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Surprising exocyclic regioselectivity in electrophilic additions to alkylidenecyclobutenes

Hillel Pizem, Ofer Sharon and Aryeh A. Frimer*

Department of Chemistry, Bar-Ilan University, Ramat Gan 52900, Israel

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Abstract—The addition of peracid, bromine, TCNE and singlet oxygen to alkylidenecyclobutenes shows a strong regioselectivity—in some cases regiospecificity—for the exocyclic double bond. Depending on the reagent, the endocyclic double bond will only undergo reaction upon the addition of a second equivalent of reagent. In the case of the first three reagents, this exocyclic regioselectivity is rationalized by invoking the formation of the more stabilized carbocation intermediate or transition state. Regarding $^1O_2$, where polar mechanisms are rare, we attribute this exocyclic regioselectivity to the improper alignment and, hence, lack of reactivity of the endocyclic allylic hydrogen.
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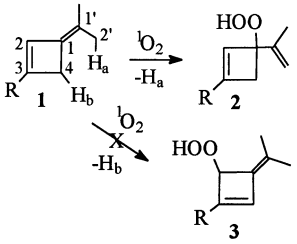
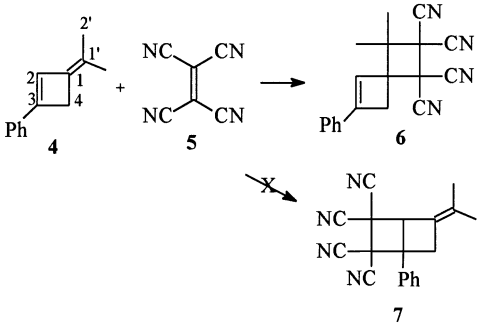
1. Introduction

Previous research in our laboratory has explored the effect of ring-strain on the mode, rate and direction of singlet oxygen attack.[1] In particular, we have focused on various small ring olefin systems in which ring-strain decreases or develops as we proceed to product. Frimer and Weiss[1h] studied the singlet oxygenation of alkylidenecyclobutenes (Eq. (1)) and observed exclusive formation of ene reaction product **2**, resulting from oxygen attack at the exocyclic double bond and abstraction of H_a. There was no evidence of oxygen attack at the endocyclic double bond and abstraction of H_b, which would have yielded cyclobutene **3**.



(1)

Frimer and Weiss[1f–h] argued that the absence of **3** may have to do with the spacial alignment of H_b, which is displaced ca. 36° from the perpendicular, far from the pseudo-axial orientation strongly preferred by singlet oxygen.[2] However, an alternate rationale is also possible: it is not the allylic hydrogen H_b of **1** that is unreactive, but rather the C_2–C_3 endocyclic double bond. Indeed, we have recently reported[3] that isopropylidenecylobutene **4** undergoes [2+2] cycloaddition with TCNE at the exocyclic C_1–$C_{1'}$ double bond to give spiroheptane **6** as the sole product (Eq. (2)); surprisingly, the endocyclic double bond proved unreactive. We decided to explore the generality of this observation with two other electrophilic additions to this system, peracid epoxidation and bromination.



(2)

2. Results and discussion

2.1. Peracid epoxidation

2.1.1. Monoepoxidation. When isopropylidenecyclobutene **4** was reacted with 1 equiv. of *m*-CPBA in CH_2Cl_2 or CH_3CN, the ^1H NMR spectrum of the reaction mixture following aqueous work-up showed the presence of a sole product which contained the typical cyclobutene olefinic hydrogen absorption at 6.67 ppm. This suggested that indeed the endocyclic double bond had remained intact. However, the ^{13}C NMR spectrum of this sample lacked absorptions corresponding to epoxide carbons (ca. 60–65 ppm), revealing instead C–O absorptions at 74 and 89 ppm. In addition, other peaks strongly suggested the

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* Corresponding author. Tel.: +972-3-5318610; fax: +972-3-5351250; e-mail: frimea@mail.biu.ac.il

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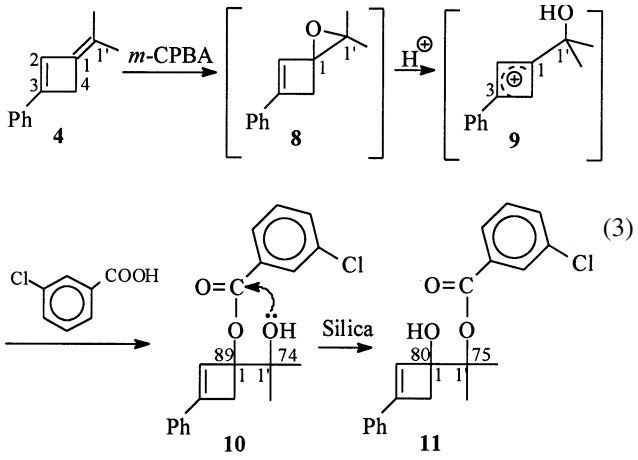
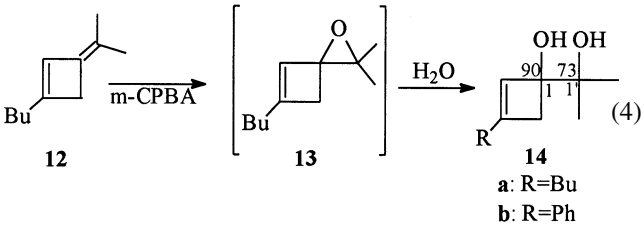
incorporation of a *m*-chlorobenzoic acid moiety into the observed product. Silica gel chromatography of the reaction mixture gave a 30% yield of a new isomeric product which again contained a cyclobutene olefinic hydrogen absorption at 6.39 ppm, but had C–O absorptions at 75 and 80 ppm. Based on this and other spectral data (vide infra), we suggest that the initially formed labile epoxide **8** (see Eq. (3)) undergoes acid-catalyzed opening and nucleophilic attack by *m*-chlorobenzoic acid at C-1, yielding butenol **10**. The latter undergoes silica mediated intramolecular *trans*-esterification to the sterically less congested isomer **11**.



(3)

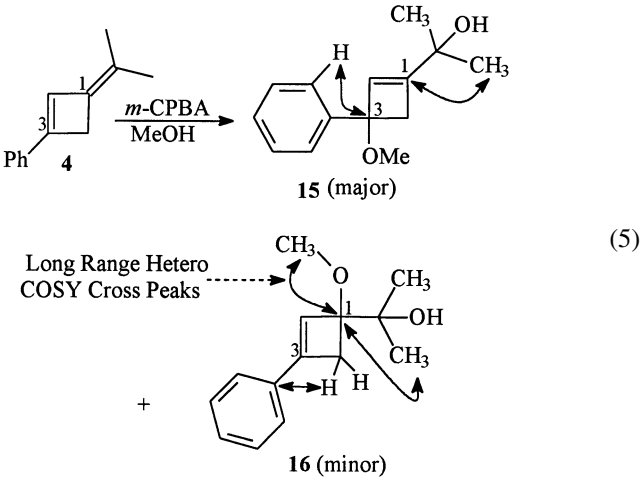
Our rationale for the assignments of **10** and **11** is based on the following considerations. Frimer and Weiss[1h] reported that the *m*-CPBA epoxidation of the 3-butyl analog, cyclobutene **12**, yields the corresponding epoxide **13**. We have reexamined their original spectral data and now believe the authors erred; the isolated product is in fact diol **14a** (Eq. (4)). The $\Delta\delta$ between C-1 and C-1′ is 17 ppm.



(4)

Calculations[4] indicate that replacing the butyl group in **14a** with a phenyl group (**14b**) has a negligible effect on the ^{13}C NMR chemical shifts of C-1 and C-1′. We also used these calculations to explore the effect of esterification of diols **14a** and **14b** at either the C-1 or C-1′ hydroxyl groups. Thus, C-1 esterification is predicted to *increase* the $\Delta\delta$ between C-1 and C-1′ (by ca. 7 ppm), while C-1′ esterification would decrease it (by 8 ppm). These calculations confirm that, in the epoxidation of **4**, the initially formed ester possessing the larger $\Delta\delta$ (15 ppm) is in all probability the 1-benzoyl analog, butenol **10**; the rearrangement product with the smaller $\Delta\delta$ (5 ppm) is presumably the 1′-benzoyl isomer **11**.

In the mechanism outlined in Eq. (3), considering the 3° structure of the C-1 carbon of epoxide **4**, we have posited the intermediacy of an allylic carbonium ion **9**, which undergoes S_N1 attack by *m*-chlorobenzoic acid to yield **10** as the sole product. Such a process is in fact well documented in the acid catalyzed solvolysis of allylic epoxides.[5] Nevertheless, we might have expected to see, in addition to **10**, products of S_N1' attack. Interestingly, when the epoxidation was repeated in CH_3OH, two new products were obtained in a 2:1 ratio and identified as methoxycyclobutenes **15** and **16** (Eq. (5)).



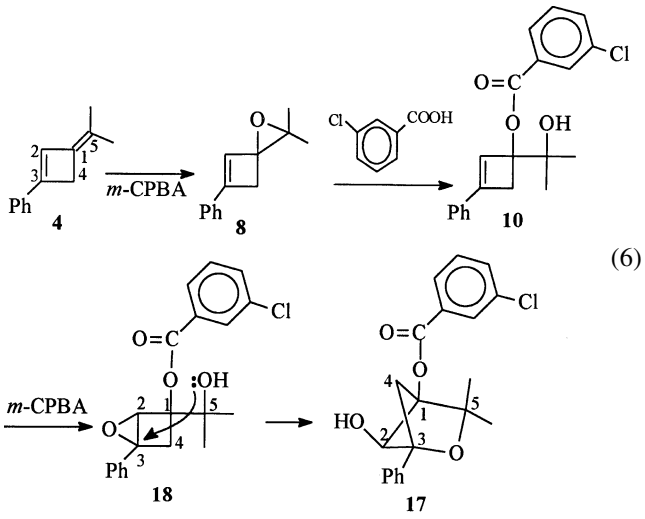
(5)

Long-range heteroCOSY experiments confirmed these assignments: in **15**, cross-peaks were observed between the *ortho* aromatic hydrogens and C-3, as well as between the methyl hydrogens and C-1; in **16**, cross-peaks were found between the ring methylene hydrogens (H-4) and the *ipso* aromatic carbon, as well as between the methyl and methoxy hydrogens and adjacent ring carbon C-1. While the minor product **16** presumably results, as before, from S_N1 attack at C-1 of **9**, the major product **15** results from S_N1' attack at the less sterically hindered carbon C-3.

The solvent dependent modes of action observed may well be linked to the protic nature of the media. In aprotic solvents such as CH_2Cl_2 and CH_3CN, the hydrogen bonding (pre-coordination) of the C-1′ hydroxyl group with the attacking carboxylic acid plays a dominant role in directing the nucleophile to the C-1 position of **9** (Eq. (3)). Such directing effects have been previously observed,[5a–c] but are expected to be attenuated in protic media, thus allowing a competing S_N1' approach.

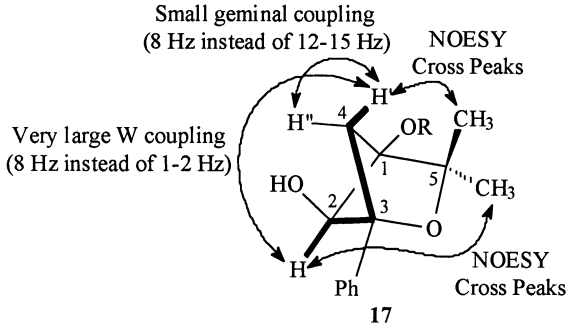
2.1.2. Diepoxidation. When alkylidenecyclobutene **4** was treated with 2 equiv. of *m*-CPBA in aprotic media, a new product was formed whose mass corresponded to the addition of two oxygen atoms and m-chlorobenzoic acid. The same product was obtained when monoepoxidation product **10** was treated with *m*-CPBA. After much spectral analysis, this product was identified as oxabicyclo[2.1.1]-hexane **17**, and a plausible mechanism of formation is shown in Eq. (6).[†]

[†] To aid the reader in following the transformation of **4** into **17**, we have kept the numbering of the carbons in these two compounds the same in Eqs. (6) and (7). The correct numbering is shown in Scheme 2 and used in Section 4.



(6)

The NMR spectral data for **17**, despite its relative simplicity, is unique. The ^{1}H NMR spectrum of the product revealed three vicinally coupled aliphatic hydrogens at 2.87 (t, J=8 Hz), 3.50 (d, J=8 Hz) and 5.03 (d, J=8 Hz). The ^{13}C NMR data further indicated the presence of a methylene and a methyne at 41.12 and 83.27, respectively. The proposal of structure **17** as drawn in Eq. (6) requires two atypical splitting constants: (1) a relatively small geminal coupling (8 rather than 12–15 Hz) for the methylene; (2) a strong W-coupling (8 rather than 1 Hz) between one of these methylene hydrogens and the methyne hydrogen across the ring (see Eq. (7)). Importantly, while such values are generally speaking unusual, they are well precedented for bicyclo[2.1.1]hexane systems.[6] NOESY cross-peaks, too, confirm the structure proposed for **17**. As further outlined in Eq. (7), the W-coupled hydrogens $H_{4'}$ and H_2 show NOE interaction with *different* C-5 methyl groups, only possible in such a bicyclo structure. This NOE interaction in turn places the C-2 hydroxyl group *endo* in the bicyclo-system (see Eq. (7)).



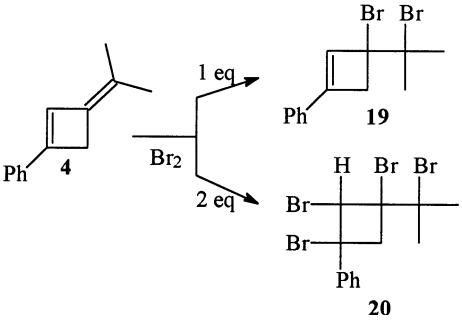
(7)

The last issue that requires elucidation is the location of the benzoate group. We have placed it at C-1 rather than C-2 for the following reasons: (1) The ester group was situated at C-1 in both the starting material and the intermediate mono-epoxidation product **10**, precursors to **17**. The C–O bonds at C-2 and C-1 are nearly perpendicular to one another and trans-esterification is, hence, highly unlikely. (2) No long range hetero-COSY interaction was observed between $H_{4''}$ and the benzoate carbonyl. (3) The $H_{4'}$ methylene resonance appears at 2.87 ppm, while the corresponding H_2 absorption is downfield at 5.03 ppm. This downfield shift of 2.2 ppm is slightly below the 2.5 ppm downfield shift typical for hydrogens geminal to hydroxyl groups. The corresponding effect observed for benzoyloxy is 3.3 ppm.[7]

In summary, we see with *m*-CPBA a sizable difference in reactivity rates of the endocyclic and exocyclic bonds of alkylidenecyclobutene **4**. In particular, no diepoxidation product is observed until the exocyclic bond has fully reacted.

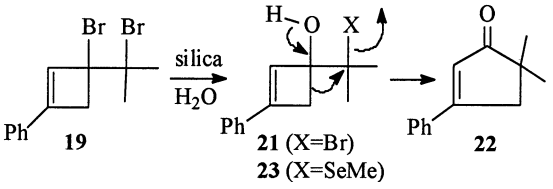
2.2. Bromination

Despite the fact that bromine is reported to react extremely rapidly with styrene,[8] 1 equiv. of bromine added exclusively to the exocyclic double bond of alkylidenecyclobutene **4**, yielding dibromide **19** (Eq. (8)). Only the second equivalent reacts at the endocyclic styrenyl double bond of **4** generating tetrabromide **20**.



(8)

Attempts to purify **19** via silica gel column chromatography yielded the known cyclopentenone **22**[9] (Eq. (9)), presumably via silica mediated hydrolysis to a β-hydroxy-bromide, cyclobutenol **21**, which ring opens to the observed cyclopentenone. Ghosez and coworkers[10] similarly report that when β-hydroxyselenide **23** is reacted with base, the corresponding cyclopentenone is obtained (Eq. (9)).

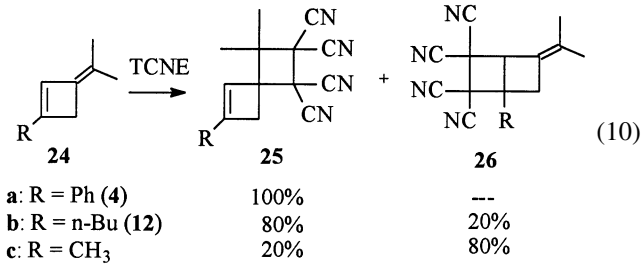


(9)

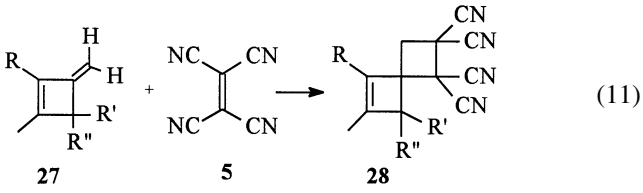
Thus, once again, we see a sizable difference in reactivity rates between the endocyclic and exocyclic bonds of alkylidenecyclobutene **4**.

2.3. Reaction with TCNE

The preference for electrophilic reaction at the exocyclic bond was observed once again in the case of TCNE addition. As noted above (Eq. (2)), 1-isopropylidene-3-phenyl-2-cyclobutene **4** (**24a** in Eq. (10)), yields spiro adduct **6** (**25a**) exclusively.[3] Similarly, we have found that the 3-butyl analog **12** (**24b**) reacts with TCNE preferentially at the exocyclic double bond, yielding adducts **25** and **26** in a 4:1 ratio. There are also several previous reports[11] that variously ring-substituted methylenecyclobutenes (e.g. **27** in Eq. (11)) react with TCNE via a facile 2+2 cycloaddition exclusively at the exocyclic olefinic linkage.



(10)



(11)

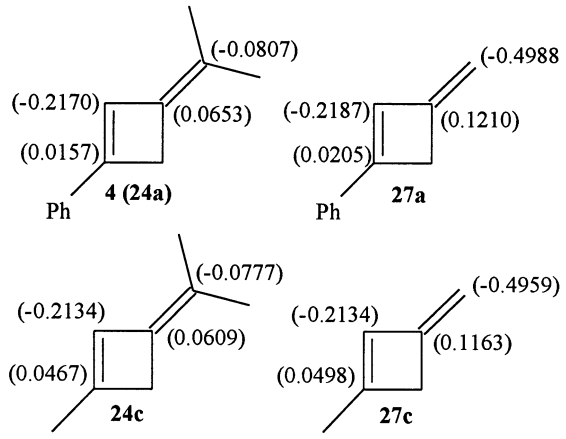
In this light, the 40 year old report of Williams[11c] regarding the reaction of 3-methyl-1-isopropylidenecyclobutene (**24c**) with TCNE is highly surprising. In particular, he reports that TCNE adds primarily at the internal cyclobutene double bond, yielding **25** and **26** in a 1:4 ratio (Eq. (10)). In comparing these latter results with the exocyclic preference of **27**, Williams[11c] and others[12] had suggested that the steric bulk of the *gem*-dimethyl groups in **24c** inhibits approach to the exocyclic bond. This rationale, however, is inconsistent with our recent results from both **24a** (**4**) and **24b** (**12**). Assuming the correctness of Williams report, we have not found an alternative explanation.

2.4. The question of mechanism

The observed exocyclic regioselectivity is somewhat surprising. Doering and coworkers[13] studied the heats of hydrogenation of various cycloolefins and report that exocyclic unsaturation in four-membered ring compounds is intrinsically slightly more stable (by ca. 0.6 kcal/mol) than *endo* unsaturation. In the specific case of olefins **24**, this difference should be increased by another 0.3 kcal/mol[14] because the exocyclic double bond is tetrasubstituted while the endocyclic unsaturation is trisubstituted. Thus the endocyclic double bond, which is about 1 kcal/mol less stable than the exocyclic one, should be more reactive.

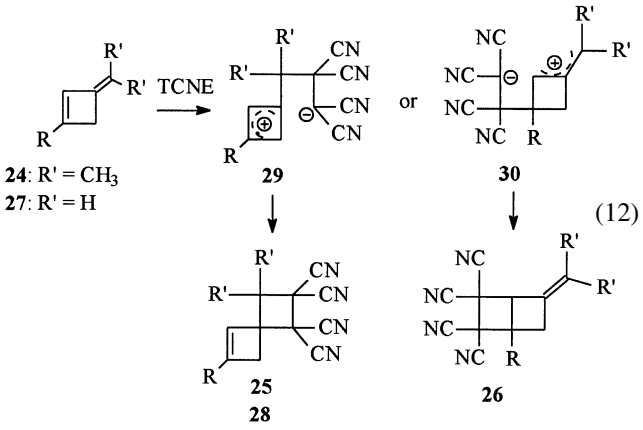
We also explored the possibility that these electrophilic processes are kinetically controlled by the electron richness of the respective double bonds. To this end, we calculated the atomic charges using a 6-31G* basis set and Mulliken population analysis of the olefinic carbons in various alkylidenecyclobutenes (see Scheme 1). The results would seem to indicate that for compounds **24** (in contradistinction to **27**) it is specifically the endocyclic double bond which is the more electron rich. Analysis of the orbital coefficients yields similar results.[1h] We are perforce lead to the conclusion that the controlling factors are not ground-state considerations.

In the case of TCNE additions, the exocyclic regioselectivity is readily rationalized considering that the mechanism for [2+2]cycloadditions of TCNE with olefins are now well established[15] to be non-concerted, ionic processes. It is likely, therefore, that the controlling factor



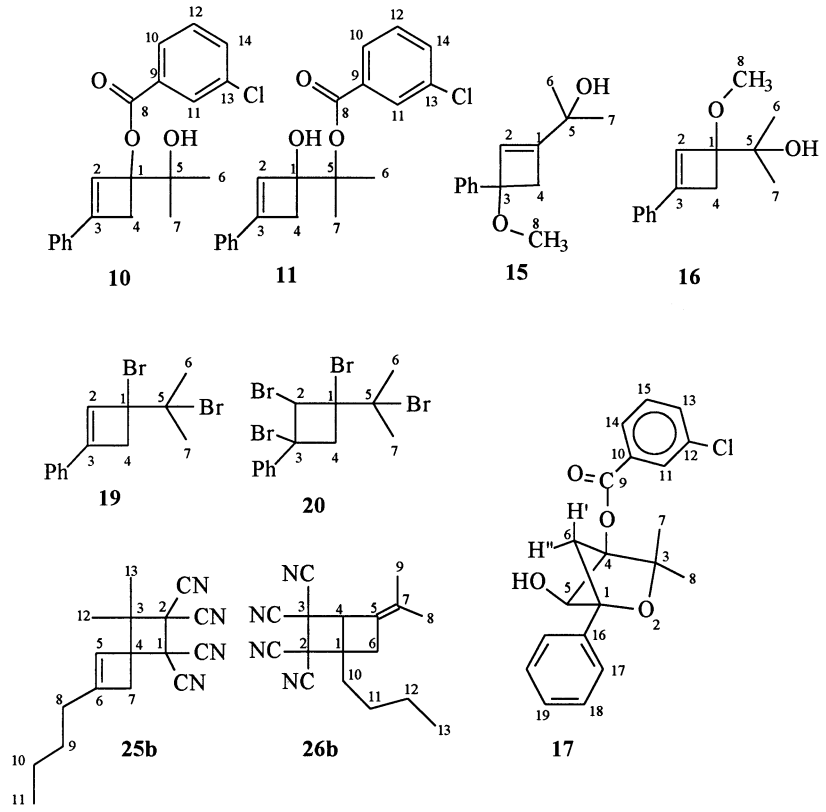
Scheme 1. Calculated electron density on selected alkylidenecyclobutenes.

is the stability of the zwitterionic intermediate. As shown in Eq. (12), addition of TCNE to the exocyclic bond of an alkylidenecyclobutene yields zwitterion **29**, while reaction at the endocyclic olefinic linkage yields **30**. The substitution pattern in the former involves an allylic carbonium ion which in the case of **24a** (**4**) is benzylic at one end and 3° at the other; while in the case of **24b** (**12**) and **27**, it is 3° at both ends. By contrast, **30** is an allylic carbonium ion which is 2° and 3° in the case of **24**, and 2° and 1° in the case of **27**. The stability difference between the various carbocations is well known to be substantial, based on heterolytic C–H dissociation energies in the gas phase. Thus 3°, benzylic and 2° are more stable than 1° carbocations by 45, 39 and 27 kcal/mol, respectively.[16]



(12)

Assuming that the exocyclic regioselectivity of the addition of TCNE to alkylidenecyclobutenes is driven by the stability of the intermediate carbocation, a similar mechanism can also be invoked to explain comparable results for the electrophilic bromination of this conjugated diene system. Indeed, Wilkins and Regulski[17] report that in a similar conjugated system, styrenes, bromination via a more open carbonium ion intervenes. Finally, turning to the reaction of *m*-CPBA with alkylidenecyclobutenes, the literature records that peracid epoxidations of olefins generally proceed via a one-step process which presumably lack carbocation character in the transition state.[18] Nevertheless, a secondary kinetic isotope effect study by Hanzlik and Shearer[19] does indicate that the transition state for the epoxidation of



Scheme 2. Numbering of the carbons used in the NMR spectral data.

arylethylenes is unsymmetrical and polar, in which only one C–O bond of the oxirane product is formed. We suggest that a similar charge development is involved in our 1,3-diene system as well.

3. Conclusion

The addition of TCNE, bromine, peracid and singlet oxygen to alkylidenecyclobutenes **24** shows a strong preference for reaction at the exocyclic double bond. For the first three reagents, we have rationalized this selectivity based on the formation of the more stabilized carbocation. Such polar mechanisms, however, are rare in the $^1O_2$ ene reactions of olefins and dienes, and are observed—if at all—in systems substituted with heteroatoms.[2] We must perforce return to the aforementioned suggestion of Frimer and Weiss[1h] who, as noted in the Introduction, attributed this exocyclic regioselectivity of $^1O_2$ with **1** to the unfavorable alignment and, hence, lack of reactivity of the endocyclic allylic hydrogen H_b (Eq. (1)).

4. Experimental

4.1. General

NMR spectra were obtained on Bruker DMX-600, DPX-300 and AC-200 Fourier transform spectrometers. Assignments were facilitated with DEPT (DPX-300), by correlating proton and carbon chemical shifts through analysis of residual couplings in off-resonance decoupled spectra (AC-200), and via long range hetero COSY and NOESY experiments (DMX-600) as needed. In all cases, TMS served as the internal standard. The carbon numbering of the various compounds used in the nomenclature and spectral assignments is shown in the Scheme 2. EI and CI (CH_4) mass spectra were run on a Finnigan-4021 GC/MS machine (at 70 eV, unless otherwise indicated), except where exact mass data is given. In the latter instance, the EI data reported is based on the high resolution mass spectra (HRMS), performed on a VG-Fison AutoSpecE High Resolution Spectrometer. Preparative thin layer chromatography (PTLC) was carried out on Merck silica gel F_{254} precoated plates and the products were extracted from the silica by stirring overnight in dichloromethane or 10% CH_3OH in $CHCl_3$. For column chromatography separation, Merck silica gel 230–400 mesh was used and the products were extracted from the silica by stirring overnight in a solution of. The retention times given are for the analytical runs. Cyclobutenes **4** (**24a**)[3] and **12** (**24b**)[1h] were prepared as previously described.

4.2. General epoxidation procedure

m-CPBA (1 or 2 equiv.) was added in one portion to a magnetically stirred solution of cyclobutene **4** (**24a**; 1 equiv.) in an appropriate solvent (ca. 25 mL of solvent per mmol of substrate). After 10 min, the solution was transferred to a separatory funnel, extracted consecutively with a 10% bisulfite solution, with a saturated bicarbonate solution, and with a saturated sodium chloride solution, dried over magnesium sulfate, and finally rotary evaporated.

4.2.1. 1-(1-Hydroxy-1-methylethyl)-3-phenyl-2-cyclobuten-1-yl *m*-chlorobenzoate (10); 1-(1-*m*-chlorobenzoyloxy-1-methylethyl)-3-phenyl-2-cyclobuten-1-ol (11). Cyclobutene **4** (**24a**) in dichloromethane was epoxidized with 1 equiv. of *m*-CPBA as described in Section 4.2, yielding ester **10** as a white solid in a 75% yield. The latter can be further purified on reverse phase preparative TLC plate eluting with 30% water in acetonitrile. Silica gel chromatography of the reaction mixture yielded as a white solid which proved to be a 7:3 mixture of **10** and isomeric benzoate **11**. The spectral data for the latter was extracted from that of the mixture. *Compound* **10**: δ_H (300 MHz, $CDCl_3$) 8.03 (s, 1H, H_{11}), 7.98 (d, J=8 Hz, 1H, H_{10}), 7.42 (d, J=8 Hz, 1H, H_{14}), 7.39 (m, 6H, aryl+H_{12}), 6.72 (s, 1H, H_2), 3.29 and 3.03 (ABq, J=13 Hz, 2H, H_4), 1.39 and 1.36 (each s, each 3H, C_6 and C_7 methyls); δ_C (75.5 MHz, $CDCl_3$) δ 166.28 (C_8), 148.64 (C_3), 134.59 (C_9), 133.14 (C_{14}), 132.47 and 132.71 (C_{13} and *ipso*), 129.72, 129.84 and (C_{10}, C_{11} and C_{12}), 128.50 (*meta*), 127.93 (*para*), 126.02 (C_2), 125.61 (*ortho*), 89.14 (C_1), 73.68 (C_5), 38.17 (C_2), 25.71 and 25.91 (C_6 and C_7); *m/z* (DCI, CH_4) 345 (MH^++2, 1.3%), 343 (MH^+, 4%), 325 (MH^+-H_2O, 21%), 284 (MH^+−*i*-PrOH, 44%), 187 (MH^+−chlorobenzoic acid); HRMS (DCI, CH_4): MH^+, found 343.1078. $C_{20}H_{20}O_3Cl$ requires 343.1100. *Compound* **11**: δ_H (300 MHz, $CDCl_3$) 8.10 (s, 1H, H_{11}) 8.09 (d, J=8 Hz, 1H, H_{10}) 7.60 (d, J=8 Hz, 1H, H_{14}) 7.40 (m, 6H, aryl+H_{12}) 6.39 (s,1H, H_4) 3.11 and 2.63 (ABq, J=13 Hz, 2H, H_2) 1.48 and 1.42 (each s, each 3H, C_6 and C_7 methyls); δ_C (75.5 MHz, $CDCl_3$) 164.33 (C_8), 79.51 (C_1), 74.82 (C_5), 40.16 (C_2), 22.29 and 21.45 (C_6 and C_7).

4.2.2. 1-(1-Hydroxy-1-methylethyl)-3-methoxy-3-phenyl-1-cyclobutene (15); 1-(1-hydroxy-1-methylethyl)-1-methoxy-3-phenyl-2-cyclobutene (16). Cyclobutene **4** (280 mg, 1.64 mmol), dissolved in dichloromethane (2 mL) and methanol (40 mL), was epoxidized with 1 equiv. of *m*-CPBA as outlined in the general epoxidation procedure. Work-up yielded a mixture of **15** and **16** (290 mg, 1.33 mmol, 81%) as a white solid in a 2:1 ratio (by NMR). The NMR spectral data for each was readily extracted from that of the mixture. The MS and HRMS data for each component was obtained with the help of GC/MS using a 0.32 mm×30 m DB-23 (J&W Scientific) fused silica capillary column, temperature programmed from 130 to 200°C. *Compound* **15**: δ_H (600 MHz, $CDCl_3$) 7.41 (m, 5H, aromatic ring), 6.36 (s, 1H, H_2), 3.33 (s, 3H, H_8), 2.90 and 2.71 (ABq, J=12.5 Hz, 2H, H_4), 1.40 and 1.39 (each s, each 3H, C_6 and C_7 methyls); δ_C (150.9 MHz, $CDCl_3$) 158.24 (C_1) 141.91 (*ipso*), 128.87 (*para*), 128.37 (*meta*), 125.47 (*ortho*), 126.84 (C_2), 79.79 (C_1), 69.51 (C_5), 52.41 (C_8), 41.67 (C_4), 27.35 and 27.43 (C_6 and C_7); *m/z* (GC/MS, CI, CH_4) 219 (MH^+, 14.57%), 218 (M^+, 5.94%), 201 (MH^+-H_2O, 100%), 187 (MH^+−MeOH, 50.51%), 169 (MH^+−MeOH−H_2O), 160 (M^+−*i*-PrOH); HRMS (CI, CH_4): MH^+, found 219.1400. $C_{14}H_{19}O_2$ requires 219.1385. *Compound* **16**: δ_H (600 MHz, $CDCl_3$) 7.41 (m, 5H, aromatic ring), 6.33 (s, 1H, H_2), 3.39 (s, 3H, H_8), 2.84(s, 1H, H_4), 1.29 (s, 3H, H_6), 1.25 (s, 3H, H_7); δ_C (150.9 MHz, $CDCl_3$) 149.01 (C_3) 133.16 (*ipso*), 128.87 (*para*), 128.48 (*meta*), 125.47 (*ortho*), 127.50 (C_2), 85.36 (C_1), 73.68 (C_5), 51.68 (C_8), 33.73 (C_4), 24.50 and 22.71 (C_6 and C_7); *m/z* (GC/MS, CI, CH_4) 219 (MH^+, 11.46%), 203 (MH^+-H-CH_3 or $M-CH_3$, 24.57%), 201 (MH^+-H_2O, 10.21%), 187 (MH^+−MeOH, 100%), 186 (M^+−MeOH), 171 (M^+−MeOH−CH_3). HRMS (CI, CH_4): MH^+, found 219.1390. $C_{14}H_{19}O_2$ requires 219.1385.

4.2.3. 4-(*m*-Chlorobenzoyloxy)-3,3-dimethyl-1-phenyl-2-oxa[2.1.1]bicyclohexane-5-ol (17). Cyclobutene **4** in CH_2Cl_2 was reacted with 2 equiv. of *m*-CPBA as described in Section 4.2. After 2 days of reaction, workup afforded oxabicyclo **17** in 54% yield as a white solid. The product can be further purified on a preparative TLC plate eluting with 10% 2-methyl-2-butanol in hexane. *Compound* **17**: δ_H (600 MHz, $CDCl_3$) 8.03 (s, 1H, H_{11}), 7.95 (d, J=8 Hz, 1H, H_{14}), 7.59 (d, J=8 Hz, 1H, H_{13}), 7.40 (m, 6H, aryl+H_{15}), 5.03 (d, J=8 Hz, 1H, H_5), 3.50 (d, J=8 Hz, 1H, $H_{6''}$), 2.87 (t, J=8 Hz, 1H, $H_{6'}$) 1.51 and 1.49 (each s, each 3H, C_7 and C_8 methyls); δ_C (150.9 MHz, $CDCl_3$) δ 165.53 (C_9), 134.77 (C_{10}), 134.38 (C_{16}), 133.80 (C_{13}), 131.05 (C_{12}), 130.01 (C_{11} and C_{15}), 128.30 (C_{18} and C_{19}), 128.14 (C_{14}), 126.67 (C_{17}), 84.31 (C_3), 83.27 (C_5), 82.74 (C_1), 77.53 (C_4), 41.12 (C_6), 24.70 and 23.54 (C_7 and C_8); *m/z* (GC/MS, CI, CH_4) 361 (MH^++2, 3.04%), 359 (MH^+, 9.14%), 203 (MH^+−*m*-chlorobenzoic acid, 100%), 203 (MH^+−chlorobenzoic acid−H_2O, 50.51%); HRMS (CI, CH_4): MH^+, found 359.1090. $C_{14}H_{19}O_2$ requires 359.1050.

4.2.4. 1-Bromo-1-(1-bromo-1-methylethyl)-3-phenyl-2-cyclobutene (19); 5,5-dimethyl-3-phenyl-2-cyclopenten-1-one (22). Bromine (0.54 mmol) in CH_2Cl_2 (1.15 mL of 0.468 M bromine solution) was added dropwise to a stirred solution of cyclobutene **4** (91.7 mg, 0.53 mmol) in CH_2Cl_2 (20 mL). The solvent was removed in vacuo, and the residue recrystallized from hexane, yielding pure dibromocyclobutene **19** as a white solid (100 mg, 3.06 mmol, 58% yield). Attempts to purify **19** via column chromatography yielded the known cyclopentenone **22**.[9] *Compound* **19**: δ_H (300 MHz, $CDCl_3$) 7.41–7.37 (m, 5H, aryl), 6.52 (s, 1H, C_2), 3.55 and 3.35 (Abq, J=14 Hz, 2H, C_4), 2.02 and 2.01 (each s, each 3H, C_6 and C_7); δ_C (75.5 MHz, $CDCl_3$) 145.87 (C_3), 132.35 (*ipso*), 131.107 (C_2), 129.42 (*para*), 128.56 (*meta*), 125.62 (*ortho*), 73.47 (C_1), 69.45 (C_5), 45.65 (C_4), 31.45 and 31.35 (C_6 and C_7); *m/z* (EI) 332 (M+4, 3.42%), 330 (M+2, 5.04%), 328 (M^+, 3.52%), 251 ($C_{13}H_{14}Br$, 23.76%), 170 ($C_{13}H_{14}$, 100%); HRMS (EI): M^+, found 327.9488. $C_{13}H_{14}Br_2$ (M^+) requires 327.9462.

4.2.5. 1,2,3-Tribromo-1-(1-bromo-1-methylethane)-3-phenyl-2-cyclobutene (20). Bromine (0.66 mmol) in CH_2Cl_2 (1.4 mL of 0.468 M bromine solution) was added dropwise to a stirred solution of cyclobutene **4** (54.4 mg, 0.32 mmol) in CH_2Cl_2 (20 mL). The solvent was removed in vacuo. Recrystallization from hexane gave tetrabromocyclobutene **20** (80 mg, 0.165 mmol, 50% yield) as a white solid. *Compound* **20**: δ_H (300 MHz, $CDCl_3$) 7.712–7.685 (m, 2H, *ortho*), 7.414–7.371 (m, 3H, *meta* and *para*) 6.16 (d, J=1 Hz, 1H, H_2), 4.084 (dd, J=5, 1 Hz, 2H, H_4), 1.965 and 1.941 (each s, each 3H, C_6 and C_7 methyls); δ_C (75.5 MHz, $CDCl_3$) 139.00 (*ipso*), 129.00 (*ortho*), 128.65 (*para*), 127.39 (*meta*), 73.57 and 72.38 (C_3 and C_1), 62.97 (C_2), 57.47 (C_5), 49.36 (C_4), 31.54 and 30.31 (C_6 and C_7); *m/z* (EI): 494 (M+8, 0.55%), 492 (M+6, 1.44%), 490 (M+4, 1.90%), 488 (M+2, 0.84%), 486 (M^+, 0.22%), 411 ($C_{13}H_{14}Br_3$, 95.29%), 329 ($C_{13}H_{13}Br_2$, 56.28%), 248

($C_{13}H_{13}Br$, 63.36%), 169 ($C_{13}H_{13}$, 100%), 155 ($M^+-Br_2-HBr-CH_2Br$, 51.10%); HRMS (EI): M^++6, found 491.7795. $C_{13}H_{14}Br_4$ requires 491.7769; HRMS (EI): M^+-H-Br_4, found 169.1010. $C_{13}H_{13}$ requires 169.1017.

4.2.6. 3,3-Dimethyl-6-butyl-spiro[3.3]-hept-5-ene-1,1,2,2-tetracarbonitrile (25b); 1-*n*-butyl-5-isopropylidenebicyclo[2.2.0]hexa-2,2,3,3-tetracarbonitrile (26b). A flame dried two necked flask equipped with a nitrogen inlet adapter and glass stopper, was charged with a magnetically stirred suspension of 1-isopropylidene-3-butyl-2-cyclobutene **12**[3] (**24b**; 0.20 g, 1.33 mmol) in 30 ml dichloromethane. Tetracyanoethylene **5** (0.242 g, 1.89 mmol) was added in one portion yielding a blue solution, which turned green after several minutes and yellow overnight. The solvent was removed and the blue-gray residue (297 mg) was chromatographed over alumina eluting with 20% ethyl acetate in petroleum ether yielding a pale orange viscous liquid (121 mg, 0.435 mmol, 33% yield, R_f=0.603). Spectral analysis revealed it to be a 4:1 mixture of tetranitriles **25b** and **26b**. *Mixture of compounds* **25b** *and* **26b**: ν_{max} (KBr) 2969, 2933, 2874, 2248, 2196, 1715, 1635, 1466, 1396, 1379, 1269, 1149, 855 cm^{-1}; *m/z* (CI, CH_4) 279 (MH^+, 77.05%), 173 ($MH^+-C_6H_6N_2$, 62.63%), 151 ($MH^+-C_6N_4$, 28.21%), 150 ($M^+-C_6N_4$, 100%); HRMS (CI, CH_4): MH^+, found 279.1609. $C_{17}H_{18}N_4$ requires 279.1610. *Compound* **25b**: δ_H (600 MHz, $CDCl_3$) 5.97 (1H, t, *J*=1.5 Hz, H_5), 2.81 and 2.78 (2H, Abq of t, *J*=14.5, 1 Hz, H_7), 2.17 (2H, bt, *J*=7.5 Hz, H_8), 1.61 (3H, s, H_{12}), 1.54 (3H, s, H_{13}), 1.47 (2H, quint, *J*=7.5 Hz, H_9), 1.36 (2H, sex, *J*=7.5 Hz, H_{10}), 0.93 (3H, t, *J*=7.5 Hz, H_{11}); δ_C (150.1 MHz, $CDCl_3$) 159.22 (C_6), 124.11 (C_5), 110.45 (CN), 110.04 (CN), 109.43 (CN), 109.38 (CN), 57.12 (C_4), 50.32 (C_3), 42.78 (C_2), 41.43 (C_1), 37.30 (C_7), 30.33 (C_8), 27.77 (C_9), 24.00 and 23.92 (C_{12} and C_{13}), 22.13 (C_{10}), 13.62 (C_{11}); *Compound* **26b**: δ_H (300 MHz, $CDCl_3$) 3.86 (s, 1H, H_4), 3.35 and 3.05 (2H, Abq, *J*=18 Hz, H_6), 2.05 (2H, ddd, *J*=14, 11, 5.5 Hz, $H_{10'}$) 1.85 (ddd, *J*=14, 11, 6 Hz, $H_{10''}$), 1.73 and 1.71 (each s, each 3H, C_8 and C_9 methyls), 1.43 (2H, m, H_{12}), 1.30 (2H, m, H_{11}), 0.96 (3H, t, *J*=7.5 Hz, H_{13}); δ_C (150.1 MHz, $CDCl_3$) 139.42 (C_5), 117.97 (C_7), 110.82 (CN), 109.61 (CN), 109.43 (CN), 109.01 (CN), 57.62 (C_4), 48.39 (C_1), 45.10 and 44.35 (C_2 and C_3), 38.55 (C_6), 33.54 (C_{10}), 25.00 (C_{11}), 22.30 (C_{12}), 19.58 and 18.98 (C_8 and C_9), 13.57 (C_{13}).

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