2a** in solution, the ^{13}C NMR shifts of the C(2), C(3) and C(4) signals could also be used as a conformational diagnosis for the enamino carbonyl compounds.[20] ^{13}C NMR data of **2a-2h** and **4a** are listed in Table 4. Signals of olefinic carbon atoms C_3 and C_4 were distinguished by DEPT or APT spectra. For the β-amino compounds **2a-2f**, the deshielded signals at *ca.* 130-140 ppm corresponded to carbons C_4, while those occurring at *ca.* 123-131 ppm were attributed to C_3. The latter are upfield shifted with respect to the same carbon atom of olefins **1** (151 ppm),[7] since a large charge density is centered on C_3 of **2** by the β-position electron-donor group, and by a compressing effect bearing on C_3, because of the steric repulsion between the groups in the *syn* relative position (γ effect).[21] Nevertheless, the latter is minimized by the increase in the N-C_4-C_3 angle to 133° and the lengthening of the bond distance of **C_3-O**COAr more than expected for an enol ester,[19] as shown by the crystal structure of **2a** (Tables 2 and 3). Chemical shifts of C_3 and C_4 of the sulphur and bromine derivatives **2g, 2h** and **4a** are opposite, C_3 being at low field. A slight variation of δC_2 (*ca.* 185 ppm) would suggest a similar conformation of the conjugated enone skeleton in the series **2a** to **2h**.[21a] The *ca.* 4 ppm upfield shift of the C_2 resonance observed in this series in comparison with **1a** could be accounted for as a shielding effect caused by C_4 substitution.

Thermal reaction of the series of olefins **2a** to **2h** with cyclopentadiene (**6**) was unsuccessful, even at high temperatures (170°C) and for long periods of time (15-24 h). The mixture of reaction with **2a** and **2b** indicated both traces of expected adducts **7/8** (Scheme 4), and a high decomposition of the olefin. Even using Lewis acid catalysts, such as $AlCl_3$, $ZnCl_2$, $TiCl_4$, $MgBr_2$ and $BF_3{\cdot}Et_2O$, which have been traditionally used to improve the cycloaddition even for unreactive olefins,[22] failed to produce any cycloadduct and the olefin decomposition was increased. Other olefins of the series (**2d** and **2h**) were treated under similar conditions, but they did not react either. Low dienophilicity has also been described for unactivated trisubstituted olefins[2d] or they react preferentially as heterodienes.[3,23]



2a, Y = NMe_2
2b, Y = NEt_2
4a, Y = Br

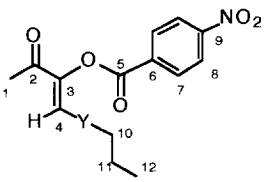
6

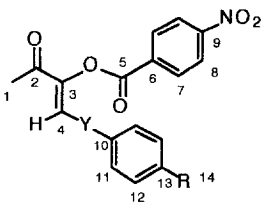
7a, Y = NMe_2
7b, Y = NEt_2
9, Y = Br

8a, Y = NMe_2
8b, Y = NEt_2
10, Y = Br

Scheme 4. Diels-Alder reaction of olefins **2a, 2b** and **4a** with cyclopentadiene (**6**).

Table 4. ^{13}C NMR Spectral Data (DMSO-d_6) of Olefins **2a-2h** and **4a.**





	2a	2b	2c	2d	2e	2f	2g	2h	4a
C-1	23.6	23.8	23.8	23.5	23.7	23.7	24.5	24.8	25.5
C-2	185.1	185.1	185.1	184.7	186.0	185.8	186.7	187.3	188.6
C-3	123.5	123.2	123.7	131.1	127.2	127.0	141.4	142.3	148.8
C-4	142.5	140.6	135.6	139.5	133.2	131.3	138.5	135.4	115.3
C-5	162.9	162.6	162.5	163.1	162.5	162.5	161.4	161.3	161.3
C-6	134.6	134.8	134.8	134.7	135.2	135.3	133.3	133.5	132.7
C-7	131.0	131.0	130.9	131.0	131.3	131.3	131.9	131.5	131.4
C-8	123.9	124.0	124.0	123.9	123.6	123.6	124.1	124.4	124.4
C-9	150.3	150.5	150.4	150.3	150.1	150.2	150.4	151.2	150.9
C-10	42.0	47.5	47.9	52.3	138.3	134.0	34.9	131.4	
C-11		14.4	21.8	24.9	129.7	117.6	23.5	129.8	
C-12					116.0	114.6	12.6	130.6	
C-13					131.5	155.0		128.3	
C-14					20.1	55.3			

The low reactivity provided by these olefins could be explained by an effective delocalization of the lone-pair of the heteroatom on C_4.[24] This effect decreases the double bond character of the olefin; hence, the dienophile character is decreased as well. From the point of view of the perturbational theory,[25] the Diels-Alder reaction is slowed down when the dienophile is electron rich, because the electron releasing substituents will produce a LUMO destabilization and, consequently, the energy gap of the frontier orbital interaction with the HOMO of the diene, under *normal electronic demand* conditions, will be greater.[26] Therefore, the interaction between these cycloaddents, as well as their reactivity, will decrease. This could account for the low reactivity of olefins **2a-2h** as dienophiles towards dienes **6** and **11** (*vide infra*). A further support for this picture with respect to thio olefins **2g** and **2h**, is the role of sulfur as a control element by an electron donnating distribution, rather than oxygen, onto the regiochemistry of disubstituted dienes.[27] In the particular case of α-alkylthio acrylates and cyanoacrylates, the captodative effect was invoked to compensate for this deactivation.[28] Even though our low temperature ^1H NMR experiments with these olefins suggested rather that sulfur lone pair delocalization to the enone π system is not as strong as for the amino group for freezing the *s-cis/s-trans* conformation, this electronic interaction could participate by decreasing the dienophilic character of these olefins. In addition to this, the steric hindrance provided by the thioalkyl and thiophenyl substituents would improve the destabilizing interactions at the transition state. Other contributing causes such as closed-shell repulsions[29] might also be considered.

A higher reactivity was observed for **4a** in the presence of diene **6**. Thus, when they were heated to 130°C or the reaction was carried out in the presence of catalysts, the addition occurred in modest yields (~34%) to give the desired adducts **9/10** (Scheme 4). Surprisingly, for the thermal trials, *exo* stereoisomer **10** was the only observed adduct; whereas, the Lewis acid catalyzed trials were less selective (Table 5). This contrasts with the usual role of Lewis acids in improving selectivity.[22] The multiple complexation sites on dienophile **4a** and the great number of possible conformeric species formed with the Lewis acid[30] prevent a prediction about the stereocontrol factors in this process. The *exo* selectivity could be associated with a low stability of the transition state leading to *endo* isomer **9**, since repulsive non-bonding interactions of the methylene bridge of **6** with the two bulky groups of the dienophile would destabilize this approach (Figure 4).[31] It has been argued that electronic effects in the transition state play a major role in determining stereoselectivity; however, these studies have been generally restricted to unsubstituted enones.[32] On the other hand, secondary orbital interactions from the donor group on the *alpha* carbon might also stabilize the *exo* transition state.[33] The *exo* approach preference of **4a** in this cycloaddition also reflect minimal contribution from possible electrostatic repulsions between the heteroatom lone pairs, i.e., bromine and oxygen, and the cyclopentadiene π electrons,[34] since this factor would predict the unobserved *endo* transition state (Figure 4) to be more stable.[35]

The relative configuration of the major adduct **10** was established by NMR. A $J = 3.4$ Hz coupling was determined between the bridgehead proton H-4 and the *exo* bromo base proton H-3.[36]

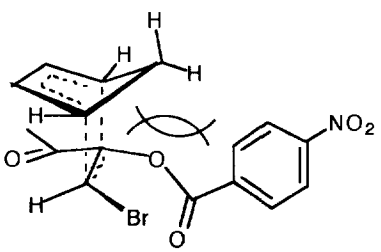


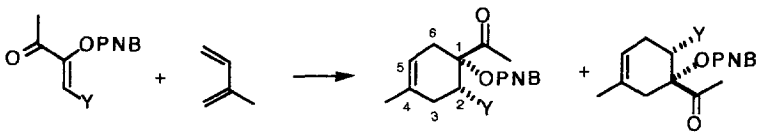
Figure 4. Steric interactions in the *endo* approach of **4a** and **6**.

Table 5. Diels-Alder Cycloadditions of Olefin **4a** with Diene **6** and **11**.

Diene[a]	Lewis Acid[b]	Solvent	T (°C)	t (h)	Products[c]	Yield (%)[d]
6[b]	---	xylene	100	31	**9/10** (<5 : >95)	25
6	$AlCl_3$	CH_2Cl_2	25	72	**9/10** (25 : 75)	37
6	$ZnCl_2$	CH_2Cl_2	25	72	**9/10** (37 : 63)	40
11[b]	---	xylene	130	15	**14/15** (70 : 30)	41
11	$AlCl_3$	CH_2Cl_2	25	5	**14/15** (85 : 15)	43
11	$ZnCl_2$	CH_2Cl_2	25	5	**14/15** (90 : 10)	41

[a] 5 mol eq. [b] 10 mol eq. [c] Ratio determined by ^1H NMR of the crude mixture. [d] After recrystallization.

The non-reaction and gradual decomposition of amino olefins **2a-2f** with isoprene (**11**), under thermal and catalytic conditions, confirmed the low reactivity of **2** as dienophiles. Derivative **2h** was added to **11** up to 170°C, giving very poor yields (<10%, estimated by NMR) of corresponding adducts **12/13** (Scheme 5), as a part of a complex side-product mixture. In contrast, thermal (130°C) cycloaddition of **4a** with **11** furnished a mixture of isomers **14/15** (70:30), in which the *para* isomer **14** was the major one (Table 5). The regioselectivity obtained was comparable to that observed with the β-unsubstituted olefin **1a**.[4] This seems to support the assumption that the controling effect on the regioselectivity shown by **4a** would be the electronic demand of the electron-withdrawing group, i.e., the acetyl group, on the LUMO energy and polarizability of the double bond, as suggested by FMO calculations.[4] In such a case, a possible interaction of the bromine lone-pair on the π-system would also induce a regioselectivity as observed for **14**, in accordance with the expected LUMO polarization of a π bond by an electron-donnor group.[24a,b] The presence of $ZnCl_2$ improved the regioselectivity, which reached a ratio of *para/meta*, **14/15**, 90:10. Other catalysts were used, such as $BF_3{\cdot}Et_2O$ and $TiCl_4$, without success.



2h, Y = SPh
4a, Y = Br

11

12, Y = SPh
14, Y = Br

13, Y = SPh
15, Y = Br

Scheme 5. Diels-Alder reaction of olefins **2h** and **4a** with isoprene (**11**).

^1H NMR spectroscopy confirmed the structure of major isomer **14**. NOE experiments revealed vicinal correlation between the signals of protons H-6 and the vinylic proton H-5. The differentiation of methylenes CH_2-3 and CH_2-6 was readily established by homonuclear decoupling, since the former is coupled with proton H-2.

In summary, an efficient and stereoselective synthesis of novel α,β-substituted enones **2a-2h** was accomplished. They showed preferential *Z* configuration and *s-trans* conformation. These compounds failed to react with dienes **6** and **11**. Brominated precursor **4a** was a more efficient dienophile, since it was added to **6** and **11** in substantially high stereo- and regioselectivity, respectively.

EXPERIMENTAL SECTION

General. UV spectra were obtained on a Shimadzu 2100 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained on Varian Gemini-300 (300 MHz) and Gemini-200 (200 MHz) instruments, with TMS as internal standard. Further analytical procedures were described elsewhere.[6a]

Refined Coordinates for the X-ray Crystallographic Data of Olefins 2a and 4a (Tables 6 and 7).

Table 6. Crystallographic Data for **2a**·toluene.

Formula	$C_{20}H_{22}N_2O_5$	Cryst. dimens, mm	0.2 x 0.3 x 0.35
Mw	370.41	μ, cm^{-1}	0.87
Cryst syst	triclinic	D (calc), g cm^{-3}	1.289
Space group	PT	*temp*, °K	298
a, Å	8.060 (1)	Diffractometer	Enraf-Nonius CAD-4F
b, Å	11.667 (2)	Radiation	Mo
c, Å	11.836 (2)	Monochromator	graphite
V, $Å^3$	954.0 (3)	2θ scan range, deg	2-44
α, deg	64.28 (1)	No. of rflns collected	2328
β, deg	73.64 (1)	No. of unique obsvd rflns	1323
γ, deg	73.74 (1)	R (merg)	---
λ, Å	0.71073	Rf	0.0701
Z	2	Rwf	0.0655

Table 7. Crystallographic Data for **4a**.

Formula	$C_{11}H_8BrNO_5$	μ, cm^{-1}	33.31
Mw	314.10	D (calc), g cm^{-3}	1.703
Cryst syst	monoclinic	*temp*, °K	298
Space group	$P2_1$	Diffractometer	Enraf-Nonius CAD-4F
a, Å	6.9537 (8)	Radiation	Mo
b, Å	16.418 (1)	Monochromator	graphite
c, Å	10.736 (1)	2θ scan range, deg	2-44
V, $Å^3$	1225.2 (8)	No. of rflns collected	1718
β, deg	91.726 (1)	No. of unique obsvd rflns	1436
λ, Å	0.71073	R (merg)	0.028
Z	4	Rf	0.068
Cryst. dimens, mm	0.62 x 0.75 x 0.95	Rwf	0.081

3,4-Dibromo-3-(p-nitrobenzoyloxy)-2-butanone (3). To a solution of 0.5 g (2.1 mmol) of **1a** in 15 mL of dry CH_2Cl_2 at room temperature was added dropwise 0.43 g (2.7 mmol) of bromine dissolved in 10 mL of CH_2Cl_2. The mixture was diluted with CH_2Cl_2 (40 mL) and was washed with a saturated solution of $Na_2S_2O_3$ (3 x 30 mL) and brine (3 x 30 mL). The organic layer was dried (Na_2SO_4) and the solvent was removed in vacuo. The amorfous crystals were recrystallized from EtOAc/MeOH, 7:3, to give 0.77 g (92%) of white crystals of **3**: mp 63-64 °C; IR (KBr) 3100, 3060, 1720, 1600, 1520, 1420, 1370, 1280, 1190, 880, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.5 (s, 3H, CH_3CO), 4.40 (d, J = 8.6 Hz, 1H, H-4), 4.69 (d, J = 8.6 Hz, 1H, H-4), 8.25 (m, 2H, ArH), 8.37 (m, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4 (C-1), 32.9 (C-4), 86.3 (C-3), 123.9 (C-8), 131.2 (C-7), 133.7 (C-6), 151.3 (C-9), 161.3 (C-5), 194.7 (C-2). Anal. Calcd for $C_{11}H_9Br_2NO_5$: C, 33.45; H, 2.30. Found: C, 33.41; H, 2.64.

(Z)-4-Bromo-3-(p-nitrobenzoyloxy)-3-buten-2-one (4a). To a solution of 0.1 g (0.254 mmol) of **3** in 3.0 mL of dry CH_2Cl_2 at room temperature was added dropwise 0.028 g (0.28 mmol) of triethylamine dissolved in CH_2Cl_2 (2.0 mL). The mixture was stirred for 1 h at room temperature, diluted with CH_2Cl_2 (30 mL) and washed with ice-cold aqueous 5% HCl (2 x 20 mL) and brine until neutral. The organic layer was dried (Na_2SO_4) and the solvent was removed under reduced pressure, giving a brown solid. This was recrystallized from EtOAc/MeOH, 7:3 to yield 0.057 g (72%) of **4a** as pale yellow crystals: mp 104-105 °C; UV (CH_3CN): 243 (19950); (EtOH): 245 (20000); IR (KBr) 1760, 1690, 1620, 1530, 1350, 1240, 1100 cm^{-1}; ^1H

NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H, CH_3CO), 7.52 (s, 1H, CH=), 8.34 (s, 4H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$), table 4. Anal. Calcd for $C_{11}H_8BrNO_5$: C, 42.06; H, 2.57. Found: C, 41.83; H, 2.39.

General Procedure for the Preparation of β-Amino Olefins 2a-2d. A solution of 0.1 g (0.32 mmol) of **4a** in dry CH_2Cl_2 (3.0 mL) was placed in a 25-mL round-bottom flask provided with a rubber septum, under an N_2 atmosphere at room temperature, and the corresponding amine was added: For **2a**, 0.019 g (0.42 mmol) of dimethylamine; for **2b**, 0.03 g (0.42 mmol) of diethylamine; for **2c**, 0.042 g (0.42 mmol) of diisopropylamine; and for **2d**, 0.03 g (0.42 mmol) of pyrrolidine. The mixture was stirred for 1 h at room temperature, dissolved in CH_2Cl_2 (40 mL) and washed with ice-cold aqueous 5% HCl (2 x 20 mL) and brine until neutral. The organic layer was dried (Na_2SO_4) and the solvent was removed in vacuo. The amorfous crystals were recrystallized from EtOAc/MeOH, 9:1, to yield:

(Z)-4-(N,N-Dimethylamino)-3-(p-nitrobenzoyloxy)-3-buten-2-one (2a): 0.074 g (84%) as yellow crystals: mp 153-154 °C; UV (CH_3CN): 268 (17800), 293 (30000); (EtOH): 260 (23600), 297 (36300); IR (KBr) 1750, 1660, 1610, 1600, 1520, 1320, 1270, 1100 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.19 (br s, 3H, CH_3CO), 3.02 (br s, 6H, NMe_2), 7.08 (br s, 1H, CH=), 8.31 (br s, 4H, ArH); ^{13}C NMR (50 MHz, DMSO-d_6), table 4; MS (70 eV) 278 (M^+, 10), 207 (4), 150 (12), 128 (100), 100 (74), 58 (11). Anal. Calcd for $C_{13}H_{14}N_2O_5$: C, 56.11; H, 5.07. Found: C, 56.28; H, 5.16.

(Z)-4-(N,N-Diethylamino)-3-(p-nitrobenzoyloxy)-3-buten-2-one (2b): 0.082 g (84%) as yellow crystals: mp 155-156 °C; UV (CH_3CN): 293 (31800); (EtOH): 248 (41200), 297 (31500); IR (KBr) 1740, 1660, 1590, 1530, 1360, 1320, 1250, 1090 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.20 (br t, J = 6.7 Hz, 6H, $N[CH_2CH_3]_2$), 2.20 (br s, 3H, CH_3CO), 3.30 (br q, J = 6.7 Hz, 4H, $N[CH_2CH_3]_2$), 7.09 (br, 1H, CH=), 8.30 (br s, 4H, ArH); ^{13}C NMR (50 MHz, DMSO-d_6), table 4; MS (70 eV) 306 (M^+, 3), 156 (100), 150 (10), 128 (25), 86 (7). Anal. Calcd for $C_{15}H_{18}N_2O_5$: C, 58.82; H, 5.92. Found: C, 58.69; H, 6.05.

(Z)-4-(N,N-Diisopropylamino)-3-(p-nitrobenzoyloxy)-3-buten-2-one (2c): 0.054 g (51%) as yellow crystals: mp 159-160°C; UV (CH_3CN): 260 (16600), 295 (28200); (EtOH): 260 (15500), 299 (23300); IR (KBr) 1740, 1660, 1590 , 1520 , 1300, 1260, 1090 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.30 (d, J = 7.0 Hz, 12H, $N[CH(CH_3)_2]_2$), 2.26 (br s, 3H, CH_3C=O), 4.05 (br, 2H, $N[CH(CH_3)_2]_2$), 7.38 (br s, 1H, CH=), 8.44 (br s, 4H, Ar-H); ^{13}C NMR (75 MHz, DMSO-d_6), table 4; MS (70 eV) 334 (M^+, 4), 319 (1), 291 (5), 249 (2), 184 (100), 150 (27), 142 (56), 114 (28), 104 (20), 72 (44). Anal. Calcd for $C_{17}H_{22}N_2O_5$: C, 61.07; H, 6.63. Found: C, 61.03; H, 6.36.

(Z)-4-Pyrrolidino-3-(p-nitrobenzoyloxy)-3-buten-2-one (2d): 0.015 g (16%) as yellow crystals: mp 163-164 °C; UV (CH_3CN): 260 (15600), 299 (33700); (EtOH): 260 (15600), 303 (29800); IR (KBr) 1740, 1650, 1600, 1270, 1100 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.90 (br s, 4H, 2 CH_2), 2.25 (br s, 3H, CH_3C=O), 3.50 (br s, 4H, $(CH_2)_2N$), 7.35 (br s, 1H, CH=), 8.36 (s, 4H, Ar-H); ^{13}C NMR (75 MHz, DMSO-d_6), table 4. Anal. Calcd for $C_{15}H_{16}N_2O_5$: C, 59.21; H, 5.30. Found: C, 59.08; H, 5.36.

General Procedure for the Preparation of β-Anilino Olefins 2e-2f. A solution of 0.1 g (0.32 mmol) of **4a** in 3.0 mL of dry DMF was placed in a 25-mL round-bottom flask provided with a rubber septum, under an N_2 atmosphere and at room temperature, and the corresponding aniline was added: For **2e**, *p*-toluidine (0.043 g, 0.4 mmol); and for **2f**, *p*-anisidine (0.052 g, 0.042 mmol). The mixture was vigorously stirred until complete dissolution and 0.042 g (0.42 mmol) of triethylamine were added. The mixture was stirred at room

temperature for 24 h, was dissolved in CH_2Cl_2 (30 mL); then, it was washed with ice-cold aqueous 5% HCl (2 x 20 mL) and brine until neutral. The organic layer was dried (Na_2SO_4) and the solvent was removed in vacuo. The remaining solid was recrystallized from EtOAc/MeOH, 7:3, to give:

(Z)-3-(p-Nitrobenzoyloxy)-4-[N-(p-toluidino)]-3-buten-2-one (2e): 0.06 g (56%) as orange crystals: mp 172-173°C; UV (CH_3CN): 267 (15700), 293 (31400), 323 (50700); (EtOH): 260 (6000), 301 (5900), 331 (12900); IR (KBr) 3250, 1740, 1670, 1600, 1520, 1350, 1260, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.58 (s, 3H, CH_3Ar) , 2.33 (s, 3H, CH_3CO), 6.49 (br d, J = 13.5 Hz, 1H, CH=), 6.91 (m, 2H, *p*-toluidyl-H), 7.15 (m, 2H, *p*-toluidyl-H), 7.76 (d, J = 13.5 Hz, 1H, NH), 8.37 (s, 4H, PNB-H); ^{13}C NMR (75 MHz, DMSO-d_6), table 4. Anal. Calcd for $C_{18}H_{16}N_2O_5$: C, 63.52; H, 4.74. Found: C, 63.17; H, 4.75.

(Z)-4-[N-(p-Anisidino)]-3-(p-nitrobenzoyloxy)-3-buten-2-one (2f): 0.046 g (41%) as yellow crystals: mp 168-169°C; UV (CH_3CN): 262 (33600), 297 (62200), 328 (63000); (EtOH): 260 (9400), 307 (8800), 334 (10600); IR (KBr) 3360, 1750, 1670, 1610, 1510, 1280, 1230, 1090 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.38 (s, 3H, CH_3CO), 3.74 (s, 3 H, OMe) , 6.92 (m, 2H, *p*-anisidyl-H), 7.28 (m, 2H, *p*-anisidyl-H), 8.05 (br d, J = 13.5 Hz, 1H, CH=), 8.33 (m, 2H, PNB-H), 8.42 (m, 2H, PNB-H), 9.10 (d, J = 13.5 Hz, 1H, N-H); ^{13}C NMR (75 MHZ, DMSO-d_6), table 4. Anal. Calcd for $C_{18}H_{16}N_2O_6$: C, 60.67; H, 4.53. Obtenido: C, 60.42; H, 4.71.

General Procedure for the Preparation of β-Thio Olefins 2g-2h. A solution of 0.1 g (0.032 mmol) of **4a** in 3.0 mL of dry DMF was vigorously stirred at room temperature under an N_2 atmosphere, and the corresponding mercaptan was added: For **2g**, *n*-propanethiol (0.032 g, 0.42 mmol); and for **2h**, thiophenol (0.046 g, 0.42 mmol). Then, triethylamine (0.042 g, 0.42 mmol) was added and the mixture was stirred for 1 h at room temperature. The mixture was diluted with CH_2Cl_2 (30 mL) and washed with ice-cold aqueous 5% HCl (2 x 20 mL) and brine until neutral. The organic layer was dried (Na_2SO_4) and the solvent was removed in vacuo. The remaining solid was recrystallized from EtOAc/MeOH, 7:3, to give:

(Z)-3-(p-Nitrobenzoyloxy)-4-(n-thiopropoxy)-3-buten-2-one (2g): 0.091 g (93%) as colorless needles: mp 119-120 °C; UV (CH_3CN): 265 (10300), 288 (12100); (EtOH): 267 (5900), 294 (7300); IR (KBr) 3050, 1750, 1680, 1600, 1540, 1360, 1275, 1230, 1110 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, J = 7.3 Hz, 3H, $CH_3CH_2CH_2$), 1.75 (sext, J = 7.3 Hz, 2H, $CH_3CH_2CH_2$), 2.35 (s, 3H, CH_3CO), 2.89 (t, J = 7.3 Hz, 2H, $CH_3CH_2CH_2$), 7.48 (s, 1H, CH=), 8.35 (s, 4H, Ar-H); ^{13}C NMR (75 MHz, DMSO-d_6), table 4. Anal. Calcd for $C_{14}H_{15}NO_5S$: C, 54.36; H, 4.89. Found: C, 54.16; H, 5.00.

(Z)-3-(p-Nitrobenzoyloxy)-4-thiophenoxy-3-buten-2-one (2h): 0.092 g (85%) as pale yellow crystals: mp 63-64 °C; UV (CH_3CN): 260 (31200), 294 (33000); (EtOH): 254 (30200), 297 (24700); IR (KBr) 1730, 1680, 1530, 1340, 1270, 1100 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.33 (s, 3H, CH_3CO), 7.40-7.50 (m, 5H, PhH), 7.52 (s, 1H, CH=), 8.45 (s, 4H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6), table 4. Anal. Calcd for $C_{17}H_{13}NO_5S$: C, 59.47; H, 3.81. Found: C, 59.44; H, 4.00.

2-endo-Acetyl-3-exo-bromobicyclo[2.2.1]hept-5-en-2-exo-yl p-Nitrobenzoate (9) and 2-exo-Acetyl-3-endo-bromobicyclo[2.2.1]hept-5-en-2-endo-yl p-Nitrobenzoate (10). Method A. A mixture of 0.1 g (0.32 mmol) of **4a**, 0.21 g (3.2 mmol) of **6** and hydroquinone (3 mg) in anhydrous xylene (2 mL), under an N_2 atmosphere, was heated to 100 °C for 31 h. The crude was purified by column chromatography on silica gel (12 g, hexane/EtOAc, 9.5:0.5), giving a mixture of adducts **9/10** (<5 : >95) as

white crystals, which were recrystallized from EtOAc/MeOH, 3:7, giving 0.03 g (25%): mp 149-150 °C; IR (KBr) 1730, 1680, 1510, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.78 (br s, 2H, H-7), 2.26 (s, 3H, CH_3CO), 3.30 (m, 1H, H-1), 3.45 (m, 1H, H-4), 5.05 (d, *J* = 3.4 Hz, 1H, H-3), 6.35 (dd, *J* = 5.5, 2.9 Hz, 1H, H-6), 6.48 (dd, *J* = 5.5, 3.3 Hz, 1H, H-5), 8.23 (m, 2H, ArH), 8.34 (m, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5 (C-9), 44.5 (C-7), 48.9 (C-1), 49.5 (C-4), 53.3 (C-3), 90.0 (C-2), 123.7 (C-13), 131.2 (C-12), 134.1 (C-6), 134.4 (C-11), 139.5 (C-5), 151.0 (C-14), 164.2 (C-10), 201.9 (C-8); MS (70 eV) 300 (M^+-Br, 1), 270 (1), 151 (7), 135 (16), 120 (100), 93 (3). Anal. Calcd for $C_{16}H_{14}BrNO_5$: C, 50.55; H, 3.71. Found: C, 50.38; H, 3.88.

Method B. To a mixture of **4a** (0.1 g, 0.32 mmol), $ZnCl_2$ (0.44 g, 3.2 mmol) or $AlCl_3$ (0.43 g, 3.2 mmol) in dry CH_2Cl_2 (2.0 mL), under an N_2 atmosphere at room temperature, was added **6** (0.053 g, 0.8 mmol). The mixture was stirred at room temperature for 48 h and **6** (0.053 g, 0.8 mmol) was added. The mixture was stirred for 24 h and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (15 g, hexane/EtOAc, 9:1), to yield: With $ZnCl_2$, 0.048 g (40%) of a mixture of adducts **9/10** (37:63); and with $AlCl_3$, 0.045 g (37%) of a mixture of adducts **9/10** (25:75).

(1R*,2R*)-1-Acetyl-2-bromo-4-methylcyclohex-4-en-1-yl p-Nitrobenzoate (14) and (1R*,2R*)-1-Acetyl-2-bromo-5-methylcyclohex-4-en-1-yl p-Nitrobenzoate (15). Method A. A mixture of **4a** (0.1 g, 0.32 mmol), **11** (0.109 g, 1.6 mmol) and hydroquinone (3 mg) in anhydrous xylene (5 mL) was placed under an N_2 atmosphere in a screw cap flask. After being stirred at 130 °C for 10 h, 0.109 g (1.6 mmol) of **11** was added. The mixture was heated for 5 h more. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (12 g, hexane/EtOAc, 9:1) to yield 0.05 g (41%) of a mixture of adducts **14/15** (7:3).

Method B. To a mixture of **4a** (0.1 g, 0.32 mmol), $AlCl_3$ (0.43 g, 3.2 mmol) or $ZnCl_2$ (0.44 g, 3.2 mmol) in dry CH_2Cl_2 (2.0 mL) under an N_2 atmosphere at room temperature was added **11** in fourfold amounts of 0.027 g (0.4 mmol) every hour. The mixture was stirred at room temperature for 5 h and the solvent was removed in vacuo. The solid residue was purified by column chromatography on silica gel (12 g, hexane/EtOAc, 8:2), to yield: With $AlCl_3$, 0.052 g (43%) of a mixture of adducts **14/15** (85:15); and with $ZnCl_2$, 0.05 g (41%) of a mixture of adducts **14/15** (90:10). IR (KBr) 3020, 1710, 1520, 1300 cm^{-1}; data of **14**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.70 (br s, 3H, CH_3C=), 2.30 (s, 3H, CH_3CO), 2.80 (m, 2H, H-3), 3.02 (dm, *J* = 18.7 Hz, 1H, H-6), 3.14 (dm, *J* = 18.7 Hz, 1H, H-6), 4.58 (dd, *J* = 6.3, 6.0 Hz, 1H, H-2), 5.37 (br s, 1H, CH=), 8.25 (m, 2H, ArH), 8.35 (m, 2H, ArH). Further signals attributed to isomer **15**: 2.33 (s, 3H, CH_3CO), 4.52 (dd, *J* = 11.0, 6.0 Hz, 1H, H-2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5 (C-7), 26.5 (C-9), 30.4 (C-3), 39.0 (C-6), 50.0 (C-2), 86.2 (C-1), 116.6 (C-5), 123.7 (C-13), 131.1 (C-12), 131.5 (C-4), 135.0 (C-11), 151.0 (C-14), 163.7 (C-10), 204.0 (C-8). Anal. Calcd for $C_{16}H_{16}BrNO_5$: C, 50.28; H, 4.22. Found: C, 50.44; H, 4.46.

Acknowledgment. We are grateful to Dr. Eusebio Juaristi, Dra. María Rosales and Dr. Francisco Delgado for helpful comments. We thank F. Labarrios and H. Nguyen for their help in spectrometric measurements and Dr. M. Schwartz for advice on MOPAC. J.T. acknowledges financial support from

DEPI/IPN (Grant 921769) and CONACYT (Grant 411300-5-3305E). J.P. thanks COSNET for a scholarship awarded.

REFERENCES AND NOTES

1. For recent examples, see: (a) Martin, S. F.; Daniel, D.; Cherney, R. J.; Liras, S. *J. Org. Chem.* **1992**, *57*, 2523-2525, and references cited therein. (b) Rossi, R.; Carpita, A.; Cossi, P. *Tetrahedron Lett.* **1992**, *33*, 4495-4498. (c) Katritzky, A. R.; Barcock, R. A.; Long, Q.-H.; Balasubramanian, M.; Malhotra, N.; Greenhill, J. V. *Synthesis* **1993**, 233-236. (d) Bland, J.; Shah, A.; Bortolussi, A.; Stammer, C. H. *J. Org. Chem.* **1988**, *53*, 992-995. (e) Das, J.; Reid, J. A.; Kronenthal, D. R.; Singh, J.; Pansegrau, P. D.; Mueller, R. H. *Tetrahedron Lett.* **1992**, *33*, 7835-7838. (f) Nunami, K.-i.; Hiramatsu, K.; Hayashi, K.; Matsumoto, K. *Tetrahedron* **1988**, *44*, 5467-5478. (g) Cecchetti, V.; Fravolini, A.; Schiaffela, F.; Tabarrini, O.; Zhou, W.; Pagella, P. G. *J. Heterocycl. Chem.* **1992**, *29*, 375-382. (h) Schmidt, U.; Griesser, H.; Leitenberger, V.; Lieberknecht, A.; Mangold, R.; Meyer, R.; Riedl, B. *Synthesis* **1992**, 487-490. (i) Armstrong, R. W.; Tellew, J. E.; Moran, E. J. *J. Org. Chem.* **1992**, *57*, 2208-2211. (j) Nakatani, S.; Yoshida, J.-i.; Isoe, S. *J. Chem. Soc., Chem. Commun.* **1992**, 880-881. (k) Yamanaka, H.; Yamashita, S.; Ishihara, T. *Synlett* **1993**, 353-354. (l) Coleman, R. S.; Carpenter, A. J. *J. Org. Chem.* **1993**, *58*, 4452-4461. (m) Hagiwara, H.; Abe, F.; Uda, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2651-2655.
2. (a) Cativiela, C.; Díaz de Villegas, M. D.; Mayoral, J. A.; Avenoza, A.; Peregrina, J. M. *Tetrahedron* **1993**, *49*, 677-684. (b) Sasaki, T.; Ishibashi, Y.; Ohno, M. *Tetrahedron Lett.* **1982**, *23*, 1693-1696. (c) Kim, K. S.; Cho, I. H.; Joo, Y. H.; Yoo, I. Y.; Song, J. H.; Ko, J. H. *Tetrahedron Lett.* **1992**, *33*, 4029-4032. (d) Dauben, W. G.; Kowalczyk, B. A.; Lichtenthaler, F. W. *J. Org. Chem.* **1990**, *55*, 2391-2398. (e) Katagiri, N.; Yamamoto, M.; Kaneko, C. *Chem. Lett.* **1990**, 1855-1858. (f) Rehnberg, N.; Sundin, A.; Magnusson, G. *J. Org. Chem.* **1990**, *55*, 5477-5483. (g) Ishihara, K.; Gao, Q.; Yamamoto, H. *J. Org. Chem.* **1993**, *58*, 6917-6919.
3. Haag-Zeino, B.; Schmidt, R. R. *Liebigs Ann. Chem.* **1990**, 1197-1203. Tietze, L. F.; Fennen, J.; Wichmann, J. *Chem. Ber.* **1992**, *125*, 1507-1511.
4. Reyes, A.; Aguilar, R.; Muñoz, A. H.; Zwick, J.-C.; Rubio, M.; Escobar, J.-L.; Soriano, M.; Toscano, R.; Tamariz, J. *J. Org. Chem.* **1990**, *55*, 1024-1034.
5. Jiménez, R.; Pérez, L.; Tamariz, J.; Salgado, H. *Heterocycles* **1993**, *35*, 591-598.
6. (a) Orduña, A.; Zepeda, L. G.; Tamariz, J. *Synthesis* **1993**, 375-377. (b) Andrade, R. M.; Muñoz, A. H.; Tamariz, J. *Synth. Commun.* **1992**, *11*, 1603-1609. (c) Gómez, A.; Aguilar, R.; Muñoz, A. H.; Tamariz, J. *Rev. Latinoamer. Quím.* **1990**, *21*, 39-41.
7. Tamariz, J.; Vogel, P. *Helv. Chim. Acta* **1981**, *64*, 188-197.
8. Ben Ayed, T.; Amri, H.; El Gaied, M. M. *Tetrahedron* **1991**, *47*, 9621-9628.
9. Dabrowski, J.; Kozerski, L. *J. Chem. Soc. (B)* **1971**, 345-348, and references cited therein.
10. (a) Dabrowski, J.; Kozerski, L. J. *Org. Magn. Reson.* **1972**, *4*, 137-144. (b) Jachak, M.; Krießmann, U.; Mittelbach, M.; Junek, H. *Monatsh. Chem.* **1993**, *124*, 199-207. (c) Leitenberger, V.; Lieberknecht, A.; Mangold, R.; Meyer, R.; Riedl, B. *Synthesis* **1992**, 487-490.

11. Dabrowski, J.; Kozerski, L. *J. Chem. Soc., Chem. Commun.* **1968**, 586-587.
12. Oki, M. *Applications of Dynamic NMR Spectroscopy to Organic Chemistry*; VCH Publishers: Weinheim, 1985; pp 76-78.
13. Juaristi, E. *Introduction to Stereochemistry & Conformational Analysis*; John Wiley & Sons: New York, 1991; p 254. Ref. 12, p 5.
14. Dahlqvist, K.-I. *Acta Chem. Scand.* **1970**, *24*, 1941-1952. Shvo, Y.; Shanan-Atidi, H. *J. Am. Chem. Soc.* **1969**, *91*, 6689-6696.
15. Dudek, G. O.; Volpp, G. P. *J. Am. Chem. Soc.* **1963**, *85*, 2697-2702.
16. Sandstrom, J.; Wennerbeck, I. *J. Chem. Soc., Chem. Commun.* **1969**, 306-307.
17. Dabrowski, J.; Kozerski, L. *Org. Magn. Reson.* **1973**, *5*, 469-470.
18. Alkaabi, S. S.; Shawali, A. S. *Can. J. Chem.* **1992**, *70*, 2515-2519.
19. Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. II* **1987**, S1.
20. Kozerski, L.; Dabrowski, J. *Org. Magn. Reson.* **1973**, *5*, 459-462.
21. (a) Marr, D. H.; Stothers, J. B. *Can. J. Chem.* **1965**, *43*, 596-607. (b) Wehrli, F. W.; Marchand, A. P.; Wehrli, S. *Interpretation of Carbon-13 NMR Spectra;* John Wiley & Sons: New York, 1988; pp 40-42
22. Yates, P.; Eaton, P. *J. Am. Chem. Soc.* **1960**, *82*, 4436-4437. Pagni, R. M.; Kabalka, G. W.; Bains, S.; Plesco, M.; Wilson, J.; Bartmess, J. *J. Org. Chem.* **1993**, *58*, 3130-3133. Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876-889. Alston, P.V.; Ottenbrite, R. M. *J. Org. Chem.* **1975**, *40*, 1111-1116. Houk, K. N.; Strozier, R. W. *J. Am. Chem. Soc.* **1973**, *95*, 4094-4096.
23. Spino, C.; Liu, G. *J. Org. Chem.* **1993**, *58*, 817-819. Mérour, J.-Y.; Mérour, A. *Synthesis* **1994**, 767-769. Coutts, S. J.; Wallace, T. C. *Tetrahedron* **1994**, *50*, 11755-11780.
24. (a) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779-807. (b) Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361-369, and references cited therein. (c) Anh, N. T.; Canadell, E.; Eisenstein, O. *Tetrahedron* **1978**, *34*, 2283-2288.
25. Sustmann, R. *Tetrahedron Lett.* **1971**, 2721-2724.
26. Houk, K. N.; Munchausen, L. L. *J. Am. Chem. Soc.* **1976**, *98*, 937-946.
27. Kahn, S. D.; Pau, C. F.; Overman, L. E.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7381-7396, and references cited therein.
28. Boucher, J.-L.; Stella, L. *Tetrahedron* **1988**, *44*, 3595-3605.
29. Caramella, P.; Houk, K. N.; Domelsmith, L. N. *J. Am. Chem. Soc.* **1977**, *99*, 4511-4514.
30. Loncharich, R. J.; Schwartz, T. R.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 14-23. Rebiere, F.; Riant, O.; Kagan, H. B. *Tetrahedron: Asymmetry* **1990**, *1*, 199-214. Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1993**, *115*, 3133-3139. Odenkirk, W.; Rheingold, A. L.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 6392-6398.
31. Martin, J. G.; Hill, R. K. *Chem. Rev.* **1961**, *61*, 537-562. Mellor, J. M.; Webb, C. F. *J. Chem. Soc., Perkin Trans. II* **1974**, 17-22. Cantello, B. C. C.; Mellor, J. M.; Webb, C. F. *J. Chem. Soc., Perkin Trans. II* **1974**, 22-25. Houk, K. N.; Luskus, L. J. *J. Am. Chem. Soc.* **1971**, *93*, 4606-4607. Houk, K. N. *Tetrahedron Lett.* **1970**, 2621-2624. Vedejs, E.; Stults, J. S.; Wilde, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 5452-5460.

32. Stammen, B.; Berlage, U.; Kindermann, R.; Kaiser, M.; Günther, B.; Sheldrick, W. S.; Wenzel, P.; Roth, W. R. *J. Org. Chem.* **1992**, *57*, 6566-6575, and references cited therein.
33. Bueno, M. P.; Cativiela, C.; Finol, C.; Mayoral, J. A.; Jaime, C. *Can. J. Chem.* **1987**, *65*, 2182-2186.
34. McCarrick, M. A.; Wu, Y.-D.; Houk, K. N. *J. Org. Chem.* **1993**, *58*, 3330-3343.
35. Kakushima, M. *Can. J. Chem.* **1979**, *57*, 2564.
36. Usually, in the norbornene skeleton, the coupling constant between the bridgehead proton and the *endo* proton is unobserved or very small: Davis, J. C., Jr.; Van Auken, T. V. *J. Am. Chem. Soc.* **1965**, *87*, 3900-3905. Brügel, W. *Handbook of NMR Spectral Parameters*; Heyden: London, 1979; V 1, pp 105-107.

(*Received in USA* 20 *October* 1994; *revised* 9 *February* 1995; *accepted* 10 *February* 1995)