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Rearrangements and Interconversions of Heteroatom-Substituted Isocyanates, Isothiocyanates, Nitrile Oxides, and Nitrile Sulfides, RX−NCY and RY−CNX

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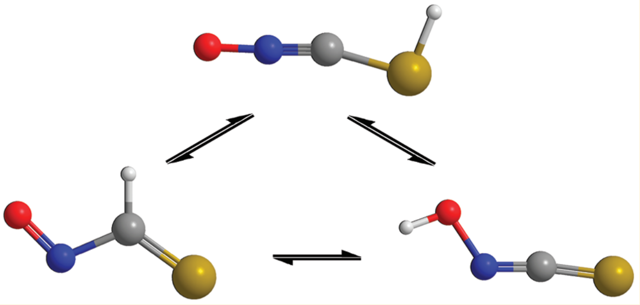
S Supporting Information



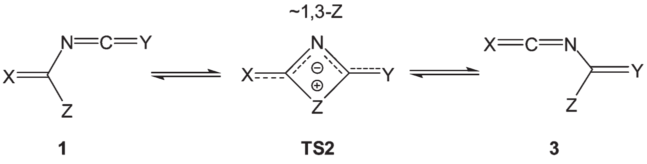
ABSTRACT: Isocyanates and isothiocyanates of the type RX−NCY (X and Y = O or S) and the isomeric nitrile oxides and nitrile sulfides RY−CNX are highly reactive compounds. A number of potential 1,4-shifts of substituent groups of the type R−Y−CNX $\rightarrow$ R−X−N=C=Y, 1,3-shifts R−C(=Y)−N=X $\rightarrow$ R−X−N=C=Y, and 1,2-shifts R−C(=Y)−N=X $\rightarrow$ R−Y−CNX have been evaluated computationally. The results obtained for the relatively new functional MPW1K and the well-established B3LYP, together with a triple-ζ quality basis set, are very similar. The 1,3- and 1,4-halogen shifts in the title compounds are usually highly exothermic and possess low activation barriers. 1,3-Aryl shifts are feasible for for **5e** $\rightarrow$ **6e** (Ar−CO−NSO$_2$ $\rightarrow$ Ar−SO$_2$−NCO) with activation barriers of less than 40 kcal/mol. Additionally, several 1,3- and 1,4-hydrogen shifts and the 1,4-methyl-shift in methoxynitrile sulfide MeO−CNS to methylsulfenyl isocyanate MeS−NCO (**4c** $\rightarrow$ **6c**) are potentially feasible. The 1,2-shift reactions **4b** $\rightarrow$ **5b** (HO−NCS $\rightarrow$ H−CS−NO) and **4c** $\rightarrow$ **5c** (Ar−O−CNS $\rightarrow$ Ar−CO−NS) are good candidates for experimental observation with activation energies around 30 kcal/mol.

INTRODUCTION

Thermal 1,3-shifts of substituents Z in isocyanates **1a** result in a degenerate interconversion with isocyanates **3a** through the transition state **TS2a**. Similarly, acyl isothiocycnates **1b** interconvert with thioacyl isocyanates **3b** (Scheme 1).[1,2]

The energies of the transition states **TS2** are lowered when the migrating groups Z possesses a lone pair that can interact with the isocyanate LUMO, which will make a formally “forbidden” reaction feasible. Therefore, these so-called pseudopericyclic 1,3-migrations of halogen, alkoxy, alkylthio, and amino groups are very facile, taking place in **1a** with a barrier of 49 kcal/mol for the H-shift, 24 kcal/mol for N(CH$_3$)$_2$, and 20 kcal/mol for Cl (calculations at the G2(MP2,SVP) level).[1,2] The interconversion of acyl isothiocyanates and thioacyl isocyanates (**1b** $\rightarrow$ **TS2b** $\rightarrow$ **3b**, Scheme 1) has been demonstrated experimentally[3−7] and computationally.[2] Calculations at the G2(MP2,SVP) and B3LYP/6-31G(d) levels provided the following order of 1,3-migratory aptitudes: Br > Cl > NMe$_2$ > F, SH > OMe, NH$_2$ > OH ≫ H ≫ Me (E_a = 17−68 kcal/mol)[2] in good agreement with the experimental sequence.[3,8] These results and related investigations of 1,3-shifts of the R groups in compounds of the type R−CX−CR′=C=Y,[9] viz. acylketenes,[1,10,11] imidoylketenes,[12−15] acylthioketenes,[16] and acylallenes[17] motivated us to investigate the potential occurrence of other substituent migrations in heterocumulenes.

Scheme 1



Z = H, Ar, Hal, OR, SR, NR$_2$
a: X = Y = O
b: X = O, Y = S

Isocyanates, isothiocyanates, and nitrile oxides have found widespread use in preparative chemistry. Compounds of the type RX−NCY (X = NR′, O or S; Y = O or S; R, R′ = H, alkyl or aryl) are usually unstable compounds, often with the characteristics of reactive intermediates, but several aminoisocyanates R$_2$N−NCO,[18−20] alkoxy isocyanates RO−NCO,[18] sulfenyl isocyanates RS−NCO,[21,22] and alkoxy isothiocyanates RO−NCS[23,24] have been prepared and isolated in low temperature matrices. Aminoisothiocyanates R$_2$N−NCS are in some cases persistent at room

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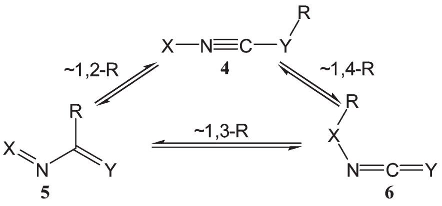
temperature for a short time, and their synthetic potential has been explored.[25−30] In contrast, sulfenyl isothiocyanates RS−NCS have not been characterized securely.[31]

Alkyl cyanate *N*-oxides RO−CNO[32] and dimethyl cyanamide *N*-sulfide Me_2N−CNS[33] have been generated as reactive intermediates in solution and trapped in 1,3-dipolar cycloaddition reactions. The existence of H_2N−CNS, CH_3S−CNS,[34] and MeO−CNS[35] in the gas phase has been established by neutralization−reionization mass spectrometry experiments. Several reviews on the classes of compounds described here are available.[36−40]

Here we report a theoretical investigation of possible rearrangements and interconversions of reactive compounds of these types (Scheme 2), e.g., the rearrangement of nitrile oxides and nitrile sulfides to iso(thio)cyanates RY−CNX **4** → RX−NCY **6**, and of acyl (thio)nitroso compounds to iso(thio)cyanates, RC(═Y)−N═X **5** → RX−NCY **6**. The potential 1,3-rearrangements of *N*-sulfinyl- and *N*-sulfonylamines to sulfinyl and sulfonyl iso(thio)cyanates RSO_x−NCY **6d**−**f** (x = 1, 2; Y = O, S), will also be described, i.e., R−CO−N═S═O → R−SO−NCO, R−CO−N═SO_2 → R−SO_2−NCO and R−CS−N═S═O → R−SO−NCS. A complete list of the investigated reactions is given in Table 1, and details of the migrating groups R can be found in Tables 2−4.

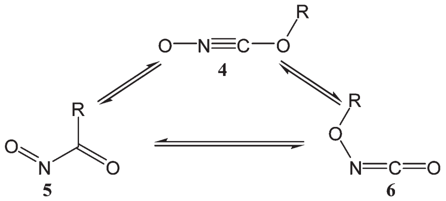
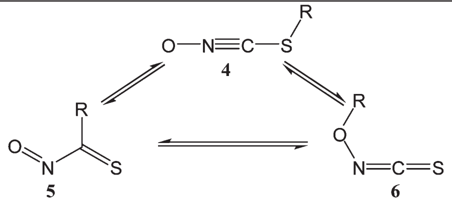
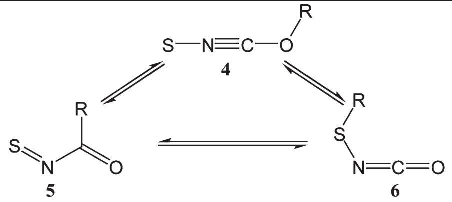
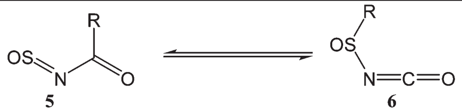
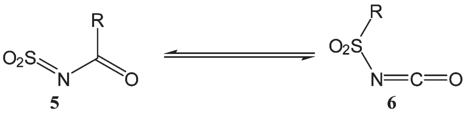
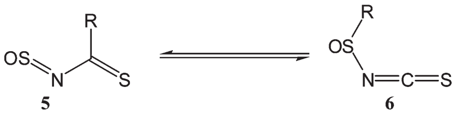
Scheme 2. General Reaction Scheme



COMPUTATIONAL DETAILS

All calculations were performed with the program package Gaussian 03.[41] Density functional theory (DFT) with the B3LYP[42,43] and MPW1K[44] functionals together with Pople's 6-31G(d)[45−47] and 6-311++G(d,p)[48−50] basis sets was used as levels of theory. The nature of all stationary points as true minima or as first-order transition states was confirmed by calculating harmonic frequencies. Scaled zero-point vibrational energy corrections have also been taken into account.[51,52] For selected reactions, CCSD(T)/6-311++G(d,p) energies[53,54] based on the B3LYP/6-311++G(d,p) geometries have been calculated. The transition states of the reactions in Scheme 2 could possess significant open-shell character; therefore, the stability of the solution wave function had been tested. In almost all cases, no wave function with a lower energy could be found. In several cases an instability has been indicated; however, reoptimization did not provide a triplet or open shell

Table 1. Investigated 1,x-Rearrangements (x = 2−4)

	X	Y	
a	O	O	
b	O	S	
c	S	O	
d	SO	O	
e	SO_2	O	
f	SO	S	

singlet wave function with (significantly) lower energy (i.e., the energy differences were invariably within 1 kcal/mol).

B3LYP has proved itself as a reliable approach in the study of systems related to the title compounds, e.g., isocyanates,[2] ketenes,[55] and iminopropadienones.[56,57] A triple-ξ basis set with diffuse functions is necessary to correctly treat the weak interactions in loose complexes between cumulenes and nucleophiles (such as amines) and the zwitterions formed therefrom.[57] In recent years, however, several new DFT methods have been developed. One of them, MPW1K, has not only been used successfully in our group[9,58] but has been applied to a variety of chemical problems.[52,59−67] We tested the applicability of this DFT approach to several pericyclic reactions (ene/retro-ene reaction, 1,5-H shift, Diels−Alder [2 + 4] cycloaddition, and Cope rearrangement, all of which can also take place in cumulenic systems) and compared its performance with the well-established B3LYP hybrid functional method (Scheme S1 and Table S1, Supporting Information). The results led us to the conclusion that both functionals together with a valence triple-ζ basis set predict similar activation barriers, in agreement with other theoretical studies on pericyclic reactions.[68−71] They are therefore used in the following section.

■ RESULTS AND DISCUSSION

1,*x*-Shifts in Isocyanates, Nitrile Oxides, and Thio Analogues. For the combinations **a**−**c** (X,Y = O,O; S,O; O,S), all 1,*x*-rearrangements between **4**, **5**, and **6** have been studied, while for the sulfinyl and sulfonyl variants **d**−**f** only the 1,3-shift between **5** and **6** has been investigated. All rearrangements are calculated for hydrogen and several aryl groups as migration substituents and the 1,4-shifts also for R = Me. Additionally, 1,3-shifts of halogens are considered. The choice of these substituents is based largely on experience with the reactions depicted in Scheme 1. The two above-mentioned levels of theory have been employed for the six systems outlined in Table 1. Careful inspection of the two sets of data does not reveal any significant difference between the two methods in the description of the 1,2-, 1,3-, and 1,4-shifts. As expected and in accord with previous findings,[52] the B3LYP-derived activation barriers are somewhat lower compared to their MPW1K counterparts. There are minor differences in the ability to find transition states: MPW1K gives a high-lying transition structure for the 1,3-chlorine shift between compounds **5a** and **6a** (61 kcal/mol) but, in contrast to the B3LYP method, fails to find transition states for the 1,4-shifts in the three aryl-substituted aryloxynitrile sulfides **4c** to arylsulfenyl isocyanates **6c**. Since the two theoretical levels give otherwise very similar results at similar computational costs,[72] only the B3LYP/6-311++G(d,p) data are presented herein (Tables 2−4); the corresponding MPW1K results can be found in Tables S2−S4 (Supporting Information). Selected CCSD(T)/6-311++G(d,p) ground-state and activation energies usually differ by as little as 5 kcal/mol from the DFT data and hence provide confidence in the latter results. In the single observed exception, the activation barrier for the 1,2-shift **4c** → **5c** (R = H) is calculated at 60 kcal/mol with the coupled cluster approach, compared to 47 kcal/mol with B3LYP, therefore making this reaction even less likely.

In Tables 2−4 numbers in italics refer to endothermic reactions; the barriers for the energetically favored pathway can be calculated by subtracting the positive numbers in parentheses from the given barriers.

1,2-Rearrangements. The 1,2-shifts between the nitrile oxides and sulfides **4a**−**c** → (thio)acyl (thio)nitroso compounds **5a**−**c** have activation barriers in the range 35−51 kcal/mol (Table 2). Some of these reactions should be feasible under FVT conditions, in particular the reactions **4c** → **5c** (aryloxynitrile sulfides to aroyl thionitroso compounds; E_a = 35−36 kcal/mol). The reactions leading to thioacyl nitroso compounds **4b** → **5b** are endothermic in contrast to the other 1,2-shifts, which are strongly exothermic. The reaction **5b** → **4b** (R = H) is experimentally feasible with E_a = 27 kcal/mol; the corresponding transition state is shown in Figure 1. The structures in Figure 1 are good representatives for this rearrangement, as all related transitions states possess similar structural features. Bond lengths and angles vary in the usual range, depending on the substituents X, Y and the migration group R.[73]

1,3-Rearrangements. For the discussion of the 1,3-shifts between (thio)nitroso compounds **5** and iso(thio)cyanates **6** (Table 3), we deal first with the nonhalogen (R = H, Ar) 1,3-

Table 2. B3LYP/6-311++G(d,p)-Calculated Relative Gibbs Free Energies of Activation (kcal/mol at 298 K) for the 1,2-Shift 4 → 5 (Nitrile Oxide (Sulfide) to (Thio)acyl (Thio)Nitroso Compound) (Scheme 2)[a]

reaction	H	Ph	*p*-NCPh	*p*-MeOPh
4a → **5a**	51 (−11)	43 (−25)	43 (−24)	42 (−27)
4b → **5b**	*38 (11)*	*44 (2)*	*44 (4)*	*47 (1)*
4c → **5c**	47 (−1)	36 (−16)	35 (−16)	36 (−17)

[a] Values in parentheses are the free energies of reaction, ΔG_R.

Table 4. B3LYP/6-311++G(d,p)-Calculated Relative Gibbs Free Energies of Activation (kcal/mol at 298 K) for the 1,4-Shift 4→6 (Nitrile Oxide (Sulfide) to Iso(thio)cyanate) (Scheme 2)[a]

reaction	H	Ph	*p*-NCPh	*p*-MeOPh	Me
4a → **6a**		61 (−35)	60 (−36)	55 (−34)	52 (−34)
4b → **6b**	55 (−12)	60 (−9)	62 (−10)	56 (−7)	69 (−4)
4c → **6c**	36 (−38)	48 (−45)	51 (−46)	46 (−45)	37 (−48)

[a] Values in parentheses are the free energies of reaction, ΔG_R.

Table 3. B3LYP/6-311++G(d,p)-Calculated Relative Gibbs Free Energies of Activation (kcal/mol at 298 K) for the 1,3-Shift 5 → 6 ((Thio)acyl (Thio)nitroso Compound to Iso(thio)cyanate) (Scheme 2)[a]

reaction	H	F	Cl	Br	Ph	*p*-NCPh	*p*-MeOPh
5a → **6a**				*38 (20)*	63 (−10)	63 (−12)	66 (−7)
5b → **6b**	57 (−23)	*67 (56)*	*43 (23)*	*34 (13)*	60 (−11)	58 (−14)	63 (−8)
5c → **6c**	44 (−37)	37(−10)	23 (−24)	17 (−29)	44 (−29)	44 (−30)	38 (−28)
5d → **6d**	38 (−4)	21 (−5)	12 (−9)	8 (−14)	47 (−1)	48 (−1)	44 (0)
5e → **6e**	33(−24)	14 (−20)	9 (−20)	7 (−24)	34 (−22)	37 (−22)	29 (−20)
5f → **6f**	33 (−5)	22 (−11)	13 (−14)	9 (−18)	48 (−3)	49 (−3)	44 (−3)

[a] Values in parentheses are the free energies of reaction, ΔG_R.

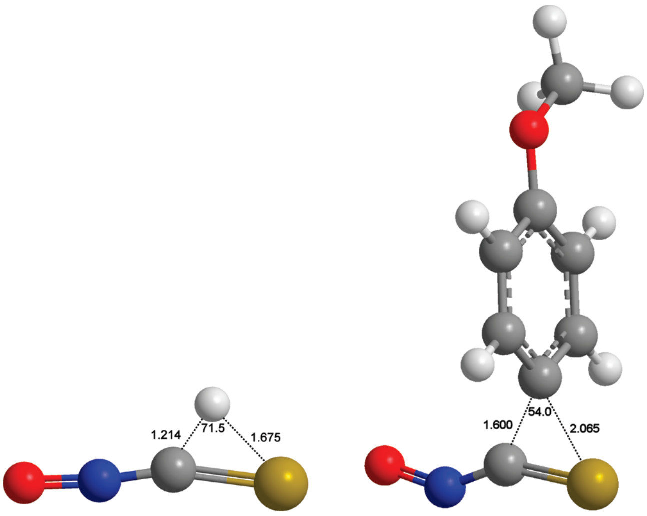


Figure 1. Transition states for 1,2-shifts (left: R = H, right: R = *p*-$MeOC_6H_4$) connecting nitrile oxide **4b** with thioacyl nitroso compound **5b**, together with selected bond lengths (Å) and angles (deg).

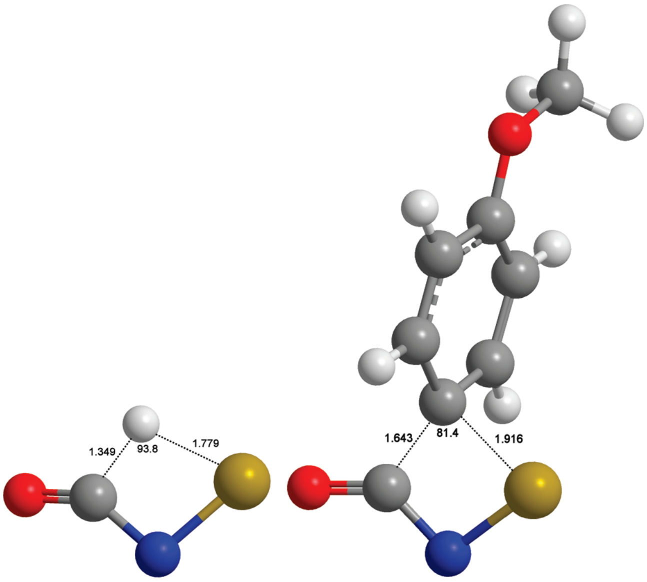


Figure 2. Transition states for 1,3-shifts (left: R = H, right: R = *p*-$MeOC_6H_4$) connecting acyl thionitroso compound **5c** with isocyanate **6c**, together with selected bond lengths (Å) and angles (deg).

shift reactions **5** → **6** described in Scheme 2: the reactions **5a,b** → **6a,b** (R-CO-NO → R-O-NCO and R-CS-NO → R-O-NCS) are unlikely to occur, as their calculated activation barriers are 57−67 kcal/mol.[74] In contrast, the reactions R-CO-N=S → R−S-N=C=O (**5c** → **6c**), R-CO-N=S=O → R-SO-N=C=O (**5d** → **6d**), R-CO-N=SO_2 → R-SO_2−N=C=O (**5e** → **6e**), and R-CS-N=S=O → R-SO-N=C=S (**5f** → **6f**) are mostly strongly exothermic with activation barriers in the range of 29−49 kcal/mol. Most of them should be accessible on thermolysis under FVT conditions or even in solution. The reactions forming sulfonyl isocyanates **5e** → **6e** are very favorable for all substituents ($E_a <$ 40 kcal/mol). In addition, the hydrogen shifts **5d,f** → **6d,f** and the migration of the *p*-anisyl group in **5c** → **6c** are particularly facile (E_a = 33−38 kcal/mol). The TS is shown in Figure 2.

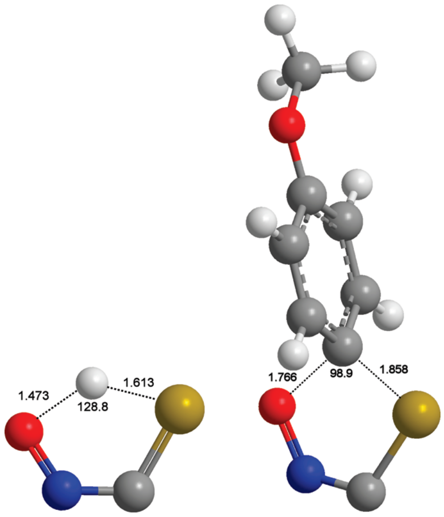


Figure 3. Transition states for 1,4-shifts (left: R = H, right: R = *p*-$MeOC_6H_4$) connecting nitrile oxide **4b** with isothiocyanate **6b**, together with selected bond lengths (Å) and angles (deg).

Similarly to the 1,2-rearrangements, the two TSs in Figure 2 are representative for all investigated 1,3-migrations.

The 1,3-rearrangements involving halogen atoms have mostly modest activation barriers in the 15−30 kcal/mol range. The reactions **5a,b** → **6a,b** have significantly higher barriers (34−67 kcal/mol), and the directions are reversed, i.e. the exothermic reactions are **6a,b** → **5a,b** with low barriers in the 10−20 kcal/mol range. There is also a distinct trend toward lower activation energies when going from fluorine to bromine. This is similar to the observations made for the reactions described in Scheme 1.

1,4-Rearrangements. All the 1,4-shifts have relatively high barriers (Table 4); those involving aryl groups require activation energies of 46−62 kcal/mol and may therefore be difficult to observe by thermal means (Figure 3). The 1,4-shifts of H and Me in R−O−CNS → R−S−NCO (**4c** → **6c**; E_a = 36−37 kcal/mol) are potentially feasible reactions. Unsurprisingly, all these reactions are exothermic, the iso(thio)cyanates being more stable than the isomeric nitrile oxides and nitrile sulfides.

CONCLUSION

The evaluation of activation energies for several pericyclic reactions shows very good agreement with the reference data for the established B3LYP functional and the newly developed MPW1K functional when employing a valence triple-ζ basis set. Further, both methods give very similar results when applied to a series of 1,4-, 1,3-, and 1,2-shifts of substituent groups of the types RY−CNX → RX−NCY, R−CY−NX → RX−NCY, and R−CY−N− → RY-CNX.

Generally, 1,3-halogen shifts in these compounds are highly exothermic and possess low activation energies in the range of 15−38 kcal/mol. Hence, they should be experimentally feasible under thermolysis conditions in the gas phase or in some cases even in solution.

Several 1,3-shifts have activation energies in the 30−40 kcal/mol range and are therefore potentially possible. All the reactions forming sulfenyl, sulfinyl, and sulfonyl isocyanates R−S−N=C=O, R−SO−N=C=O, and R−SO_2−N=C=O (**5c**−**f** → **6c**−**f**) are energetically feasible. 1,4-Shifts of H and alkyl (methyl) in $\mathrm{R{-}CO{-}N{=}S} \rightarrow \mathrm{R{-}S{-}N{=}C{=}O}$ (**4c** → **6c**) are potentially observable.

Some 1,2-H shifts are good candidates for experimental observation. The activation energy is calculated to be as low as 27 kcal/mol for HCS−NO **5b** → HS−CNO **4b**. The 1,2-aryl shifts rearranging aryloxynitrile sulfides to aroyl thionitroso compounds, ArO−CNS **4c** → ArCO−NS **5c**, are also among the most favorable (35−36 kcal/mol).

As indicated in the Introduction, methods exist for the generation of several of the classes of compounds described herein.[36] The present study indicates that many of the activation barriers for the 1,*x*-rearrangements are experimentally accessible. This should lead to a rich intramolecular chemistry, which merits further investigation. The technique most suitable for experimental investigation will be FVT coupled with matrix isolation spectroscopy.

ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Tables containing MPW1K/6-311++G(d,p) and B3LYP/6-311++G(d,p) calculated energies for pericyclic reactions (ene/retro-ene reaction, 1,5-H shift, [2 + 4] cycloaddition, and Cope rearrangement) and for all reactions and structures described herein. Absolute energies and Cartesian coordinates for all calculated ground and transition states. This material is available free of charge via the Internet at http://pubs.acs.org.

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(73) Within a given series of X and Y, the distances between the migrating group R and the two atoms of the bond breaking and bond forming centers increase with larger R due to the increased steric demand of R. As a consequence, the angle formed by the three atoms (leaving center—R—arriving center) is reduced.

(74) The transition state for the hydrogen shift in variant **a** could not be located. An estimate (PES scan with fixed distances) of this barrier **6a**—**5a** is about 70 kcal/mol; hence, it is unlikely to occur. In the same series, there are two more 1,3-shifts for which no activation energies could be calculated (R = F, Cl). The estimated barriers are in the 45—60 kcal/mol region.