Registry No. 1, 61-19-8; 2·2NH$_3$, 120311-44-6; KHSO$_5$, 10058-23-8; Poly A (potassium salt), 26763-19-9.

Comparison of the Relative Rates of Radical Addition versus Diradical Intermediate Formation in [2 + 2] Cycloaddition Reactions of Similarly Substituted Alkenes and Alkynes

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Numerous studies have focused on the determination of the relative reactivities of substituted alkenes and alkynes toward free-radical addition. The available data indicates that free-radical additions occur more rapidly to the substituted alkenes than to the similarly substituted alkynes. The relative reactivities for trapping R (R = *n*-butyl or *tert*-butyl generated by the reduction of RHgCl with NaBH$_4$) are $H_2C{=}CHCO_2Et$ (1.0) and $HC{\equiv}CCO_2Et$ (0.19), and $H_2C{=}CHC_6H_5$ (0.15) and $HC{\equiv}CC_6H_5$ (0.02).[1] In a similar type of study the relative reactivities for the trapping of the cyclohexyl radical were found to be $H_2C{=}CHCO_2Et$ (6.7) and $HC{\equiv}CCO_2Et$ (2.1), and $H_2C{=}CHC_6H_5$ (1.0) and $HC{\equiv}CC_6H_5$ (0.25).[2] The addition of substituted benzenethiyl radicals to $H_2C{=}CHCO_2Et$ and $HC{\equiv}CCO_2Et$ favored the alkene by factors of 24–47.[3] And finally, the rates have been measured for the gas-phase addition of the methylthiyl radical to ethylene and acetylene (2.8 and $<2 \times 10^{15}$ cm^3/s) and propene and propyne (10 and $<6 \times 10^{15}$ cm^3/s).[4] In all of these comparative cases the addition of the free radical to the alkene occurred faster than to the alkyne by factors that range from 1.4 to 47.

Recent studies in our laboratories have shown that the [2 + 2] cycloaddition reactions of 1,1-dimethylallene (DMA) with substituted alkynes occur very cleanly to produce substituted methylenecyclobutenes.[5] Qualitatively, these reactions appeared to proceed considerably more rapidly than did the [2 + 2] cycloaddition reactions with substituted alkenes,[6] which prompted us to carry out relative rate comparisons of similarly substituted alkenes and alkynes toward cycloaddition with DMA. The two pairs of substituted alkenes and alkynes used in this study are $H_2C{=}CHCO_2Et$ and $HC{\equiv}CCO_2Et$, and $H_2C{=}CHC_6H_5$ and $HC{\equiv}CC_6H_5$.[7] *In both cases the substituted alkyne was essentially completely reacted; there was no indication of any reaction having occurred with the substituted alkene. In these* [2 + 2] *cycloaddition reactions the substituted alkynes are more reactive than the corresponding alkene by a factor of* $>$*100*!

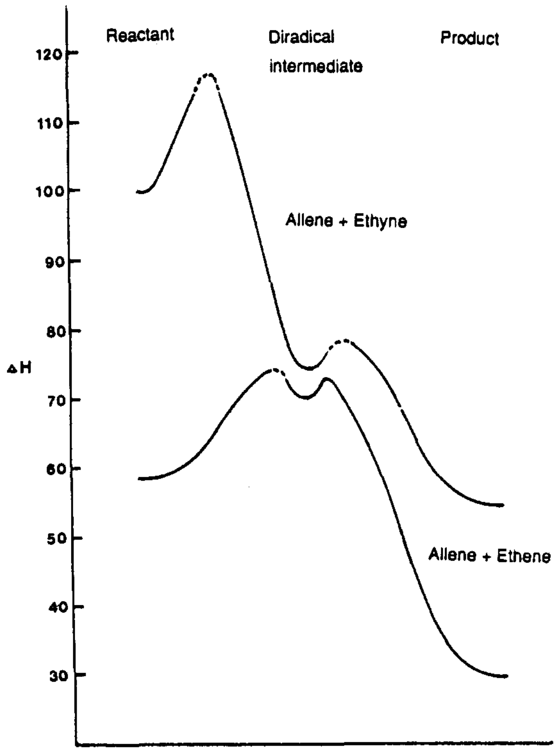

Figure 1. Heats of formation of reactants diradical intermediates and products.

What accounts for this dramatic change in relative reactivities in radical addition reactions versus the cycloaddition reactions with DMA? In the addition of an alkyl radical to a C=C or C≡C, a C—C bond is formed, a C=C π-bond is cleaved, and one radical center disappears while another radical center is formed. Overall, this reaction will be quite exothermic, and, thus, the transition state for the addition should occur early along the reaction coordinate. In this case the relative reactivities will be controlled by FMO properties. The calculated energies (4-31G fully geometry optimized structures)[8] for the HOMO's and LUMO's of ethylene and acetylene are −10.21 and −11.04 eV, and +5.07 and +6.16 eV, respectively; with c_i's of 0.564 and 0.911, and 0.558 and 0.986, respectively. In radical addition reactions there is an interaction between the SOMO of the radical (whose energy lies between the HOMO and the LUMO of the π-system) with both the HOMO and the LUMO of the π-system of the alkene or alkyne. According to PMO theory the alkene is thus expected to react more rapidly than the alkyne in reactions involving very early transition states.

In the [2 + 2] cycloaddition reactions of substituted allenes all of the data collected in the author's laboratories indicate that these cycloaddition reactions occur via diradical intermediates that are formed via transition states that occur late along the reaction coordinate.[6] This is fully consistent with the nature of the process: two C=C bonds being cleaved, one C—C bond being formed along with two radical centers, which will result in a rather endothermic process. At first glance, the greater reactivity of the substituted alkynes in the cycloaddition process would appear to suggest that the vinyl radical portion of intermediate 1 is lower in energy than the alkyl radical portion in 2. However, this is not consistent with the well-recognized relative stabilities of the ethyl and vinyl radicals as indicated by C–H bond dissociation energies and heats of formation, which indicate that the ethyl radical is lower in energy than the vinyl radical. An understanding of the

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[2] Giese, B.; Lachhein, S.; Meixner, J. *Tetrahedron Lett.* 1980, *21*, 2505.

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[4] Balla, R. J.; Weiner, B. R.; Nelson, H. H. *J. Am. Chem. Soc.* 1987, *109*, 4804.

[5] Pasto, D. J.; Kong, W. *J. Org. Chem.* 1988, *53*, 4807.

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[7] All of the cycloadducts except that of styrene with DMA have been previously characterized (ref 5 and 6).

[8] Carnegie-Mellon Quantum Chemistry Archive, Carnegie-Mellon University, Pittsburgh, PA.

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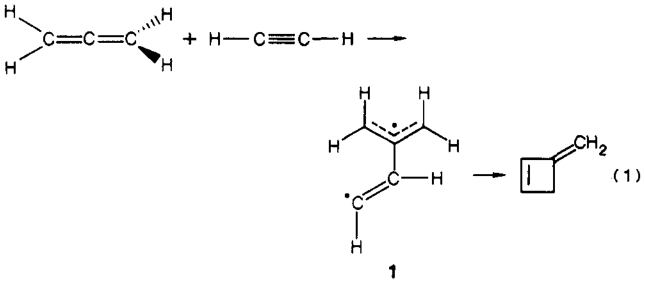
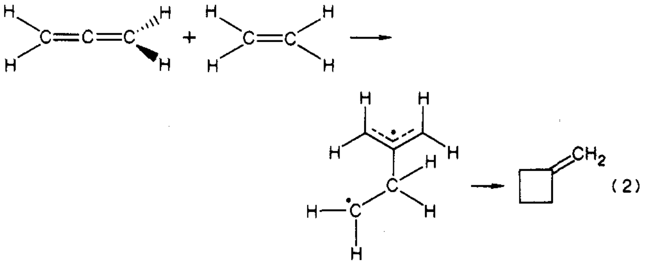
greater reactivity of the alkynes in the [2 + 2] cycloaddition reactions with DMA can be gained by consideration of the relative changes in the heats of formation on going from the reactants to the intermediate diradicals and on to the products, which are shown in Figure 1 for the hypothetical reactions shown in eq 1 and 2. The formation of **2** is accompanied by a positive *increase* in the heat of formation as expected. The formation of **1**, however, is accompanied by a *decrease* (in a positive sense) in heat of formation, giving a heat of formation of **1** *lower* than that of the reactants! This is due to the considerably larger positive heat of formation of acetylene (54.2 kcal mol^{-1}) compared to that of ethene (12.5 kcal mol^{-1}).[9] The much lower heat of formation of **1** versus **2** relative to the heats of formation of the reactants would suggest that the energy barrier for the formation of **1** should be considerably lower than that for the formation of **2**, which is consistent with the presently observed relative reactivity data.


1 (1)


2 (2)

Experimental Section

Relative Rate Measurements. The competitive cycloaddition reactions were carried out by placing 0.5 mmol each of the substituted alkene and alkyne and DMA in 0.4 mL of toluene-d_8 in an NMR tube. Dioxane (20 μL) was added as an internal standard for NMR integration purposes, and 1 mg of hydroquinone was added as a polymerization inhibitor. The contents of the tubes were triply freeze degassed, and the tubes were sealed under reduced pressure. The NMR spectra of the reactant solutions were recorded and the tubes were then heated in a sand bath at 160 °C for 5 days. The NMR spectra of the reaction solutions were recorded, the integrals were measured and compared with those of the reactant solutions, and the extent of reaction of the substituted alkene and alkyne was calculated. The resonances in the reactions mixtures were identified by the comparison of chemical shifts with those recorded previously.[5,6]

Acknowledgment. This research was supported by National Science Foundation Grant CHE87-09725.

Registry No. DMA, 598-25-4; $H_2C{=}CHCO_2Et$, 140-88-5; $HC{\equiv}CCO_2Et$, 623-47-2; $H_2C{=}CHC_6H_5$, 100-42-5; $HC{\equiv}CC_6H_5$, 536-74-3.

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[9] The heats of formation of the reactants, diradical intermediates, and the products have been calculated by the Benson group additivity approach (Benson, S. W. *Thermochemical Kinetics*; John Wiley & Sons: New York, 1976) using the group additivities in Table 2.14 (pg 73) and Appendix A.1. The group additivities for C-(C_d)(C)(H) and C_d-(H) were assumed to be −5 and +25, respectively, based on comparisons with other group values.

(±)-Aspidofractinine Derivatives

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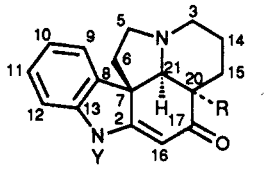
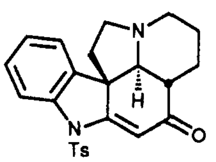
In connection with studies in the field of Aspidosperma alkaloid synthesis the pentacyclic intermediate **1a** has been prepared recently[2] and now has been used for the construction of some aspidofractinine derivatives.

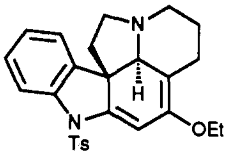
Exposure of pentacycle **1a** to *p*-tolylsulfonyl chloride and sodium hydroxide under phase-transfer conditions yielded a mixture of the *N*-tosyl derivatives **1b** and **2**. Treatment of either product with ethyl iodide and potassium hydride gave ketone **1c** (in 13% yield) and diene **3** (61%).[3]



1a: R = Y = H
b: R = H; Y = $SO_2C_6H_4Me(\text{-}p)$
c: R = Et; Y = $SO_2C_6H_4Me(\text{-}p)$
d: R = Et; Y = H



2



3

The acquisition of a fair amount of diene **3** permitted its use in Diels–Alder reactions en route to the kopsane skeleton (e.g. aspidofractinine, **5a**).[4] Interaction of the diene with methyl acrylate afforded hexacycle **4a** (82%). Acid-induced, partial hydrolysis of the latter yielded keto ester **5b** (87%), whose stereostructure was confirmed by single-crystal, X-ray crystallographic analysis.[6] Similarly, cycloaddition of diene **3** and phenyl vinyl sulfone produced a ca. 4:1 mixture (66%) of adducts **4b** and **6**. Hydrolysis of each enol ether furnished ketones **5c** (81%) and **7** (84%), respectively. Exposure of either product to sodium amalgam reduction led to 17-oxoaspidofractinine (**5d**) (70

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[2] Wenkert, E.; Orito, K.; Simmons, D. P.; Kunesch, N.; Ardisson, J.; Poisson, J. *Tetrahedron* **1983**, *39*, 3719.

[3] Hydrolysis of ketone **1c** with 2 N potassium hydroxide in methanol has led to colorless, amorphous 2,16-dihydro-17-oxoaspidospermidine (**1d**) (76%): UV λ_{max} 241 nm (log ϵ 4.08), 300 (3.85), 348 (4.10); IR NH 3140 (br m), NCH 2760 (m), 2700 (w), C═O 1680 (s), C═O, C═C 1625 (s), 1603 (s) cm^{-1}, ^{1}H NMR δ 0.25 (t, 3, J = 7 Hz, Me), 3.47 (s, 1, H-21), 5.46 (s, 1, H-16), 6.8–7.7 (m, 4, Ar Hs), 10.03 (s, 1, NH); *m/e* 294 (M^+, 6), 140 (9), 126 (37), 124 (base), 110 (7).

[4] For previous Diels–Alder reactions on **3**-like substances, see: (a) Ohnuma, T.; Oishi, T.; Ban, Y,. *J. Chem. Soc., Chem. Commun.* **1973**, 301. (b) Ban, Y.; Honma, Y.; Oishi, T. *Tetrahedron Lett.* **1976**, 1111. (c) Magnus, P.; Gallagher, T.; Brown, P.; Pappalardo, P. *Acc. Chem. Res.* **1984**, *17*, 35. (d) Kuehne, M. E.; Seaton, P. J. *J. Org. Chem.* **1985**, *50*, 4790.[5] (e) Ogawa, M.; Kitagawa, Y.; Natsume, M. *Tetrahedron Lett.* **1987**, 3985.[5]

[5] Wenkert, E.; Pestchanker, M. J. *J. Org. Chem.* **1988**, *53*, 4875.

[6] Toffoli, P.; Rodier, N.; Le Mênez, P.; Kunesch, N., unpublished observation.

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