Merging of 4+2 and 2+4 cycloaddition paths in the regiospecific dimerization of methacrolein. A case of concerted crypto-diradical cycloaddition

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Abstract—The regiospecific dimerization of methacrolein takes place through a very asynchronous and symmetrical transition structure, which shows a merging of the 4+2 and 2+4 cycloaddition paths. The geometrical features of the transition structures correspond well to a case of diradical formation. A cage of secondary orbital interactions restricts the flexibility of the diradical transition structure and stabilizes it. © 2001 Elsevier Science Ltd. All rights reserved.

The simplest α,β-unsaturated aldehyde and ketone, acrolein and methyl vinyl ketone **1** (R=H), undergo a regiospecific dimerization to the dihydropyrans **2** under relatively mild thermal conditions (80–120°C).[1] Several other α,β-unsaturated aldehydes and ketones **1** having α substituents but no substituents at the β-carbon undergo a similar and even easier thermal dimerization[2] affording the dimers **2**, which are versatile intermediates in many valuable synthetic elaborations.[3]

The mechanism of these regiospecific Diels–Alder (DA) dimerizations has attracted high interest since the exclusive products are the adducts **2** and not the electronically favored regioisomeric adducts **3**. In the early studies the neat head-to-head union of the addends in adducts **2** was taken as indicative of some sort of diradical intermediates, crypto[4] or equipped with special attractive forces.[5] Later, however, frontier orbital (FO) theory could account for the observed regiochemistry[6] in the framework of concerted DA cycloadditions and since then the regiospecific dimerization of acrolein was included in the collection of venerable pericyclic reactions and has even become a textbook example[7] of the power of FOs in accounting for regiochemical phenomena.

We have recently located at the B3LYP/6-31G* level the eight possible DA transition structures (TSs) of the acrolein dimerization leading to the dimers **2a** and **3a**.[8] The two lowest and viable TSs are the *exo* and *endo* TSs **2aCX** and **2aCN** (Fig. 1). Both the TSs involve the less stable cisoid conformation of the acrolein dienophile and lead to the observed dimer **2**. The heteroatoms play a determining role in the stabilization of the two TSs and we suggested a mechanism of neighboring group participation through the bridging (dotted lines in formulas) of the nucleophilic diene oxygen to the proximal carbonyl carbon of the cisoid dienophile. The coiled TS **2aCN** is further stabilized by a classical secondary orbital interaction (SOI)[6a,b] as well as by Coulombic attraction.

Although the interpretation of the stabilizing effects of **2aCX** and **2aCN** rested on the well-known Bürgi–Dunitz model[9] and the extensively used,[10] albeit debated,[11] SOI concepts, we were nevertheless worried
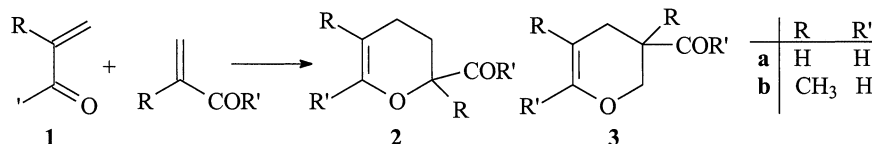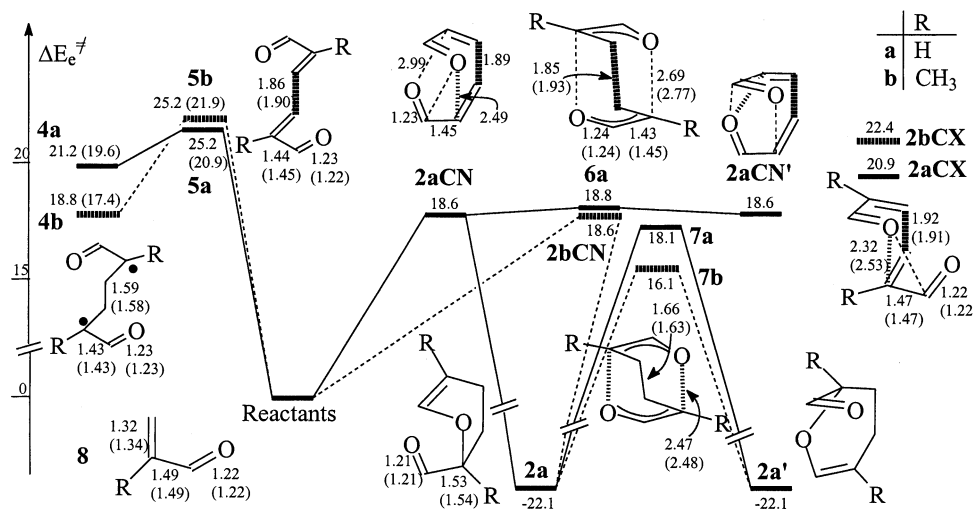
Figure 1. Transition structures and diradical intermediates for the acrolein (full lines) and methacrolein (dashed lines) dimerization. Numbers near the levels are electronic energies in kcal/mol relative to the reactants and in parentheses are the relative energies of the diradical species after spin projection.[12c] Numbers near the forming bonds are bond distances in Å for the acrolein (methacrolein) structures.

by some intriguing aspects of TS **2aCN**. While the geometrical features of TS **2aCX** still correspond to expectations for a concerted asynchronous DA cycloaddition, the lowest TS **2aCN** displays an asynchronicity significantly magnified, showing a rather long (2.49 Å) forming C···O bond and a distressingly short (1.89 Å) forming C···C bond. Such a distance is in the typical range reported in several TSs of diradical formation.[12] In brief, although TS **2aCN** energetically looks like a normal saddle point of a concerted asynchronous DA (1 imaginary frequency), its geometrical features show an uncanny resemblance to a TS of diradical formation.

We have then located[13] a few other relevant points on the potential energy surface of acrolein dimerization (Fig. 1 and Table 1). At the UB3LYP/6-31G* level the reference singlet diradical in the *anti* conformation **4a** is only 2.6 kcal/mol above TS **2aCN** while the TS **5a** leading to the diradical is 6.6 kcal/mol higher. The energies of the diradical species lower somewhat after spin correction,[12c] but remain above TS **2aCN** by 1.0 and 2.3 kcal/mol, respectively. As far as the 4+2 saddle point **2aCN** is concerned, it lies on a quite flat plateau and only a little energy expenditure (0.2 kcal/mol) is required to convert it into the 2+4 saddle point **2aCN′** through a symmetrical 2nd order saddle point **6a**. The Cope TS **7a**,[14] interconnecting the dimers **2a** and **2a′** is 0.5 kcal/mol below **2aCN**.

Clearly Fig. 1 shows that the reference diradical **4a** and TS **5a** are anyway higher in energy than the concerted TS **2aCN**. Does it mean that radicals are not involved at all in TS **2aCN**? Why then is the surface of **2aCN** so flat, allowing the ready interconversion of the 4+2 and 2+4 TS **2aCN** and **2aCN′** with such a minuscule barrier? Further perplexities arise because of the almost identical geometrical features of the acrolein dipolarophile in TS **2aCN** and in the diradical TS **5a**. In the DA cycloaddition the C1–C2 bond (1.49 Å) of the s-*cis*

acrolein dipolarophile **8** lengthens to 1.52 Å in the cycloadduct **2a** while a remarkable shortening occurs in TS **2aCN** (1.45 Å) as well as in TS **5a** (1.44 Å) and in diradical **4a** (1.43 Å), as expected for an acetyl radical moiety.[15]

Following the idea of testing the consequences of a possible diradical stabilization through the aid of substituents we have investigated the related dimerization of methacrolein. In this case the diradical **4b** and the Cope TS **7b** drop by ca. 2 kcal/mol and TS **2bCX** is lifted by 1.5 kcal/mol, while TS **5b** and **2bCN** are almost unaffected.[16] The most striking effects of the methyl substitution are however, the increase in asyn-

Table 1. B3LYP/6-31G* electronic activation energies $\Delta E_e^{\neq}$ relative to the reactants (kcal/mol), activation enthalpies,[a] forming C···C and C···O bond lengths (Å) of the TSs and the singlet diradical species of acrolein[b] and methacrolein[c] dimerization

	$\Delta E_e^{\neq}$	$\Delta H^{\neq}$	C···C	C···O
2can[b]	18.6	20.5	1.89	2.49
2bCN	18.7	20.1	1.93	2.77
2aCX[b]	20.9	22.7	1.92	2.32
2bCX	22.4	23.7	1.91	2.53
4a[d]	21.2 (19.6)	23.1 (21.5)	1.59	
4b[d]	18.8 (17.4)	20.7 (19.3)	1.58	
5a[d]	25.2 (20.9)	26.3 (22.1)	1.86	
5b[d]	25.2 (21.91)	26.1 (22.8)	1.90	
6a	18.8	20.1	1.85	2.69
7a	18.1	20.4	1.66	2.47
7b	16.1	18.1	1.63	2.47

[a] Thermodynamic values at 298.15 K from unscaled vibrational frequencies in the harmonic approximation.
[b] Ref. 8.
[c] s-*trans* Methacrolein, −231.233628 hartree, correction to enthalpy $\delta H = 60.7$; s-cis methacrolein, $\Delta E_e = 2.9$; dimer **2b**, $\Delta E_e = -19.0$.
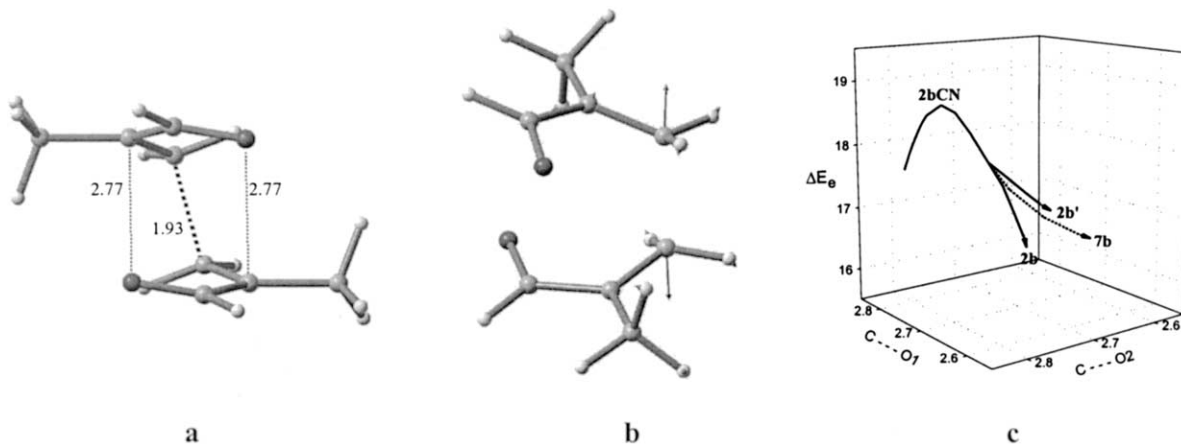[d] UB3LYP/6-31G* singlets; energies after spin correction[12c] are given in parentheses.

Figure 2. Geometric features (a) and displacement vectors (b) of the methacrolein TS **2bCN** and the reaction coordinate (c) of the dimerization path. The dotted path refers to the symmetrical crest toward Cope TS **7b**.

chronicity and the neat geometrical change occurring in the lowest cycloaddition pass **2bCN** which shows up fully symmetrical (Fig. 2a). The 4+2 and 2+4 cycloaddition paths have no longer a separate identity and have fully merged in this TS.

The displacement vectors associated with the imaginary frequency of TS **2bCN** involve essentially the C···C vibration while the in phase C···O vibrations play only a secondary role (Fig. 2b). Accordingly, IRC calculations[17] shows that the Reaction Coordinate (RC) steps symmetrically from TS **2bCN** toward the reactants as well as the products, with only minor changes of the C···O distances (Fig. 2c). On the product side the RC steps at the beginning toward the Cope TS **7b** but at about half way the antisymmetric CO/CO vibration (which is imaginary frequency of the Cope TS **7b**) becomes negative and the RC splits into two symmetrical branches, which point finally toward the cycloadducts **2b** and **2b′**, respectively. Clearly the RC of Fig. 2c does not properly belong to a normal DA cycloaddition.

The extreme asynchronicity and shape of TS **2bCN** corresponds almost exactly[18] to the imaginative picture of the formation of a *gauche* diradical kept together by secondary attractive forces as hypothesized in 1959 by Woodward and Katz[5] for the acrolein dimerization. As foreseen by Woodward the primary process is a C···C bond formation assisted by the SOIs between the developing oxaallyl moieties, which interact in a fashion similar to a Cope boat TS. The SOIs stabilize the diradical species and restrict its mobility, providing concertedness to the cycloaddition path. For this sort of immobilized diradical the Alder's term crypto-diradical[4] seems to us quite appropriate. The dimerization of acrolein still shows a slight preference for an extreme 4+2 cycloaddition path but this predilection can be easily overcome as indicated by the flatness of the surface connecting the 4+2 and 2+4 paths.

Merging of 4+2 and 2+4 DA paths has been reported and dismissed in the DA cycloadditions of butadiene to

Lewis acids complexes of acrolein.[19] The dimerization of methacrolein provides a neat example of merging and a case of a concerted crypto-diradical cycloaddition as well. Current investigations with better radical stabilizing substituents (Cl, OCH_3, CN) show further cases of merging in which the asynchronicity of the symmetrical TSs increases only a little more.

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16. When comparing the energies of the acrolein and methacrolein structures the changes shown in Fig. 1 are somewhat misleading, since they include a conformational bias due to the sizeably different energies of the s-*cis* conformers of acrolein and methacrolein (1.7 and 2.9 kcal/mol, respectively) relative to the corresponding more stable s-*trans* conformers. When the energies of s-*cis* conformers are taken as the reference point the acrolein and methacrolein structures of Fig. 1 are to be lowered by 3.4 and 5.9 kcal/mol, respectively. In this case the methacrolein structures become actually lower than the corresponding ones of acrolein, as expected on the basis of simple FO considerations. The α-methyl substitution in acrolein raises the HOMO and polarizes it toward the β-carbon, favoring the head to head dimerization. The STO-3G eigenvalues and coefficient of the s-*cis* acrolein (methacrolein) FOs are: HOMO, $\varepsilon = -8.68$ (-8.31) eV, O 0.402 (0.357), C1 0.194 (0.154), C2 -0.563 (-0.555), C3 -0.586 (-0.604); LUMO, $\varepsilon = 6.08$ (6.23) eV, O 0.580 (0.578), C1 -0.505 (-0.513), C2 -0.436 (-0.436), C3 0.642 (0.632).

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18. In the original formulation Woodward and Katz[5] hypothesized that, "after passage of the barrier, the reaction proceeds to the Cope TS and thence to the products."

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