Novel formation of phenylcyclopropanes from the reaction of β-cyanostyrenes and related compounds with 2-methoxyfuran: experimental and theoretical studies

Kuniaki Itoh* and Shigehisa Kishimoto

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As a diene, 2-methoxyfuran fails to generate a Diels–Alder adduct when it reacts with β-cyanostyrenes (cinnamonitriles). However, in the reaction with β-cyanostyrenes possessing additional electron-withdrawing groups (CN, CO_2Et and SO_2Ph), it yielded two new phenylcyclopropanes. We have used computational methods to investigate the mechanism and to probe the regioselectivity observed in the rearrangement reactions. We used a B3LYP/6-31G* level density functional calculation to locate the transition states (TS), and to account for the selectivity observed in these reactions, we examined the global electronic index involved. An analysis of the results for the reaction pathways of two adducts (the *endo* and *exo* isomers) shows that the reaction takes place *via* a polar stepwise mechanism. The first step involves a side-on nucleophilic attack by the α-carbon atom of the furan ring on the vinyl carbon of the cyanostyrene to give a zwitterionic intermediate. An intramolecular substitution within the intermediate (IN) gives the cyclopropane ring, together with fission of the furan ring. The potential energy barriers for these reactions had the following values: at the nucleophilic addition step, 14.6 and 13.7 kcal mol^{-1} for **2b**, and 18.4 and 17.8 kcal mol^{-1} for **2c**; at the rearrangement step, 22.3 and 22.8 kcal mol^{-1} for **2b**, and 25.1 and 23.1 kcal mol^{-1} for **2c**. Solvent effects in chloroform stabilized the rearrangement steps by 5–6 kcal mol^{-1}, but the nucleophilic addition step appeared to be slightly affected. From the theoretical results, in the case of **2b**, the energy of TS2-*endo* is lower than that of TS2-*exo*, so more *trans*-cyclopropane product from the *endo* form is formed under kinetic conditions. Conversely, in the case of **2c**, the energy of TS2-*exo* is lower and more of the *cis*-product is formed. Density functional theory analysis of these reactions is in complete agreement with the experimental results.

Introduction

Over the last two decades, Diels–Alder cycloaddition reactions using furans as the diene have been extensively studied by many research groups as one method for the construction of valuable synthetic intermediates,[1] and we have also been studying the Diels–Alder reactions of furans with some electron-deficient dienophiles.[2] Recently, we reported that 2-methoxyfuran reacts with β-nitrostyrenes to give not only the Michael adducts, but also the unexpected new isoxazoline *N*-oxide,[2d,g] without the formation of a Diels–Alder adduct. Furans are known to be rather unreactive dienes[3] and hence, reactions of furans require stronger dienophiles to make them proceed.[1b,3a,4] Cyano-olefins are powerful and versatile reagents, which have found extensive applications in organic synthesis.[5] Due to the strong electron-withdrawing properties of the cyano group, acrylnitriles are excellent Michael and Diels–Alder acceptors, and the cyano group can be further transformed into a wide range of functionalities.[5,6] In Diels–Alder reactions, they react with dienes to give not only bicyclonitriles, but also azabicyclo compounds.[7] The use of cyanostyrene derivatives in combination with benzaldehyde affords pyrrole derivatives.[8] Recently, we reported some interesting novel reactions for the formation of phenylcyclopropane from the reaction of β-cyanostyrenes with 2-methoxyfurans (see Scheme 1).[2e] In this paper, our aim is to contribute to a better understanding and interpretation of the mechanistic features of these processes, including of the addition and rearrangement reactions (see Scheme 2), especially by locating and characterizing all of the stationary points involved along the reaction coordinate in this type of reaction, using a computational approach.

It is well known that the furan ring opening in Diels–Alder reactions occurs in the case of donor-substituted furans with reactive olefins possessing an electron-withdrawing group, which undergo rapid smooth cycloaddition with the furan.[1b] The resulting adducts are easily transformed into cyclohexanols and phenols *via* furan ring opening in the presence of Lewis acids.[9,10] An abnormal Diels–Alder reaction of 2-methoxyfuran with benzopyranylidene resulted in the formation of a three-membered ring product.[11] Furthermore, Huisgen *et al.*[12] have reported that the reaction between 2-methoxyfuran and ethylene substituted with very strongly electrophilic groups (two trifluoromethylene and two cyano groups) also leads to the formation of a cyclopropane ring. The high yield of the

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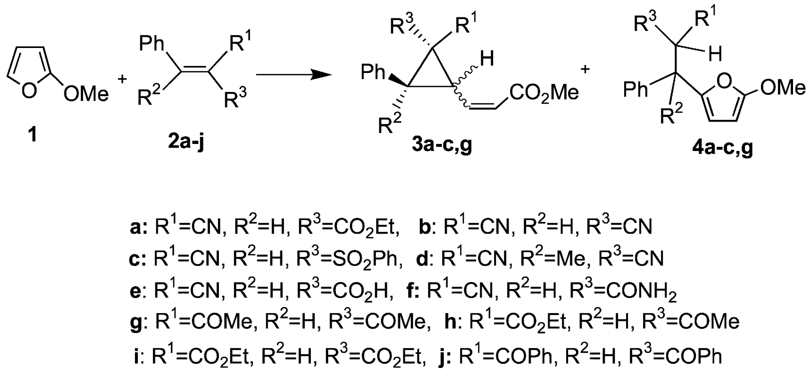
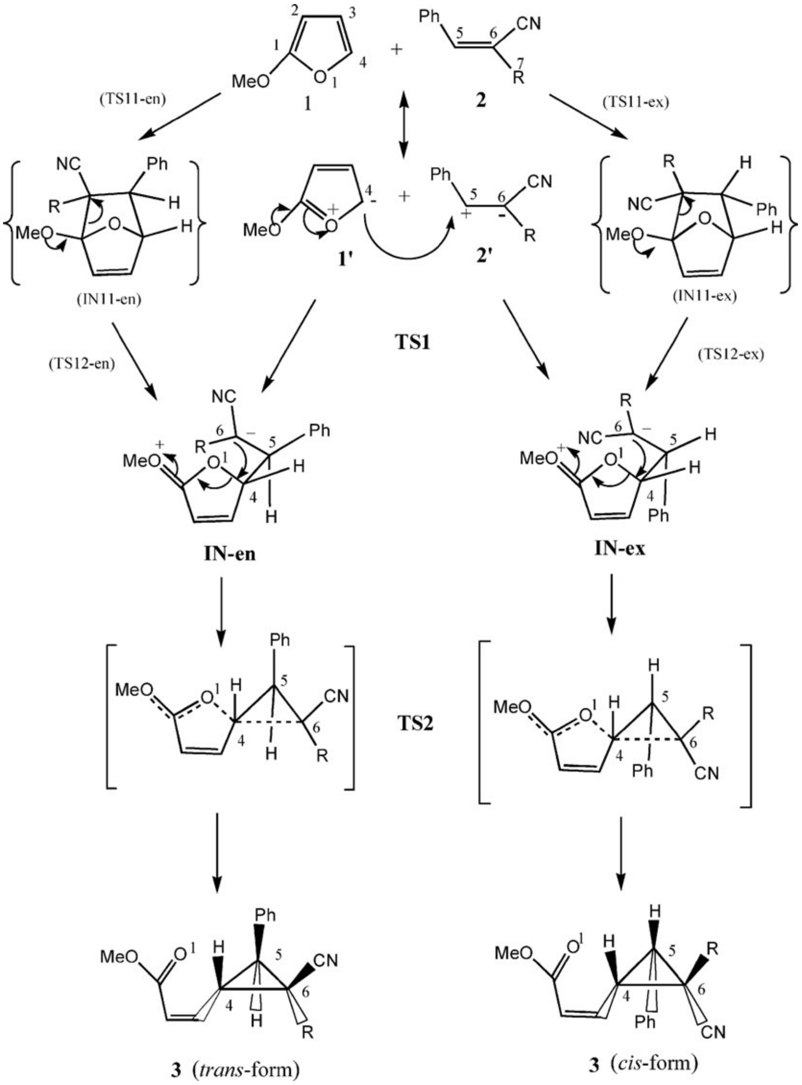
Department of Chemistry, Faculty of Science, Kobe University, Nada-ku, Kobe, 657-8501, Japan. E-mail: kuitoh@kobe-u.ac.jp; Fax: +81 78-803-5770; Tel: +81 6-6436-4865



Scheme 1 The reaction of β-cyanostyrene (**2**) with 2-methoxyfuran (**1**).



Scheme 2 Formation mechanism of phenylcyclopropane.

isolated product, coupled with the disappearance of the strong color associated with charge-transfer in a few seconds at low temperatures, indicates that these strongly electrophilic groups may stabilize the initially formed intermediate.

This reaction presents some interesting points, that is to say, it features an electron-donating group on the furan in the diene system, and not only electron-withdrawing cyano and phenylsulfonyl groups in the dienophile system, but also an electron-donating phenyl group. In the reaction with **2a** (CO_2Et) and **2b** (CN), the *trans*-product is favored, but with **2c** (SO_2Ph), the *cis*-product is more favored. Furthermore, the presence of a phenyl group allows for effective stabilization of the developing electric charge, which favors a stepwise mechanism *via* a zwitterionic intermediate (see Scheme 2).[13] In addition, after the formation of the zwitterionic intermediate, the rearrangement reaction proceeds simultaneously with a stepwise process of fission of the carbon–oxygen bond of the furan ring, similar to the reaction of 1-methylpyrrole with dimethyl acetylenedicarboxylate reported by Domingo *et al.*[5b] and the reaction of 2-methoxyfuran with β-nitrostyrene by us.[2d,g]

Results and discussion

Experimental results

No reaction between cyanostyrenes and furan or 2-methylfuran took place; therefore, in the present study we used 2-methoxyfuran as a more reactive diene.[1b,14]

A typical experimental procedure was as follows: to a stirred solution of 2-methoxyfuran (**1**; 2.5 mmol) in chloroform (3 mL) was added ethyl 1-cyano-cinnamate (**2a**; 1.2 mmol) at room temperature under a nitrogen atmosphere. After being stirred for 4 d, the resulting mixture was concentrated under reduced pressure to give an oil, which was separated by column chromatography on silica gel (eluent solvent: ethyl acetate–hexane, 1 : 4).

The results of the reactions of **1** with various β-cyanostyrenes (**2**) are given in Table 1. In general, the β-cyanostyrenes with relatively weak electron-withdrawing groups (**2d–2f**) failed to produce an adduct with **1**, even after a reaction time of one week (Table 1, runs 4–6). However, we expected that β-cyanostyrene derivatives with stronger electron-withdrawing groups (**2a–2c**) might react with **1** to give the adducts, as was the case in previous reaction with electron deficient dienophiles.

Ethyl 1-cyanocinnamate (**2a**) produced a mixture of the adducts (*trans*-**3a** (major) and *cis*-**3a** (minor): 46% yield, and **4a**: 5% yield; Table 1, run 1), but gave no Diels–Alder adducts. The NMR and IR spectra of **3a** showed no evidence for the presence of a furan ring (δ = 6.2 and 7.4; ν = 1260 cm^{-1}) or a methoxy group (δ = 3.5; ν = 1200 cm^{-1}). The ^1H and ^{13}C NMR spectra of the major adduct indicate the presence of a methyl ester group (CO_2CH_3: δ_H = 3.73, s, 3H; δ_C = 63.3 and 165.1) and a vinyl group (CH═CH, *cis* (*syn*) configuration: δ = 6.00, dd, J = 1.0, 11.7 Hz and 6.24, dd, J = 9.3, 11.7 Hz), and the *cis* configuration was confirmed by an NOE experiment. These signals indicate that scission of the furan ring had occurred. Furthermore, the proton signal at higher field (δ = 4.44, ddd, 1H, J = 1.0, 8.3, 9.3 Hz) is correlated with that of a vinyl group proton (δ = 6.24, dd, J = 9.3, 11.7 Hz). On the other hand, the stereochemistry of the minor adduct was found to have a *cis* (*syn*) configuration (based on prominent NOE signals from protons with δ = 3.48, d, J = 9.7 Hz and 4.17, dd, J = 9.7, 10.3 Hz). Finally, the elemental structure of the adduct was determined by single-crystal X-ray diffraction using the major adduct obtained from the reaction of **2c** to be a vinylcyclopropane derivative (Fig. 1). A similar stereoselectivity was also observed in the reaction of **1** with **2b**. However, in case of compound **2c**, which has a bulky phenylsulfonyl group, the amounts of the *cis*-cyclopropanes were greater than those of the *trans* products, in spite of the similar configuration to **2a**.

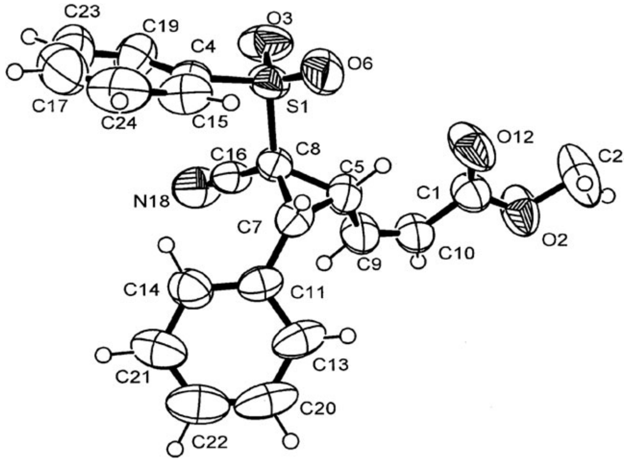


Fig. 1 The structure (ORTEP) of phenylcyclopropane **3c**.

Also, we are currently conducting further investigations of rearrangements utilizing styrenes with non-cyano groups (*e.g.* Table 1, runs 7–10) and the reaction in run 7 indicates their possible applications in the cases where the styrenes have powerful electron-withdrawing groups (β,β′-diacetylstyrene; **2g**).

Geometries and energies

Figs. 2, 3, 4 and 5 show the geometries of the calculated transition structures (TS2) including selected bond lengths, Fig. 6 shows the free energy levels on the reaction coordinate, and Fig. 7 shows the local function, while Tables 2 and 5 show the relative energies of the stationary points and thermodynamic parameters. In Tables 3 and 4, the corresponding geometries obtained from a B3LYP/6-31G* calculation are reported for the intermediates and TSs. In Table 6, the geometric parameters from X-ray analysis are reported with the

Table 1 The reactions of β-cyanostyrenes and related compounds (**2**) with 2-methoxyfuran (**1**)

Run	Cyanostyrene	Cyclopropane	Yield (%)	*trans* : *cis*	Michael adduct	Yield (%)
1	**2a**	**3a**	46	3.5 : 1.0	**4a**	5
2	**2b**	**3b**	84	4.5 : 1.0	**4b**	8
3	**2c**	**3c**	77	1.0 : 1.5	**4c**	4
4	**2d**	—	No reaction	—	—	—
5	**2e**	—	No reaction	—	—	—
6	**2f**	—	No reaction	—	—	—
7	**2g**	**3g**	36	3.3 : 1.0	**4g**	51
8	**2h**	—	—	—	—	Trace
9	**2i**	—	No reaction	—	—	—
10	**2j**	—	No reaction	—	—	—

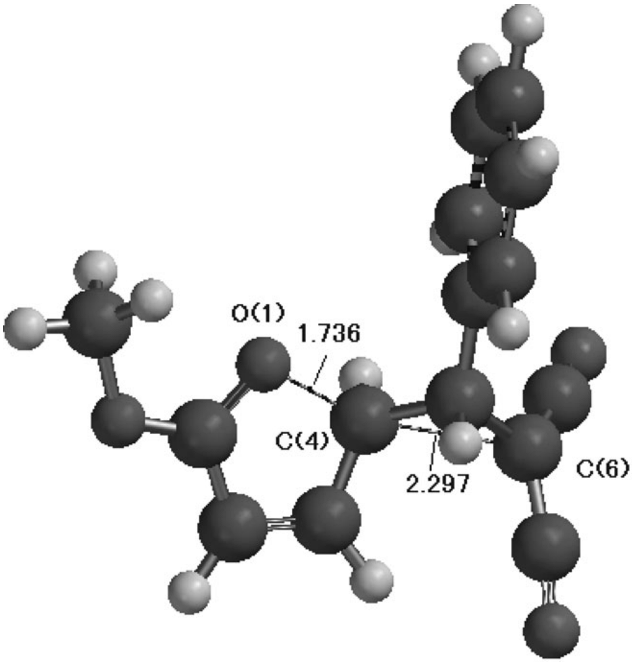


Fig. 2 The transition structure (**TS2-en**) of **1** and **2b**. O(1)–C(4)–C(6) distances in Å.

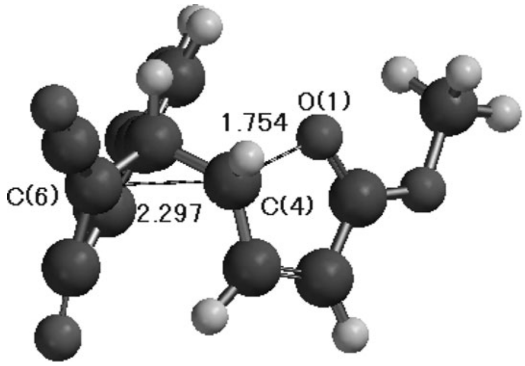


Fig. 3 The transition structure (**TS2-ex**) of **1** and **2b**. O(1)–C(4)–C(6) distances in Å.

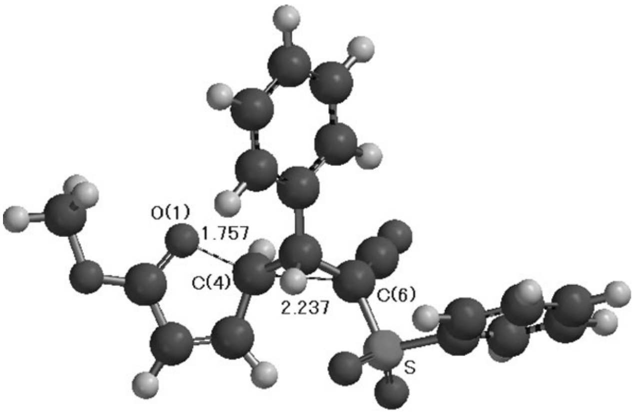


Fig. 4 The transition structure (**TS2-en**) of **1** and **2c**. O(1)–C(4)–C(6) distances in Å.

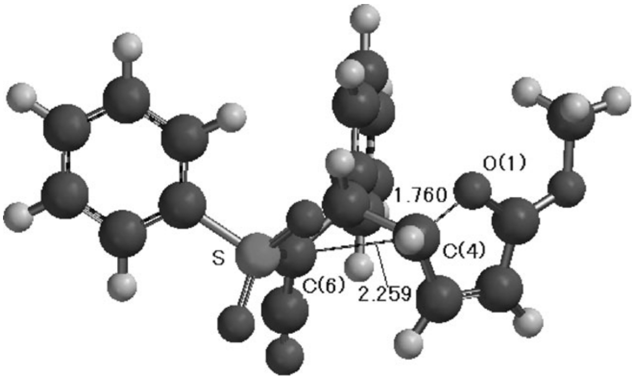


Fig. 5 The transition structure (**TS2-ex**) of **1** and **2c**. O(1)–C(4)–C(6) distances in Å.

calculation values, and in Table 7, the parameters of the global properties are reported.

Scheme 2 illustrates that these reactions take place *via* a stepwise mechanistic pathway. The reaction is initiated by nucleophilic attack of the unsubstituted C4 carbon atom of **1** on the C5 carbon atom (the carbon atom attached to the cyano group) of β-cyanostyrene **2** to give a zwitterionic intermediate. The attack of **1** on **2** can take place *via* two stereoisomers formed from the *endo* and *exo* approach of the 2-methoxyfuran ring to the phenyl group belonging to the styrene. Thus, these regioisomers are two *erythro* isomers (**IN-en**: gauche conformation between H4 of the furan and H5 of the styrene, and **IN-ex**: synclinal conformation between H4 and H5). The reactive carbanion of the cyanostyrene moiety attacks the nucleophilic C4 position of the methoxyfuran moiety in the intermediate accompanied by the carbon–oxygen bond fission of the furan ring to yield the cyclopropane product, **3**.

Structures and energetics of gas-phase calculation

At the first two transition states from the nucleophilic attack of **1** on **2** (see Scheme 2), the potential energy barriers associated with **TS1-en** and **TS1-ex** are 14.6 and 13.7 kcal mol^{-1} for **2b**, and 18.4 and 17.8 kcal mol^{-1} for **2c**. An analysis of the relative energies indicates that **TS1-ex** is slightly less favorable than **TS1-en**. In the structure of **TS1**, the lengths of the C4–C5 bond being formed in the two stereoisomers are both 1.86 Å for **2b**, and 1.88 and 1.83 Å for **2c**, whereas the distances between C1 and C6 are about 3.0 Å for both compounds. This large difference might be due to steric hindrance between the methoxy group and the cyano or sulfonyl group. The values of the unique imaginary frequency of **TS1** are 284i and 288i for **2b**, and 308i and 324i for **2c**. These similar vibrational frequencies indicate that these **TSs** are mainly associated with the motion of the C4 and C5 carbon atoms along the C–C bond formation direction. A measure of the extent of bond formation or bond breaking along a reaction pathway is provided by the bond order (BO) of the Weinberg index, derived from the natural bond orbital (NBO) basis.[15] The values of the C4–C5 BOs are 0.61 for **2b** and 0.58 for **2c**, whereas the values of the C1–C6 BOs are 0.08 for **2b** and 0.07 for **2c**. Thus, the high values for the C4–C5 bond indicated that these C–C single bonds are forming, while

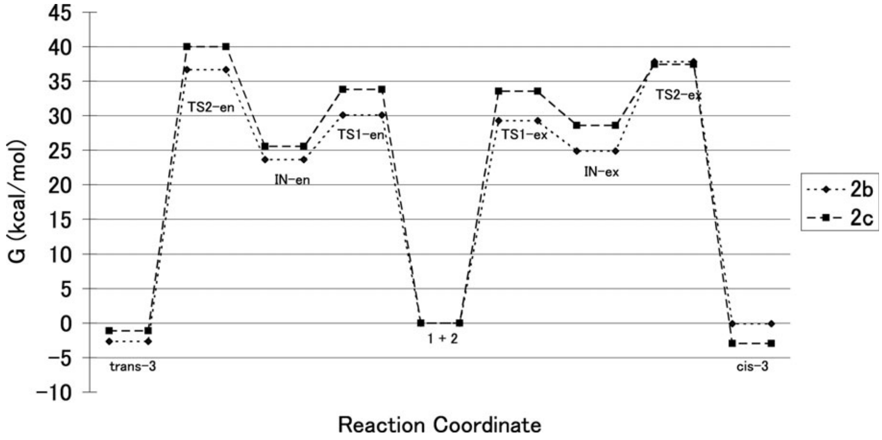


Fig. 6 The Gibbs free energy for the reaction between furan **1**, and styrenes **2b** and **2c**.

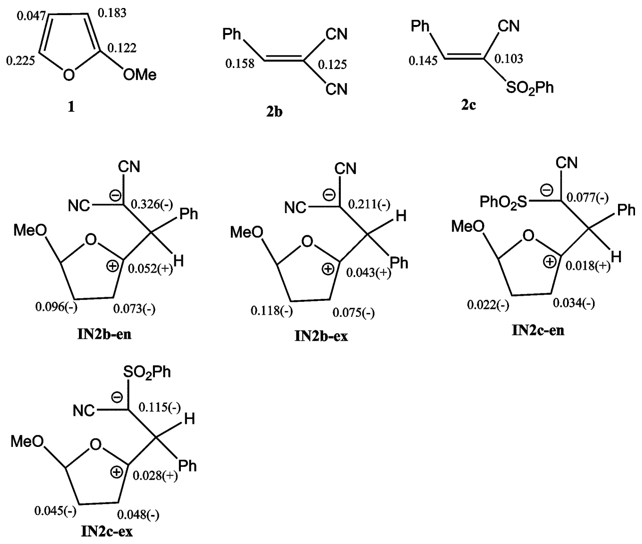


Fig. 7 Fukui functions for furan **1**, styrenes **2b** and **2c**, and intermediates **IN2b** and **IN2c**.

on the other hand, the very low C1–C6 values indicate that C1 and C6 atoms are becoming bonded. Furthermore, the values of the C5–C6 BOs in **TS1** (about 1.2) show that the double bond present in styrene is approximately a single bond in the transition state.

The formed zwitterionic intermediates are two configurationally favorable stereoisomers (**IN-en** and **IN-ex**). The potential energy barrier for the intermediate of **IN-en** and **IN-ex** for **2b** indicates similar values (6.4 and 7.6 kcal mol^{-1}, respectively), but for **2c**, **IN1-en** is 4.6 kcal mol^{-1} more favorable than that of **IN-ex** (5.8 and 10.4 kcal mol^{-1}, respectively). This result is due to the Coulombic interactions that appear between the positively charged donor 2-methoxyfuran and the negatively charged sulfonyl groups of the acceptor styrene at the *endo* form. In the structures of all the intermediates, the lengths of the C4–C5 bond are about 1.6 Å, which are similar to that of **TS1**. However, the lengths of the C1–C6 bond are 1.60–1.66 Å, which indicates a large difference (about 1.4 Å) from that of **TS1** (non bonding structure). In these intermediates, both the C4 and C5 carbon atoms are completely pyramidalized, while the C1 and C6 atom centers have a planar arrangement, in agreement with sp^2 hybridization. This situation is similar to that of the Diels–Alder adduct product. The values of the C1–C6 BOs for the intermediates are 0.86 for **2b** and 0.89 for **2c**, whereas the values of the C4–C5 BOs for the intermediates are 0.94–0.95, which indicates that a single bond is forming. The BO values for the C1–O1 and C1–C2 bonds (0.985–0.996 and 0.98–0.99, respectively) at the furan site, point to an allyl structure for the C2–C1–O1 framework that allows a favorable stabilization of the positive charge.

It is also possible that the intermediates may occur *via* the scission of a [4 + 2] cycloadduct (Diels–Alder adduct).[9,10,16] The potential energy barriers of a concerted [4 + 2] transition state for the cycloaddition reactions are 14.5 and 13.8 kcal mol^{-1} for **2b**, and 18.3 and 18.8 kcal mol^{-1} for **2c**, respectively, values which are similar to that of **TS1**. Furthermore, the energy barriers for the C1–C6 bond scission of a cycloadduct to the intermediates are 13.8 and 10.7 kcal mol^{-1} for **2b**, and 15.3 and 17.0 kcal mol^{-1} for **2c**. The forming bond (C1–C6 and C4–C5) distances of the cycloadduct are similar to those of the intermediate; however, it differs in that generally, the concerted pathway is favored over a stepwise mechanism by a few kcal mol^{-1}.[17] Nevertheless, the concerted [4 + 2] pathway can compete with the nucleophilic attack pathway, for both **TS11-ex** and **TS21-ex** are lower than **TS1-ex** in free energy. In addition, the valid *trans*/*cis* selectivity of the product may be required in this reaction.

Once formed, the intermediates can undergo further transformations. The final step of these reactions corresponds to an intramolecular nucleophilic substitution in the zwitterionic intermediate to give the final cyclopropane, **3**. This process can take place by the nucleophilic attack of the carbanion (C6) attached to the cyano group on the C4 carbon atom of the furan ring, with resulting cyclopropyl ring formation, together with a fission process in the plane of the C4–O1 bond of the furan ring, to produce the carbonyl group. In both **TS2** of **2b**, similar potential energy barriers exist (22.3 and 22.8 kcal mol^{-1}). In the transition structure of **2b-en**, (see Fig. 2) the center tetrahedral carbon C4 (C3–C4–C5: 118.7°, C3–C4–H4: 116.9°, C5–C4–H4: 111.6°, O1–C4–C5: 113.7°) is located between the C6 and O1 atoms of the furan. The O1–C4–C6 bond angle is 154.3°, that is, the O1 atom, the C4 atom and the C6 atom

Table 2 The total energies (E, au), relative energies (ΔE, kcal mol^{-1}), entropies (ΔS, cal K^{-1} mol^{-1}), enthalpies (ΔH, kcal mol^{-1}) and free energies (ΔG, kcal/mol) at 298.15 K for the stationary points corresponding to the reaction between 2-methoxyfuran (**1**), and β-cyanostyrenes (**2b** and **2c**)

	2b-en					**2b-ex**				
	E	ΔE	ΔS	ΔH	ΔG	E	ΔE	ΔS	ΔH	ΔG
1 + **2**	−838.670495	0.00	0.00	0.00	0.00	−838.670495	0.00	0.00	0.00	0.00
TS1	−838.647212	14.61	−49.45	15.36	30.10	−838.648605	13.71	−49.51	14.50	29.26
IN1	−838.660313	6.39	−54.27	7.46	23.64	−838.658323	7.64	−53.98	8.77	24.86
TS2	−838.634947	22.31	−46.24	22.88	36.67	−838.634215	22.77	−52.23	22.23	37.80
3	−838.695841	−15.90	−40.68	−14.76	−2.63	−838.692652	−13.90	−40.56	−12.17	−0.08
TS11	−838.647396	14.49	−58.04	15.89	33.19	−838.648471	13.82	−56.61	10.86	27.74
IN11	−838.660484	6.28	−54.27	8.08	24.26	−838.658464	7.55	−53.98	9.39	25.48
TS12	−838.648549	13.77	−49.45	14.72	29.46	−838.653380	10.74	−49.51	13.88	28.63
	2c-en					**2c-ex**				
	E	ΔE	ΔS	ΔH	ΔG	E	ΔE	ΔS	ΔH	ΔG
1 + **2**	−1526.052704	0.00	0.00	0.00	0.00	−1526.052704	0.00	0.00	0.00	0.00
TS1	−1526.023353	18.42	−49.26	19.14	33.82	−1526.024306	17.82	−50.24	18.56	33.54
IN1	−1526.043432	5.82	−62.70	6.87	25.56	−1526.036062	10.44	−55.47	12.06	28.60
TS2	−1526.012725	25.09	−50.09	25.04	39.98	−1526.015943	23.07	−47.99	23.11	37.42
3	−1526.077564	−15.60	−42.98	−13.94	−1.12	−1526.081185	−17.87	−43.99	−16.04	−2.93
TS11	−1526.023478	18.34	−52.04	16.47	31.98	−1526.017937	18.81	−55.04	18.06	34.47
IN12	−1526.043584	5.73	−63.02	6.23	25.02	−1526.036299	10.29	−53.59	12.61	28.59
TS12	−1526.028250	15.34	−47.78	20.03	34.87	−1526.025601	17.01	−50.78	19.66	34.80

Table 3 Selected bond lengths (Å), bond angles (°) and dihedral angles (°) for the TSs and intermediate of the reactions between 2-methoxyfuran (**1**) and β-cyanostyrenes (**2b** and **2c**)

	2b-en	**2b-ex**	**2c-en**	**2c-ex**
TS1				
C1–C6	2.963	3.047	3.000	2.994
C4–C5	1.862	1.862	1.883	1.832
C5–C6	1.449	1.446	1.437	1.442
C1–C4–C5–C6	−9.98	17.78	−9.13	11.62
IN1				
C1–C6	1.661	1.620	1.598	1.614
C4–C5	1.575	1.578	1.582	1.614
C4–C6	2.421	2.427	2.459	2.454
C5–C6	1.599	1.602	1.588	1.584
C1–O1	1.419	1.429	1.438	1.425
C6–C4–O1	69.46	68.99	67.59	69.66
C1–C4–C5–C6	0.03	2.80	4.96	2.18
H4–C4–C5–H5	−91.42	49.56	95.48	47.9
TS2				
C4–C6	2.284	2.297	2.237	2.259
C4–O1	1.736	1.754	1.757	1.760
C5–C6	1.535	1.535	1.531	1.510
C1–O1	1.273	1.270	1.268	1.267
C3–C4–C5	118.65	120.28	119.69	122.04
C3–C4–H4	116.86	116.71	116.58	116.65
C5–C4–H4	111.63	111.41	114.32	109.59
C5–C4–O1	113.68	111.46	114.32	111.55
C6–C4–O1	154.30	152.98	154.36	153.08
C6–C4–C3	101.05	102.29	104.43	101.45
H4–C4–C5–H5	−179.83	41.06	−173.49	38.59

Table 4 Weinberg bond indices for the TSs and intermediate of the reactions between 2-methoxyfuran (**1**) and β-cyanostyrenes (**2b** and **2c**)

	2b-en	**2b-ex**	**2c-en**	**2b-ex**
TS1				
C1–C6	0.081	0.072	0.078	0.072
C4–C5	0.611	0.603	0.581	0.568
C5–C6	1.194	1.203	1.239	1.250
C4-O1	0.893	0.888	0.893	0.900
C1–O1	1.094	1.099	1.098	1.103
IN1				
C1–C2	0.987	0.980	0.982	0.991
C1–C6	0.861	0.857	0.892	0.895
C4–C5	0.941	0.939	0.939	0.954
C4–C6	0.005	0.004	0.006	0.005
C5–C6	0.912	0.917	0.939	0.951
C1–O1	0.996	0.996	0.985	0.986
TS2				
C4–C6	0.109	0.108	0.223	0.221
C4–O1	0.413	0.398	0.518	0.517
C5–C6	0.850	0.862	0.981	0.983
C1–O1	1.088	1.090	1.368	1.369
C1–C6	0.006	0.006	0.015	0.016
C4–C5	0.847	0.851	0.962	0.965

are arranged nearly on a straight line. The value of this bond angle indicates that the C4 center has sp hybridization, in which the charge located at C4 occupies a p atomic orbital. The length of the C4–C6 bond being formed in **TS2** is 2.28 Å and the length of the C4–O1 bond being cleaved is 1.74 Å. The value of the H4–C4–C5–H5 dihedral angle (−179.83°) for **2b-en** is consistent with formation of the *trans*-form of the product (**3b**). Also, in the transition structure of **2b-ex** (see Fig. 3), the O1–C4–C6 bond angle of the center carbon C4 is 153.0°; again, these atoms are arranged on almost a straight line, similar to the case of **2b-en**. However, the value of the H4–C4–C5–H5 dihedral angle is 41.06°, which translates to the *cis*-form of the product.

On the other hand, the potential energy gaps of the transformation process (**TS2**) of **2c** are 25.1 kcal mol^{-1} for the *endo* form and 23.1 kcal mol^{-1} for the *exo* form. The latter is 2.0 kcal mol^{-1} more favorable than **TS2-en**, due to a

Table 5 The total energies (E, au), relative energies (ΔE, kcal mol^{-1}) at 298.15 K and dipole moments (D) for the stationary points corresponding to the reaction between 2-methoxyfuran (**1**) and β-cyanostyrenes (**2b** and **2c**) including the solvent effects

	2b-en			**2b-ex**		
	E	ΔE	Dipole moment	E	ΔE	Dipole moment
1 + **2**	−838.688090	0.00	—	−838.688090	0.00	—
TS1	−838.6672399	13.08	7.93	−838.667795	12.74	7.88
IN1	−838.678262	6.17	5.19	−838.676302	7.40	6.09
TS2	−838.6603686	17.40	12.47	−839.659186	18.14	12.87
3	−838.713436	−15.91	5.68	−838.711247	−14.51	5.71
	2c-en			**2c-ex**		
	E	ΔE	Dipole moment	E	ΔE	Dipole moment
1 + **2**	−1526.069299	0.00	—	−1526.069299	0.00	—
TS1	−1526.042149	17.04	8.13	−1526.042748	16.66	8.03
IN1	−1526.061002	5.26	3.41	−1526.053650	9.82	5.03
TS2	−1526.039437	18.74	9.74	−1526.041919	17.18	10.76
3	−1526.095294	−16.31	4.02	−1526.097909	−17.95	5.14

Table 6 Selected bond lengths (Å), bond angles (°) and dihedral angles (°) for **3c** from X-ray analysis and calculation data

Parameters	X-ray	Calc.
C4–C5	1.489(3)	1.516
C5–C6	1.514(3)	1.520
C4–C6	1.537(3)	1.543
C3–C5	1.473(3)	1.476
C2–C3	1.319(3)	1.345
O5–C4–C6	59.79(13)	59.58
C4–C6–C5	58.87(13)	59.33
C4–C5–C6	61.34(13)	61.09
H4–C4–C6–H6	105.82(2)	106.12
C1–C2–C3–C4	106.6(1)	108.04

Table 7 The global properties of the masked furan (**1**) and styrenes (**2b**, **2c**, **IN2b**, **IN2c**, **2a** and **2g**), and yields (**2a**, **2b**, **2c** and **2g**)[a]

Molecule	HOMO	LUMO	μ/au	η/au	ω/eV	Yield (%)
1	−0.1939	0.0353	−0.0793	0.2292	0.3731	—
2b	−0.2597	−0.1067	−0.1832	0.1530	2.9833	84
2c	−0.2536	−0.0925	−0.1731	0.1611	2.5295	77
IN2b-en	−0.2530	−0.0303	−0.1417	0.2227	1.2262	—
IN2b-ex	−0.2560	−0.0368	−0.1464	0.2192	1.3298	—
IN2c-en	−0.2414	−0.0438	−0.1426	0.1976	1.3996	—
IN2c-ex	−0.2529	−0.0483	−0.1506	0.2046	1.5076	—
2a	−0.2487	−0.0909	−0.1698	0.1578	2.4855	46
2g	−0.2394	−0.0772	−0.1583	0.1621	2.1022	36

[a] The electronic chemical potential, μ, and the chemical hardness, η, are given in atomic units; the electrophilicity power, ω, is in given electron volts.

favorable arrangement. In the transition structure for this process, the O1–C4–C6 bond angle (the C6 atom attacked the cyano group and O1 atom of the furan) is 153–154°, which makes this transformation likely. The length of the C4–C6 bond being formed for **TS2-en** (see Fig. 4) is 2.24 Å and the length of the C4–O1 bond being cleaved is 1.76 Å. The value of the H4–C4–C5–H5 dihedral angle is −173.5°. These angles are consistent with the formation of the *trans*-form of product **3**, in accord with the experimental results. Also, in the transition structure of **2c-ex** (see Fig. 5), the O1–C4–C6 bond angle of the center carbon C4 is 153.1°, these atoms also being almost arranged on a straight line, while the value of the H4–C4–C5–H5 dihedral angle is 38.59°, all of which translates to the *cis*-form of the product. These comparisons for **TS2** clearly indicate that the carbonyl group forms *via* scission of the C4–O1 bond in the furan ring and imply that the *exo* form is the more favorable transition structure. Interestingly, the secondary orbital interaction determining the *exo* preference in the **2c-exo** form is due to the contribution from the phenylsulfonyl group. Thus, the dihedral angle between the S=O moiety and the C4–C6 group being formed, ∠C–C–S=O, is 25.22°, which may be attributed to electron flow from the S=O moiety to the C4–C6 group.

The BO values of the forming C1–O1 double bonds are 1.09 for **2b** and 1.37 for **2c**, and for the C4–C6 forming single bonds are 0.11 for **2b** and 0.22 for **2c**. These low BO values for the forming bonds and the large BO values for the C4–O1 cleaving bond (0.4 and 0.5) indicate that the **TSs** for the translation processes are early. Moreover, the slightly larger BO value of **2c** for these bonds (C4–C6, C5–C6, C4–C1 and C4–O1) in comparison with those of **2b** will account for a favorable stabilization due to delocalization of the sulfur lone pairs of the phenylsulfonyl group. The values of the unique imaginary frequency of **TS2** are 427i for **2b** and 420i for **2c**. Analysis of the atomic motion related to these vibrational frequencies indicates that these **TSs** are mainly associated with the motion of the forming C4–C6 bond and the dissociating C4–O1 bond accompanied by a push and pull motion of the S_N2 substitution type.

We have also computed the relative enthalpies, entropies and free energies at 25 °C for the different stationary points along the reaction coordinate (Table 2). At **TS1**, the large negative entropy change (−49 cal K^{-1} mol^{-1} for the *endo* form, −50 cal K^{-1} mol^{-1} for the *exo* form) due to the restricted geometry associated with the intermolecular nature of the process is similar to that seen in the Diels–Alder reaction due to the bimolecular nature of that process. This entropy change, similar to that created during intermolecular cycloadditions, is responsible for the increase of the activation free energy of the rate-determining step to 29–34 kcal mol^{-1}.[18] However, for the second step, the activation entropy and the activation free energy change is smaller (less than 12.6 cal K^{-1} mol^{-1} and 14.4 kcal mol^{-1}, respectively), due to the smooth intramolecular nature of the rearrangement process. This fact, together with stabilization of **TS2** by the inclusion of a solvent effect, emphasizes the stepwise nature of the transformation process.

Interestingly, the formation of cyclopropane **3b** is exothermic, −15.9 kcal mol^{-1} for the *endo* form and −13.9 kcal mol^{-1} for the *exo* form. Thus, the formation of the cyclopropane *via* the *endo* form is thermodynamically more favorable than formation *via* the *exo* form, but is kinetically almost the same at **TS1** and **TS2** in the gas phase. However, at **TS2**, the lower activation free energy and lower negative entropy of the *endo* form compared with the *exo* form leads to the favorable formation of *trans* product *via* the *endo* reaction channel. On the other hand, **3c-en** is kinetically favored by the potential energy gaps at **TS1**, but disfavored at **TS2** relative to the *exo* form. Furthermore, a comparison of the free energy and entropy at **TS2** indicates that the *exo* form is slightly favored. Therefore, the selectivity of both forms is not amenable to a kinetic explanation with gas phase calculations.

Finally the geometries of the calculated structure are compared with the structure obtained from the X-ray analysis (see Table 6). The value of the H4–C4–C6–H6 dihedral angle in **3c-ex** from the B3LYP/6-31G* calculation is 106.12°, which is in reasonable agreement with that of 105.82(2)° from the X-ray analysis. The other geometrical parameters obtained for cyclopropane **3c-ex** from the calculation are in agreement with the experimental analysis of the structure. The bond distances in the cyclopropyl ring for the calculated structure are slightly longer than those found by experiment (0.026 Å is the highest difference for the C2–C3 and C4–C5 bonds).

Solvent effects

Solvent effects on cycloaddition are well known[19] and have received considerable attention. Sustmann *et al.* reported that such effects favor the transition structure that exhibits the higher dipolar moment.[19a] Table 5 shows the energies at the stationary points corresponding to the reaction in chloroform, which was used as the experimental solvent. The energy differences of the transition state at **TS2** in solvent are stabilized by 5–6 kcal mol^{-1} over those in the gas phase. The transition structure involving nucleophilic attack is preferentially stabilized relative to the reactants, due to the large charge transfer that is developed along this polar transfer path. The intensity of the solvent effect for **2c** is slightly larger than that for **2b**. This result is due to the charge delocalization of the phenyl group compensating for the high dipole moment arising from the strong electron-withdrawing group—the sulfonyl group of **2c**. Thus, inclusion of the solvent effect may accelerate this polar reaction, thanks to a greater stabilization of the transition state corresponding to nucleophilic attack. Also, the solvent effect for **TS1** shows a slight difference (1–2 kcal mol^{-1}) in the gas phase and in solution. According to the reactions studied by Sustmann *et al.*, the high polarity of the transition structure came from the strong asynchronicity. Here, as described in the previous section, the transition structures (**TS1**) for the nucleophilic reaction are asynchronous structures, which have a high dipole moment. The fact that **2c** is more stable seems to indicate that the values of the dipole moments at **TS1** are somewhat lower than those of **TS2**. It should be noted that for the dipole moments, the values of the transition state are higher than those of the intermediate. This contrasts with the situation encountered in the intermediates, for which the values of the dipole moments are almost same, both in the gas phase and in solution. Thus, the interaction of the dipoles of the transition state with the medium should be different with each one of the intermediates. These results clearly suggest that the solvent effect should be significant in those cases where the transition structure is highly polarized. The energy barrier difference obtained for the *endo* and *exo* forms in solution is in very good agreement with the observed experimental stereoselectivity, in contrast to the poor agreement with gas phase calculations. Thus, the formation of cyclopropane **3b** *via* the *endo* form is kinetically more favorable than formation *via* the *exo* form, so the potential energy differences at **TS1** are the same (gap: 0.34 kcal mol^{-1}), but that of the *endo* form at **TS2** is more favorable than the *exo* form by 0.74 kcal mol^{-1}. Thus, the amount of the *trans*-cyclopropane produced from the *endo* form will be greater than that of the *cis* compound resulting from the *exo* form. On the other hand, with respect to the formation of cyclopropane **3c**, the potential energy difference at **TS1** is not observed (gap: 0.38 kcal mol^{-1}), but the value at **TS2** is favorable for the *exo* form by 1.5 kcal mol^{-1}. Therefore, the amount of the *cis*-cyclopropane is predicted to be greater than that of the *trans* form, as found by experiment.

Selectivity of *trans*/*cis* product

At a first glance, it will be see that the potential energy difference from the intermediate, that is, the relative **TS2** energy, may determine the selectivity of *trans*/*cis* product.

However, the barriers starting from the intermediate are much lower, so the whole process is reversible and may shift to the reagents. In order to obtain more definitive evidence, we represent the different reaction pathways calculated in Fig. 6 graphically using the Gibbs free energy (ΔG) on the ordinate axis. The dotted lines correspond to the reaction with **2b**, and dashed lines correspond to the reaction with **2c**. It is also evident that the back reaction from the intermediate to substrates **1** and **2b** has a lower barrier than the forward reaction from the intermediate to product **3b**, and that both barriers are relatively low. Under these conditions, the steady state approach for the intermediate can be used in the kinetic analysis.

We have calculated the stereoselectivity (*trans*/*cis* ratio) of products **3** using terms of relative reaction rates and equilibrium. The ratio may be combined into eqn (1) as a basis of calculation:

$$\frac{trans}{cis} = \frac{K_{\mathrm{eq},endo}}{K_{\mathrm{eq},exo}} \frac{k_{2,endo}}{k_{2,exo}} \qquad (1)$$

where K_{eq} is the equilibrium constant and k_2 is the kinetic rate constant of the second step.

Conversion of eqn (1) using the energy term results in eqn (2):

$$\frac{trans}{cis} = \frac{e^{\frac{-\Delta\Delta G_{endo-exo}}{RT}} e^{\frac{-\Delta G^{\neq}_{endo}}{RT}}}{e^{\frac{-\Delta G^{\neq}_{exo}}{RT}}} = e^{\frac{-\Delta\Delta G^{\neq}_{endo-exo}}{RT}} \qquad (2)$$

Using the free energies given in Table 2 and Table 5, the values of the ratios are obtained as follows:

	$-\Delta\Delta G^{\neq}_{endo-exo}$	
	Gas phase	Solution
2b	1.13	1.00
2c	−2.56	−2.10

The analysis results indicate that in the case of **2b**, the *trans*-cyclopropane coming from the *endo* path way is favored; on the other hand, in the case of **2c**, the *cis*-cyclopropane coming from the *exo* path way is favored. Also, solvent influence is not required to obtain the correct interpretation. This situation corresponds to pseudo-Curtin–Hammett behavior,[20] so that the energy differences in Table 2 and Table 5 correspond to the absolute Gibbs free energy difference of **TS2-en** and **TS2-ex**.

Global and local electrophilicity/nucleophilicity analysis

The reactivity and regioselectivity of these addition and rearrangement reactions have been analyzed using global and local indices.[21] In Table 7, the static global parameters, electronic chemical potential μ, chemical hardness η, and global electrophilicity ω, for 2-methoxyfuran (**1**), cyanostyrenes **2b** and **2c**, and intermediates **IN2b-en**, **IN2b-ex**, **IN2c-en** and **IN2c-ex** are displayed. Calculations carried out by Domingo's group on the addition reaction with polar character have shown that these indices are powerful tools to study both reactivity and regioselectivity.[21*b*,22]

The value of μ of cyanostyrenes **2b** and **2c** (μ = −0.1832 and −0.1731 au) is less than that of furan **1** (μ = −0.0793 au), therefore indicating that the net charge transfer will take place from **2b** and **2c** towards **1**, in agreement with the charge transfer analysis (see the previous section). Styrenes **2b** and **2c** have a large electrophilicity power (ω = 2.983 and 2.529 eV), whereas on the other hand, **1** has a low electrophilicity (ω = 0.373 eV). Thus, the global electrophilicity difference between both reactants ($\Delta\omega$ = 2.610 and 2.156 eV) indicates the normal electron demand reaction in which electron-poor dienophile **2b** or **2c** reacts with the electron-rich diene **1**. Furthermore, the value of the difference may be corrected with the reactivity (the product yield) including the case of **2a** and **2g**.

Recent studies of cycloaddition reactions with polar character have used analysis of the electrophilic and nucleophilic Fukui functions to explain the observed experimental regioselectivities.[23] The local functions for our case are summarized in Fig. 7. **1** has the largest nucleophilic activation at the non-substituted C4 position (f^- = 0.225(−)), hence, this is the more reactive site for electrophilic attack. On the other hand, for the styrene systems **2b** and **2c**, there are two electrophilic sites (at the C5 and C6 carbon atoms). Analysis of the electrophilic Fukui functions for **2b** and **2c** indicates that the C5 position has the lower electrophilic activity (f^+ = 0.158(+) > 0.125(+) for **2b**; 0.145(+) > 0.103(+) for **2c**). Thus, the most favorable interaction will take place between the C4 carbon atom of **1** and the C5 carbon atom of **2**, in agreement with the regioselectivity observed.

The second step in the reaction is the rearrangement reaction of zwitterionic intermediate **IN-en** or **IN-ex** to give cyclopropane products **3**. This process involves the nucleophilic attack of the rest (C6) of styrene **2** to the electron-poor furan residue (C4). As a consequence, for **IN-en** and **IN-ex**, the site analysis must be carried out at the electrophilic positions (C4) of the furan residues, the C4 center (f^+ = 0.052(+) and 0.043(+) for **IN-2b**, and f^+ = 0.018(+) and 0.028(+) for **IN-2c**) and the nucleophilic position of the styrene, the C6 center (f^- = 0.326(−) and 0.211(−) for **IN-2b**, and f^- = 0.077(−) and 0.115(−) for **IN-2c**; see Fig. 7). These local Fukui functions show that the more favorable interaction along the addition reaction process corresponds to attack of the nucleophilic C4 center on the electrophilic C6 one, and leads to formation of the cyclopropane. Moreover, comparison of the nucleophilic function for both isomers of **2b** and **2c** indicate a large activity at C6, but quite a large difference is found between the isomers, the value exhibiting an opposite tendency. The function has a larger value for the *endo* form of **2b** (0.326 > 0.211), but on the other hand, shows a larger value (0.077 < 0.115) for the *exo* form of **2c**, in spite of the moderate stabilities of the *exo* structure in both cases. These contrasting results allow us to explain the different ratios of the isomer products, the more reactive nucleophilic attack for the *endo* form at **2b**, and the more reactive attack for the *exo* form at **2c**. This local analysis offers a reasonable explanation for the experimental results.

Summary

This study has shown that the mechanism of the reaction of 2-methoxyfuran with β-cyanostyrenes possessing strong electron-withdrawing groups has been characterized using quantum mechanical calculations. Experimental data showed that for the reaction with **2b** (CN), more *trans*-cyclopropane is obtained (a ratio 4.5 : 1 over the *cis*-cyclopropane). With **2c** (SO_2Ph), more *cis*-product is obtained (a ratio 1.5 : 1 over the *trans*-product). We have shown that: (i) an analysis of the results shows that the reaction takes place along a polar stepwise mechanism. The first step (**TS1**) corresponds to the nucleophilic attack of the furan ring on the styrene or the concerted addition-fission reaction to give two zwitterionic intermediates (**IN-*endo*** and **IN-*exo***). For the second step (**TS2**), an intramolecular substitution in the intermediate give the formation of the cyclopropane ring together with fission of the furan ring. (ii) *Trans*-cyclopropanes come from the *endo* pathway of the cyanostyrene to the furan ring, whereas *cis*-cyclopropanes come from the *exo* pathway. (iii) From the theoretical results, the selectivity of the reaction is determined by the difference between **TS2-en** and **TS2-ex** energies (so a pseudo-Curtin–Hammett behavior is assumed). (iv) As a consequence, in the case of **2b**, the energy of **TS2-en** is lower than that of **TS2-ex**, so more *trans*-cyclopropane product from the *endo* form is formed under kinetic conditions. Conversely, in the case of **2c**, **TS2-ex** is lower in energy than **TS2-en**, so the *cis*-cyclopropane is formed. (v) The qualitative agreement with and without including solvent effects is therefore complete. (vi) This also agrees with the conclusions drafted from gas phase calculations of the local Fukui functions. (vii) The calculation analysis offers a reasonable explanation for the experimental results.

Experimental

Computational details. The density functional method computations for the gas phase calculations were performed with the Spartan '04 for Windows package[24] and the Gaussian 03 program.[25] The reactant, product and transition state (TS) geometries for the above reactions were optimized by DFT calculations at the B3LYP/6-31G* level.[26] After the optimization of all transitional structures, we carried out vibrational analyses in order to check the nature of the stationary points. The transition states are defined by exactly one imaginary frequency. Unless otherwise indicated, all energy changes in the B3LYP/6-31G* optimizations reported in this paper include zero-point energies without scaling. To calculate the free energies of solvation needed to understand the effect of the solvent on the stereoselectivity,[27] we used the Gaussian 03 program.[25] To evaluate the solvent effect, we carried out a B3LYP/6-31G* single point calculation, using the method based on the polarized continuum model (PCM).[28] The solvent used in the experimental work was chloroform; therefore, we employed the dielectric constant, $\varepsilon = 4.81$ and the solute radius, $\alpha = 3.92$. To reduce the time of the calculation, we used β,ß′-dicyanostyrene (**2b**) and β-cyano-ß′-phenylsulfonylstyrene (**2c**) in the calculations to represent the actual styrenes used in the experiments.

Global electronic indices were calculated by a very simple operational formula in terms of the one-electron energies of the HOMO and LUMO frontier molecular orbitals.[18] Electrophilic and nucleophilic Fukui functions condensed to atoms were evaluated from single point calculations performed on the ground state of molecules at the same level of theory.[18] This method evaluated Fukui functions using the gross charges of the natural population analysis (NPA).

Apparatus. The IR spectra were recorded with KBr tablets and an NaCl sandwich on a Hitachi I-2000 spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-250 and GX-400 spectrometers in deuterated-chloroform. Tetramethylsilane was used as the internal reference for the proton spectra. The mass spectra were recorded on a GCMS-QP2000A spectrometer. Melting points were determined on a Yanaco micro hot-plate apparatus and are uncorrected.

Materials. β-Cyanostyrene derivatives (**2a–2i**) were prepared either according to the Knoevenagel condensation of benzaldehyde with cyanoalkenes reported by Dornow,[29] Yamamura,[30] 2-cyanoethylcinnamate,[31] 2-diacetylstyrene,[32] 2-dicyanostyrene[33] and 2-cyano-2-phenylsulfonylstyrene.[34]

Methyl 3-((3*S*,1*R*,2*R*)-2-cyano-2-ethoxycarbonyl-3-phenylcyclopropyl)-(2*Z*)-prop-2-enoate (3a). Major (*trans* form): Mp = 65.5–66.5 °C. MS: m/z = 299 (M$^+$), 267 (M$^+$ − MeOH), 253, 221 (M$^+$ − Ph), 195, 194, 167, 166, 139, 128, 115, 98. IR: ν = 3028, 2946, 1702, 1618, 1584, 1260, 1198 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 1.28 (3H, t, J = 7.3 Hz), 3.36 (1H, d, J = 8.3 Hz), 3.73 (3H, s), 4.24 (2H, q, J = 7.3 Hz), 4.44 (1H, ddd, J = 1.0, 8.3, 9.3 Hz), 6.00 (1H, dd, J = 1.0, 11.7 Hz), 6.24 (1H, dd, J = 9.3, 11.7 Hz), 7.24–7.45 (5H, m). ^{13}C NMR (CDCl$_3$): δ = 14.1, 30.2, 34.4, 40.1, 51.7, 63.3, 115.6, 124.2, 128.4, 128.7, 128.9, 130.1, 132.2, 140.0, 165.1, 166.2. Found: C, 68.06; H, 5.63; N: 4.44; calc. for $C_{17}H_{17}NO_4$: C, 68.22; H, 5.72; N, 4.68%.

Methyl 3-((2*S*,1*R*,3*R*)-2-cyano-2-ethoxycarbonyl-3-phenylcyclopropyl)-(2*Z*)-prop-2-enoate (3a′). Minor (*cis* form): Mp = 69.8–70.8 °C. MS: m/z = 299, 253, 221, 194, 166, 140, 129, 115, 98. IR: ν = 3068, 2957, 1744, 1641, 1443, 1316, 1251, 1146 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 1.32 (3H, t, J = 7.3 Hz), 3.48 (1H, d, J = 9.7 Hz), 3.72 (3H, s), 4.17 (1H, dd, J = 9.7, 10.3 Hz), 4.28 (2H, q, J = 7.3 Hz), 5.76 (1H, dd, J = 10.3, 11.7 Hz), 6.04 (1H, dd, J = 1.0, 11.7 Hz), 7.24–7.45 (5H, m). ^{13}C NMR (CDCl$_3$): δ = 14.1, 28.1, 33.2, 38.4, 51.7, 63.4, 114.9, 124.4, 128.4, 128.7, 128.9, 129.3, 130.5, 139.9, 166.2, 166.5.

Ethyl 2-cyano-3-(5-methoxy(2-furyl))-3-phenylpropanoate (4a). Oil, ^{1}H NMR (CDCl$_3$): δ = 1.30 (3H, t, J = 3.3 Hz), 4.25 (2H, q, J = 7.3 Hz), 4.38 (1H, d, J = 7.6 Hz), 4.49 (1H, dd, J = 0.4, 7.6 Hz), 5.12 (1H, d, J = 3.3 Hz), 6.21 (1H, dd, J = 0.4, 3.3 Hz), 7.39–7.45 (5H, m) ppm.

Methyl 3-((3*S*,1*R*)-2,2-dicyano-3-phenylcyclopropyl)-(2*Z*)-prop-2-enolate (3b). *Trans* form: Mp = 53.0–54.0 °C. MS: m/z = 252 (M$^+$), 220 (M$^+$ − MeOH), 192, 165, 155, 138, 128, 115. IR: ν = 3068, 3028, 2956, 2248, 1722, 1652, 1444, 1216, 1182 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 3.21 (1H, d, J = 8.3 Hz), 3.83 (3H, s), 4.57 (1H, ddd, J = 0.6, 8.4, 9.2 Hz), 6.00 (1H, dd, J = 9.2, 11.3 Hz), 6.25 (1H, dd, J = 0.6, 11.3 Hz), 7.32–7.43 (5H, m). ^{13}C NMR (CDCl$_3$): δ = 14.9, 32.0, 41.3, 51.9, 112.1, 113.1, 126.1, 128.4, 129.2, 129.5, 138.7, 165.7. Found: C, 71.38; H, 4.79; N, 11.00; calc. for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10%.

Methyl 3-((1*R*,3*R*)-2,2-dicyano-3-phenylcyclopropyl)-(2*Z*)-prop-2-enolate (3b′). *Cis* form: Mp = 49.0–50.0 °C. MS: m/z = 252, 220, 192, 165, 155, 128, 117. IR: ν = 3136, 2960, 2208, 1734, 1432, 1052, 756. ^{1}H NMR (CDCl$_3$): δ = 3.59 (1H, d, J = 10.0 Hz), 3.84 (1H, d, J = 10.0 Hz), 3.82 (3H, s), 4.47 (1H, ddd, J = 0.6, 9.9, 10.0 Hz), 5.72 (1H, dd, J = 9.9, 11.3 Hz), 6.24 (1H, dd, J = 0.6, 11.3 Hz) 7.35–7.50 (5H, m).

[(5-Methoxy(2-furyl))phenylmethyl]-methane-1,1-dicarbonitrile (4b). Oil, MS: m/z = 252 (M$^+$), 187 (M$^+$ − CH(CN)$_2$), 155, 115. IR: ν = 2912, 2256, 1260 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 3.82 (3H, s), 4.38 (1H, d, J = 7.6 Hz), 4.49 (1H, dd, J = 0.4, 7.6 Hz), 5.12 (1H, d, J = 3.3 Hz), 6.21 (1H, dd, J = 0.4, 3.3 Hz), 7.39–7.45 (5H, m). ^{13}C NMR (CDCl$_3$): δ = 28.8, 46.6, 57.9, 80.5, 111.4, 111.5, 128.3, 128.5, 129.3, 129.4, 134.7, 138.9, 162.1. Found: C, 71.06; H, 4.86; N, 10.87; calc. for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10%.

Methyl 3-((3*S*,1*R*,2*R*)-2-cyano-2-phenylsulfonyl-3-phenylcyclopropyl)-(2*Z*)-prop-2-enoate (3c). *Trans* form: Mp = 171.5–172.7 °C. MS: m/z = 367 (M^+), 307 ($M^+ - CO_2Me$), 270, 242, 226, 194, 166, 130. IR: ν = 3036, 2939, 2222, 1696, 1593, 1453, 1324, 1159, 1122. 1077 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 3.83 (1H, d, J = 10.4 Hz), 4.64 (1H, dd, J = 10.4, 10.6 Hz), 5.65 (1H, dd, J = 10.6, 11.7 Hz), 6.05 (1H, d, J = 11.7 Hz), 7.25–7.31 (5H, m), 7.63–8.15 (5H, m). ^{13}C NMR ($CDCl_3$): δ = 30.4, 35.6, 46.1, 125.2, 125.4, 128.2, 128.7, 128.9, 129.2, 129.6, 135.0, 137.9, 165.8 ppm. Found: C, 65.38; H, 4.66; N, 3.81; calc. for $C_{20}H_{17}NO_4S$: C, 65.51; H, 4.56; N, 3.67%.

Methyl 3-((2*S*,1*R*,3*R*)-2-cyano-2-phenylsulfonyl-3-phenylcyclopropyl)-(2*Z*)-prop-2-enoate (3c′). *Cis* form: Mp = 156–157 °C. IR: ν = 3062, 2833, 2250, 1608, 1573, 1493, 1360, 1193, 1102 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 3.70 (1H, d, J = 8.4 Hz), 4.47 (1H, dd, J = 8.4, 9.2 Hz), 6.7 (1H, d, J = 10.7 Hz), 6.65 (1H, J = 9.2, 10.7 Hz), 7.8–7.35 (5H, m), 7.60–8.24 (5H, m). ^{13}C NMR ($CDCl_3$): δ = 34.2, 38.1, 51.7, 125.2, 125.4, 128.2, 128.7, 128.9, 129.1, 129.5, 135.0, 138.5, 165.8.

Methyl 3-((3*S*,1*R*)-2,2-diacetoxy-3-phenylcyclopropyl)-(2*Z*)-prop-2-enolate (3g). Mp = 78–79 °C. MS: m/z = 286 (M^+), 243 ($M^+ - COMe$), 211 ($M^+ - C_6H_5$), 197, 183, 169, 141, 128, 115. IR: ν = 3032, 2956, 1726, 1704, 1600, 1440, 1378, 1230, 1180 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.93 (3H, s), 2.32 (3H, s), 3.47 (3H, s), 3.98 (1H, d, J = 2.9 Hz), 5.89 (1H, dd, J = 2.9, 8.3 Hz), 5.90 (1H, d, J = 11.5 Hz), 6.31 (1H, dd, J = 8.3, 11.5 Hz), 7.20–7.36 (5H, m). ^{13}C NMR ($CDCl_3$): δ = 15.2, 29.7, 51.1, 56.4, 86.2, 121.1, 127.4, 127.5, 128.8, 146.6, 165.5, 168.1, 195.0. Found: C, 71.36; H, 6.16; calc. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34%.

3-[(5-methoxy(2-furyl))phenylmethyl]-pentane-2,4-dione (4g). Oil, MS: m/z = 286 (M^+), 243, 211, 187, 173, 155, 147, 129, 115. IR: 2944, 1736, 1702, 1618, 1586, 1260, 1184 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 2.16 (3H, s), 2.34 (3H, s), 3.76 (3H, s), 4.55 (1H, d, J = 12.1 Hz), 4.71 (1H, d, J = 12.1 Hz), 4.97 (1H, d, J = 3.2 Hz), 5.86 (1H, d, J = 3.2 Hz), 7.17–7.37 (5H, m). ^{13}C NMR ($CDCl_3$): δ = 27.7, 29.5, 51.5, 52.4, 83.9, 116.1, 120.8, 128.2, 129.5, 134.7, 138.7, 145.5, 165.9, 195.4, 203.6. Found: C, 71.36; H, 6.27; calc. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34%.

X-Ray analysis. X-Ray crystallographic analysis was carried out on a Rigaku AFC5R diffractometer. The diffraction data were collected with Mo Kα radiation and 3343 independent reflections were used to solve the structure using the SHELXS-97[35] program. All non-H atoms were located by direct methods using SHELXL-97[36] and refined anisotropically. Crystal data for $C_{20}H_{17}NO_4S$: formula weight = 367.41, orthorhombic, space group *Pbca*, a = 17.354(4), b = 8.865(2), c = 24.388 (5) Å, U = 3952.1(13) $Å^3$, Z = 8, D_{calc} = 1.301 g cm^{-3}, R = 0.043 (Rw = 0.1375) for 4027 refection data point with $I > 2\sigma$ and 303 variables.[37]

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