A Complete Active Space Self-Consistent Field (CASSCF) Study of the Reaction Mechanism of the α-Alkynone Rearrangement

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Dedicated to Prof. *André S. Dreiding* on the occasion of his 80th birthday

The pyrolytic rearrangement of α-alkynones has been discovered by *Karpf* and *Dreiding* [1] in 1979. The mechanism of this reaction, which involves an acetylene-vinylidene rearrangement followed by cyclization of the intermediate vinylidene carbene by insertion into a β-C−H bond, has been debated in a couple of theoretical investigations. Restricted *Hartree-Fock* (RHF) and single-point *Møller-Plesset 2* (MP2) calculations at the RHF geometries apparently indicate the carbene cyclization to be the rate-determining step, contrary to chemical intuition. However, larger-scale correlated calculations with completely optimized molecular geometries ((8,8) CASSCF/6-311G**), augmented with a perturbative account for the dynamic correlation contribution to the electronic energy, show vanishing energy barriers to the cyclization step and large activation energies for the acetylene-vinylidene rearrangement, which is thus confirmed as the rate-determining step of the title reaction.

Introduction. – The pyrolytic rearrangement of α-alkynones [1] belongs to the rich area of carbene reactions, which continue to pose mechanistic challenges to theoreticians and frequently offer elegant and unexpected synthetic paths to complex molecules. The reaction involves a transformation of alkyl ethynyl ketones to cyclopent-2-enones, and is illustrated in the *Scheme*.

Scheme
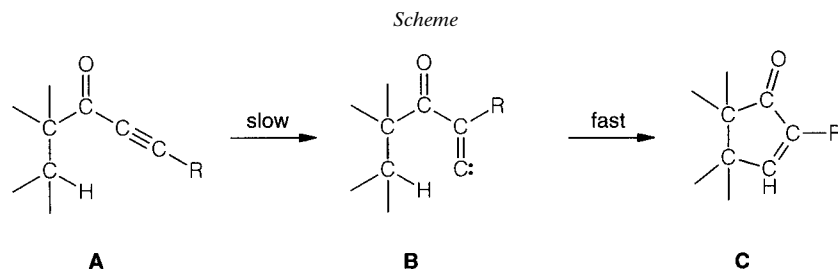
Intuitive considerations [1] assume a slow [1,2]-shift of the β-substituent in **A** to produce the reactive carbene intermediate **B**, which inserts into a C−H bond to give the final cyclopentenone **C**. This mechanism has apparently been confirmed by *ab initio* SCEP/DZ calculations [2], but was later challenged by *Nguyen* and *Hegarty* [3] on the basis of the calculated significant barrier to the insertion reactions of vinylidene carbenes [4] and their isoelectronic species, *i.e.*, carbon monoxide and isonitriles [5]. However, *Nguyen* and *Hegarty* investigated the cyclizations to cyclobutenone and

cyclopent-2-enone [3] using MP2/6-31G**//3-21G and MP4SDTQ/6-31G//3-21G calculations without considering the ring strain of cyclobutenone. Even more important in the case of the vinylidene cyclization is to account for the effect of nondynamic electron correlation. As shown in this work, the latter significantly influences the electronic structure of carbenes and vinylidenes and the size of the energy barrier limiting both the initial acetylene-vinylidene rearrangement (see **13** and **14**) and the subsequent cyclization. While at the MP4 level the energy barrier, which separates the vinylidene intermediates from stable acetylenes, is very small [6]; higher-level correlation calculations [7] bring this barrier to the limiting value of *ca.* 2.9 kcal/mol, corrected for the zero-point energy (ZPE) contribution. Extensive density-functional-theory (DFT) studies on the same energy barrier also converge around the above-mentioned value [8].

Furthermore, the mechanism of the α-alkynone rearrangement is not fully understood with respect to the participation of singlet or triplet vinylidene species in the intramolecular reaction. Carbonyl carbenes, for example, are triplet species [9][10]. Therefore, this point should be addressed as well when investigating the α-alkynone cyclization. To outline the trends in the energetics of the two possible acetylene-vinylidene rearrangement paths, namely [1,2] shift of hydrogen or alkyl *vs.* acyl migration (see **13** and **14**), calculations were carried out on six α-alkynones, propynal (**1**), but-2-ynal (**2**), but-3-yn-2-one (**3**), pent-3-yn-2-one (**4**), pent-1-yn-3-one (propio-nylacetylene; **5**), and pent-1-en-4-yn-3-one (acryloylacetylene; **6**), and the stationary points arising along their reaction paths were determined.

[1,2] Rearrangements of the selected alkynone species give the vinylidene intermediates **7** – **12**.

Cyclization of the three intermediate vinylidenes **9**, **11**, and **12** leads to enones **15**, **16**, and **17**, respectively.

Computational Details. – Geometries of all mentioned stationary points on the acetylene [1,2]-rearrangements to the corresponding vinylidenes are completely optimized by gradient molecular-orbital (MO) calculations with explicit accounting for electron correlation. To account for the nondynamic electron correlation, three levels of CASSCF calculation are used: (6,6) 6-31G*, (8,8) DZP, and (8,8) 6-311G** [11][12], using *Irix*, *Linux*, and *Windows* versions of *GAMESS* [13]. The notation (*m*,*n*) denotes the span of considered active configuration space, *i.e.*, *m* electrons in *n* active orbitals. The choice of configuration-space size is based on recent calculations of the acetylene-vinylidene rearrangement [11] and carbene additions to ethylene C=C
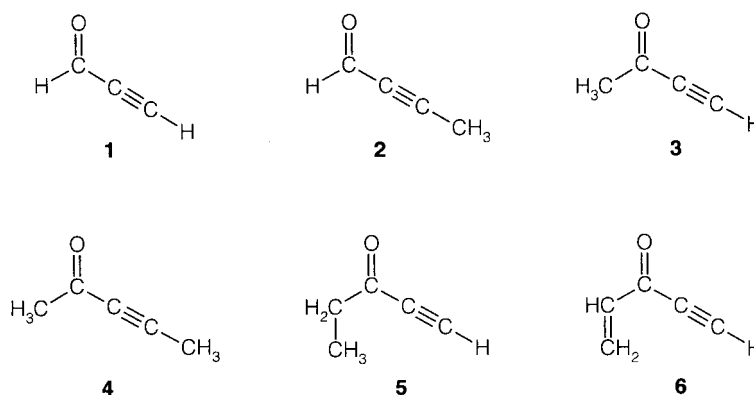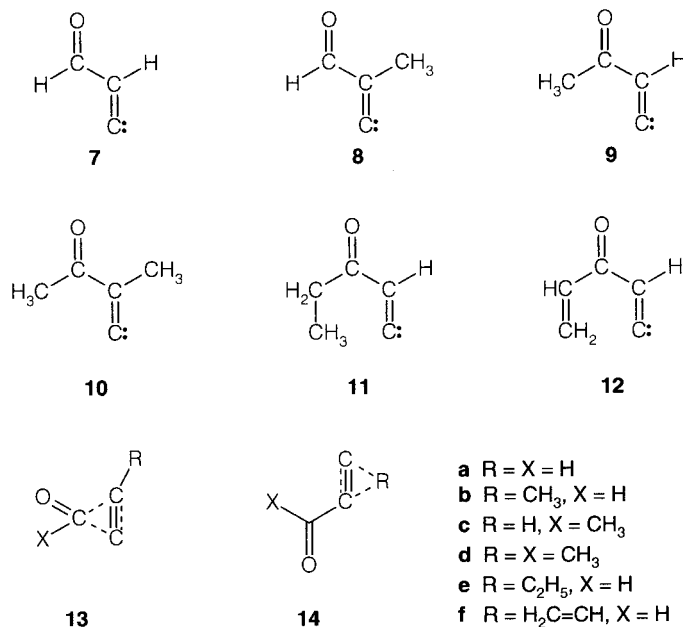
bonds [12]. The two smaller basis sets, 6-31G** [14] and DZP [15], are used for compatibility with earlier calculations [2][3], while the moderate-size 6-311G** [14] basis set is used as an indicator of convergence trends of results depending on the basis set [16]. Single-point multiconfigurational second-order perturbation calculations (MCQDPT [17]) on the optimized CASSCF geometries are used to account for dynamic electron-correlation effects on the energies of studied stationary structures of the traced carbenoid reaction paths. The effect of dynamic electron correlation on the calculated cyclization barrier of the three vinylidene carbenes, **9**, **11**, and **12** is studied at the MP4(fc)-SDQ/6-311G**//MP2(fc)/6-311G** level. ZPE Corrections for all stationary structures are calculated at the RHF/6-311G** level.

Results and Discussion. – C_3 to C_5 species (*cf.* **13** and **14**) are considered sufficient to elucidate the aforementioned aspects of the α-alkynone cyclization, as well as to bring clarity to the question of preferred participation of alkyl or acyl fragments in the initial [1,2]-rearrangement on the acetylene-vinylidene stage [2]. To define as precisely as possible the thermochemical parameters of the second reaction stage, the cyclization of the intermediate vinylidene carbene to form the corresponding five-membered enone rings, and thus to conclusively define the rate-determining stage of the studied process, larger alkyl and alkenyl substituents were included.

Present CASSCF calculations uniformly show that the singlet ground states (S) of the studied vinylidenes are lower in energy than the corresponding lowest triplet states (T) by 33–36 kcal/mol. This energy gap is significantly larger than S-T gaps of substituted carbenes and most nitrenes [18] and the extensively studied C_7H_6 [19][20]. The mentioned size of the S-T gap in studied vinylidenes justifies, therefore, the original calculation [2][3] of singlet reaction paths only. Present CASSCF calculations confirm the activation enthalpies for the [1,2]-H shift of the studied acetylenes of *ca.* 60 kcal/mol (decreasing slightly for heavier species) at the DZP/SCEP level [2], of *ca.* 60 kcal/mol for the [1,2]-Me shift, and of *ca.* 50 kcal/mol for the [1,2]-acyl shift (increasing slightly

for heavier species). Any preference for [1,2]-H, alkyl, or acyl migration of more heavily substituted acetylene species is therefore unlikely. For this reason, more attention is paid now to the comparison of calculated activation energies of model [1,2] migrations of more heavily substituted C_4 and C_5 acetylene species studied here.

The mentioned theoretical activation parameters turned out to be 20 – 25% higher than the more recently determined experimental values for the parent acetylene-vinylidene rearrangement [21]. Similar to the results obtained by highly correlated MO and DFT calculations of carbenoid species [7][8], recent CASSCF calculations corrected this overestimation, indicating activation energies of *ca*. 46 – 62 kcal/mol for the carbene-vinylidene rearrangement. Therefore, calculations that include both dynamic and nondynamic electron correlation are expected to provide reliable predictions of the relative preferences for various substituents (H, alkyl, or acyl) for the studied [1,2] shift, leading to the intermediate carbene species. Calculated activation enthalpies for the singlet [1,2] rearrangement of the studied acetylenes to corresponding vinylidenes are summarized in the *Table*.

Table. *Calculated Absolute Energies and Activation Enthalpies of the Acetylene-Vinylidene [1,2] Rearrangement* (singlets only)

| Species	MCQDPT2//(8,8)CAS SCF/6-311G** [a.u.]	ZPE and ΔH [kcal/mol]
Propynal (**1**)	− 190.1766	ZPE = 25.6
C_3-Formyl TS_{ac} (**13a**)	− 190.1033	ZPE = 22.6, ΔH = 46.0
C_3-Hydrogen TS_h (**14a**) (s-*trans*)	− 190.0998	ZPE = 21.4, ΔH = 48.2
Formylvinylidene (**7**) (s-*trans*)	− 190.1043	ZPE = 24.0, ΔH = 45.3
But-2-ynal (**2**)	− 229.3895	ZPE = 44.2
C_4-Formyl TS_{ac} (**13b**)	− 229.3101	ZPE = 42.5, ΔH = 49.8
C_4-Methyl TS_{alk} (**14b**)	− 229.3008	ZPE = 42.6, ΔH = 55.6
Formyl(methyl)vinylidene (**8**)	− 229.3127	ZPE = 42.9, ΔH = 48.2
But-3-ynone (**3**)	− 229.3996	ZPE = 44.0
C_4-Acetyl TS (**13c**)	− 229.3137	ZPE = 41.9, ΔH = 53.9
C_4-Hydrogen TS (**14c**)	− 229.3133	ZPE = 40.3, ΔH = 54.2
Acetylvinylidene (**9**)	− 229.3152	ZPE = 42.5, ΔH = 53.0
Pent-3-yn-2-one (**4**)	− 268.5983	ZPE = 63.2
C_5-Acetyl TS (**13d**)	− 268.5151	ZPE = 61.0, ΔH = 52.2
C_5-Methyl TS (**14d**)	− 268.4999	ZPE = 61.4, ΔH = 61.8
Acetyl(methyl)vinylidene (**10**) (s-*trans*)	− 268.5231	ZPE = 61.8, ΔH = 47.2
Pent-1-yn-3-one (**5**)	− 268.6003	ZPE = 63.0
C_5-Propionyl TS (**13e**)	− 268.5120	ZPE = 61.1, ΔH = 55.4
C_5-Hydrogen TS (**14e**)	− 268.5219	ZPE = 59.5, ΔH = 49.2
Propionylvinylidene (**11**)	− 268.5189	ZPE = 62.0, ΔH = 51.1
Pent-1-en-4-yn-3-one (**6**)	− 267.3745	ZPE = 48.0
C_5-Acryloyl TS (**13f**)	− 267.2912	ZPE = 45.8, ΔH = 52.3
C_5-Hydrogen TS (**14f**)	− 267.2968	ZPE = 44.2, ΔH = 48.7
Acryloylvinylidene (**12**)	− 267.2962	ZPE = 46.2, ΔH = 49.1

The above data clearly indicate that [1,2]-acyl shifts are energetically more favored than [1,2]-alkyl shifts in the studied α-alkynones in the acetylene-vinylidene rearrangement. However, a [1,2]-H shift will be preferred with ethynyl ketones, for which the probability of a vinylidene intermediate before cyclization is extremely small.

Now the geometry changes that account for nondynamic electron correlation in the calculated stationary points on the reaction path of the α-alkynone cyclization, relative to earlier 3-21G [3] and DZ [2] calculations, should be considered. The important structures to be compared are obviously found at the saddle points of the [1,2] rearrangements and of the cyclization step itself. For the [1,2]-H migration (*cf.* **14a**, **14c**, **14e**) in propionylacetylene (**5**), uncorrelated 3-21G [3] and DZ [2] calculations predict an early transition structure with significantly extended C−H bonds. The three main participating atoms form an approximately equilateral triangle of C=C and C−H bonds of 124–126 pm length. The present CASSCF calculations, however, predict a late-transition structure with the H-atom almost attached to the target sp^2-C-atom at a distance of *ca.* 118 pm, while the C$\cdots$H distance to the other C-atom is extended to 151 pm. The almost formed vinylidene C=C bond has a predicted length of *ca.* 130 pm.

More interesting is the geometry of the transition state (TS) for the [1,2]-acyl migrations (*cf.* **13a–f**). All calculations predict that the plane of the migrating acyl fragment is almost perpendicular to the plane of the C=C bond and the acyl C-atom. The TS is again predicted to be early by 3-21G [3] and DZ [2] calculations, with a C_1-C_2 distance of 183–185 pm and a $C_1-C_2-C_3$ angle of 68–72°. Furthermore, the CASSCF calculations predict a more advanced TS along the reaction coordinate, with a C_1-C_2 distance of 198 pm and a $C_1-C_2-C_3$ angle of 63°.

The transition structures predicted by the performed CASSCF calculations are once again more advanced along the reaction coordinate, as compared to the 3-21G results of *Nguyen* and *Hegarty* [3]. The incipient C−C bond has a length of 202 pm, compared to 210 pm at the 3-21G level. The distance between the migrating H-atom and the carbene C-atom is 114 pm, which has, approximately, also been found in other calculations. The distance between the H-donating C-atom and the migrating H-atom is calculated to be 142 pm at the 3-21G and 139 pm at the CASSCF level, *i.e.*, this TS has actually a typical H-bridged fragment involving the C−C bond in formation.

Four species out of the six listed in the *Table*, namely **9**, **10**, **11**, and **12**, are capable of undergoing cyclization, giving cyclobutenone (**15**), cyclopent-2-enone (**16**), and cyclopenta-2,4-dienone (**17**), respectively. Calculations of the three cyclization-reaction paths of the intermediate propionyl-, acryloyl-, and acetylvinylidenes, **11**, **12**, and **9**, resp., give the typical late, *i.e.*, H-abstraction transition structures with :C−H bond lengths of 116–118 pm (see *Fig. 1*).

15   **16**   **17**
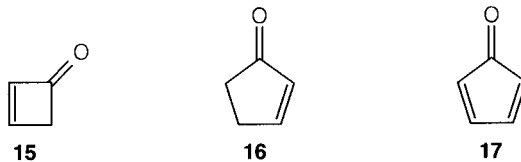
These three transition structures are in contrast to early carbene complexes with proton donors [22], in which the new :C$\cdots$H bond is merely a H-bond to the carbene with a distance of 183–244 pm. The calculated absolute energies of propionyl-, acryloyl-, and acetyl-vinylidene cyclization are shown in *Fig. 2*.
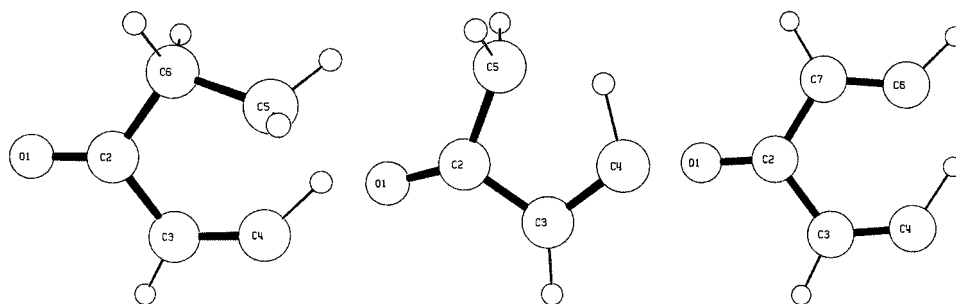
Fig. 1. *(8,8) CASSCF/6-311G** Transition structures for cyclizations* (left to right) *of propionyl-, acetyl-, and acryloylvinylidene*
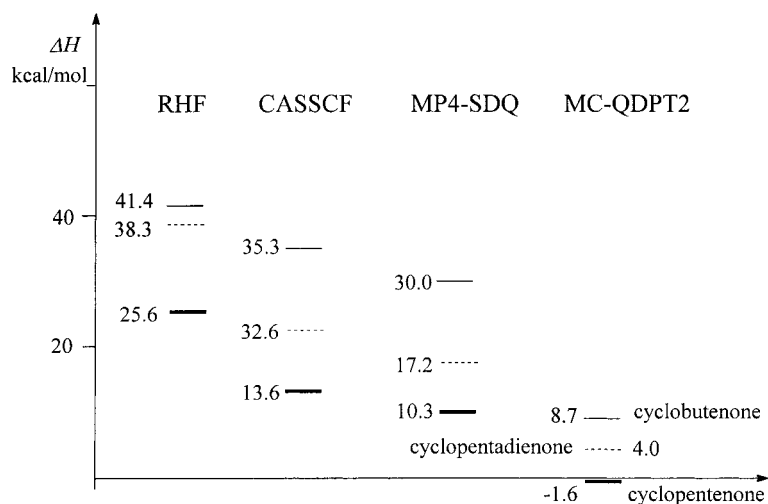

Fig. 2. *Calculated 6-311G** activation enthalpies for the cyclization of the three vinylidene carbenes* **9**, **11**, *and* **12** *at various levels of electron correlation, with resulting final enone products*

As seen in *Fig. 2*, the high energy barriers to cyclization, calculated at the RHF level, are significantly reduced by either dynamic electron correlation at the MP4-SDQ level, or nondynamic electron correlation at the (8,8) CASSCF level, provided the electron correlation is explicitly accounted for in the geometry optimization. However, to reproduce the intuitive expectation of negligible barriers to vinylidene cyclization, it is sufficient to consider simultaneously both types of electron correlation, although in this work, dynamic electron correlation is considered only perturbationally, and no further improvement of the optimized CASSCF geometry is used.

Conclusion. – The reported CASSCF and MCQDPT2 calculations of the stationary points along the α-alkynone-cyclization path convincingly demonstrate that accounting for only either dynamic or nondynamic electron correlation is insufficient to reproduce the apparent trends in acyl-vinylidene cyclization. However, the combined computation of nondynamic *and* dynamic electron-correlation effects correctly predicts the

vanishing barriers to this carbene C−H insertion reaction and confirms the earlier conclusion [1][2] that the rate-determining step of the α-alkynone cyclization is the acetylene-vinylidene [1,2] rearrangement. The subsequent cyclization TS has a slightly higher energy than the TS for the [1,2]-acetylene-vinylidene rearrangement. In addition, the combined consideration of dynamic and nondynamic electron correlation reproduces satisfactorily the expected trend of increasing activation enthalpy for the closure of strained-ring molecules, as shown by the results for the acryloyl-vinylidene cyclization to cyclopentadienone (**17**) and the acetyl-vinylidene cyclization to cyclo-butenone (**15**) (*cf. Fig. 2*), compared to the less-strained cyclopentenone (**16**). In addition, the reported CASSCF calculations show no involvement of singlet-triplet intersystem crossing, neither during the [1,2]-acetylene-vinylidene rearrangement, nor during the vinylidene-cyclization reaction.

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