Keywords: angucyclinones · antibiotics · asymmetric synthesis · cycloadditions · quinones

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[12] The relative configuration was established by comparison with a similar intermediate prepared by Sulikowski [5d] in the total synthesis of SF 2315A.
[13] When the cycloaddition was carried out in water the reaction was faster (completed in 12 h at room temperature) but with a lower enantiomeric excess (20%).
[14] The enantiomeric excesses were evaluated by ^{1}H NMR spectroscopy using chiral lanthanide shift reagents: [Eu(tfc)$_3$] for **3b** and **5d**, and [Yb(hfc)$_3$] for **7b** and **7d**. The required racemic compounds were obtained from racemic quinone **1** [8].
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[17] These results contradict those reported by Sulikowski et al. [4g], who described no reaction for a similar system with DBU in benzene at 0 °C.

Evidence for a Stepwise Addition of Carbenes to Strained Double Bonds: Reactions of Dihalocarbenes with Cyclopropenes**

Jürgen Weber and Udo H. Brinker*

Dedicated to Professor William von Eggers Doering on the occasion of his 80th birthday

The most thoroughly investigated pathway of carbene stabilization is addition to carbon–carbon double bonds. Early studies by Skell and Woodworth[1] consider the singlet carbene addition a one-step process in which two new bonds are formed simultaneously. Even though the addition of singlet carbenes is concerted, it cannot be synchronous according to orbital symmetry considerations.[2] Jones et al.[3] suggested that the concept of nucleophilicity and electrophilicity, as applied to intermolecular additions of carbenes to alkenes, can be interpreted as the different contributions of the highest occupied and lowest unoccupied molecular orbitals (HOMOs and LUMOs). For instance, during the electrophilic attack of a dihalocarbene, charge is transferred from the olefin's HOMO to the empty p orbital of the carbene (LUMO). Calculations of activated complexes[4] for addition of dihalocarbenes to simple olefins support this direction of charge transfer. These calculations also show a shorter distance from the carbene carbon to one of the carbon atoms of the double bond.

Although addition of photochemically generated monohalocarbenes to 1,2-dimethylcyclobutene was postulated to proceed via zwitterions,[5] no conclusive evidence of their intermediacy[6] was provided.[7] We present here evidence that charge transfer during reactions of dihalocarbenes with differently substituted cyclopropenes leads to polarization of the activated complex or even to an intermediate dipolar species with complete charge separation.

Only few dihalocarbene reactions with cyclopropenes are known.[8] With the exception of perfluoro-1,3-dimethylbicyclo[1.1.0]butane,[9] geminal dihalobicyclobutanes, the addition products of dihalocarbenes, have never been isolated or unambiguously identified by spectroscopy. Instead cyclobutenes, probably formed by cationic cyclopropylallyl (CCA) rearrangements,[10] were found as the only products.

We initially reported that, for the first time, 2,3-diaryl-1,1-dihalo-1,3-butadienes were formed along with 1,3-diaryl-2,3-dihalocyclo-1-butenes by the reactions of dihalocarbenes (:CF_2, :CCl_2, :CBr_2, :CFCl, :CFBr) with 1,2-diarylcyclopropenes (Scheme 1).[11] We now present evidence for a step-wise addition of dihalocarbenes to strained double bonds of cyclopropenes. For the mechanistic studies of the formation of butadienes and cyclobutenes, three different aryl substituents were utilized. In the reactions of 1,2-diphenylcyclopropene (**1**) with dichlorocarbene, the ratios of the products, that is, of butadienes **2**[12] to cyclobutenes **5**,[12] were nearly independent of the method of carbene generation (Table 1).[13] This indicates that the same

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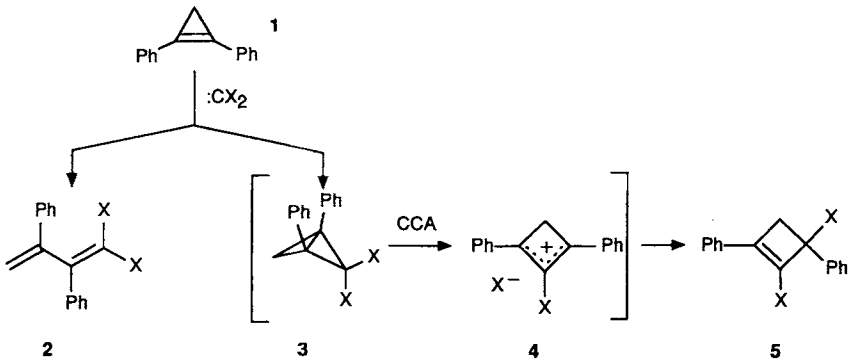


Scheme 1. Dihalocarbene addition to cyclopropene **1**: formation of 1,3-butadiene **2** and cyclobutene **5**.

Table 1. Ratios of cyclobutene **5a** to butadiene **2a** for reactions of cyclopropene **1** with the dichlorocarbene from different carbene sources.

Method	*T*	**5a**:**2a**	Yield [%] [c]
Doering–Hoffmann [13a]	−45 °C → 0 °C	79:21	20
ultrasound [a] [13b]	20 °C → 40 °C	87:13	70
Seyferth [b] [13c]	80 °C	80:20	79

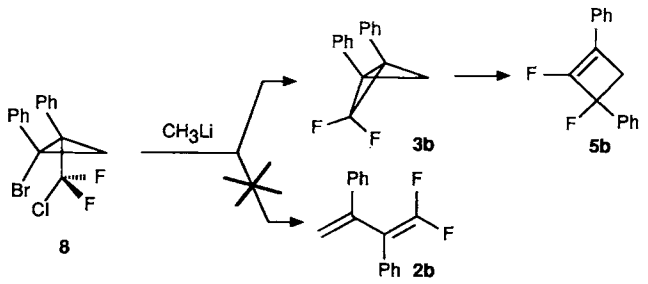
[a] Catalytic phase transfer method under ultrasound conditions. [b] $PhHgCCl_2Br$. [c] 2-Chloro-1,3-diphenylcyclobut-1-en-3-ol, the hydrolysis product from **5a**, was isolated.

reactive species, that is, a dichlorocarbene(oid), was involved in the formation of both products.

Cyclobutenes **5** may be derived from intermediate bicyclobutanes **3**. Cleavage of the central bond and loss of one halide in **3** leads to the stabilized homoaromatic cyclobutenyl cation **4**. Trapping of **4** by the halide gives **5** (Figure 1). In contrast, three different pathways can be suggested for the formation of butadienes **2** (Scheme 2).

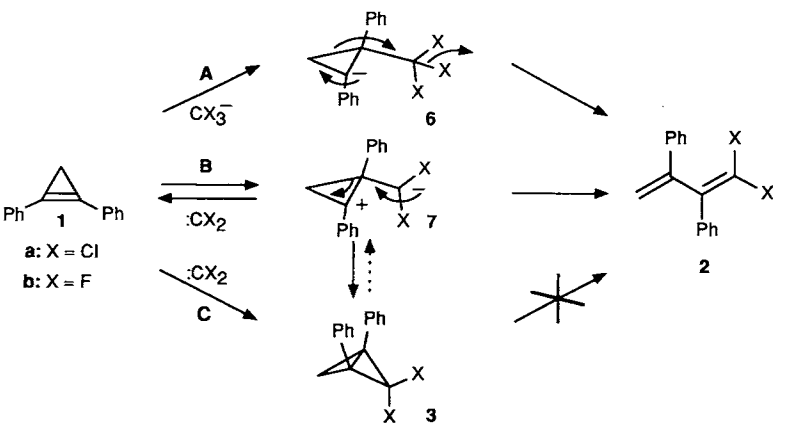
Butadienes **2** were formed when different conditions are applied for carbene generation, even at temperatures as low as −45 °C. This renders pathway C unlikely, because various substituted bicyclobutanes,[14] including several 1,3-diphenylbicyclobutanes,[15] are thermally stable at room temperature. Furthermore, attempts at an independent preparation of bicyclobutane **3b** exclude pathway C. *cis*-1-Bromo-2-chlorodifluoromethyl-1,2-diphenylcyclopropane (**8**)[12, 16–18] was chosen as the precursor to **3b**. When **8** was allowed to react with methyllithium, only difluorocyclobutene **5b**, the formal CCA-rearrangement product of bicyclobutane **3b**, was found (Scheme 3). No evidence of difluorobutadiene **2b** was present. The only plausible way to explain the formation of **5b** is through **3b**. In contrast, the reaction of difluorocarbene with cyclopropene **1** affords only **2b** and no cyclobutene **5b**. That means, if **3b** were an intermediate, the formation of **5b** would also be expected.

Intermediates **6** and **7** (Scheme 2) may result from reactions of **1** with a trihalomethyl anion or a dihalocarbene (pathways A and B), respectively. However, the product ratios of the isomeric butadienes **13a** to **13b**[12] and **14a** to **14b**[12] obtained from dichlorocarbene additions to the asymmetrically substituted cyclopropenes **9**[12] and **10**[12, 19], respectively, bearing an electron-withdrawing or electron-donating substituent at the *para* position of one of the phenylsubstituents support an electrophilic attack of the carbene (Scheme 2, pathway B). In contrast, butadienes **13b** and **14a**, which were expected to be the major isomers by nucleophilic attack of the trichloromethyl anion (pathway A), due to better stabilization of the negative charge, were found in lower amounts. Furthermore, direct generation of dichlorocarbene from phenyl(bromodichloromethyl)mercury without involvement of a trichloromethyl anion gave a butadiene to cyclobutene ratio of 20:80 when allowed to react with **1**. This ratio is nearly identical, within experimental error, to the ratios obtained by other methods of carbene generation (Table 1). Therefore, pathway A is not operative.

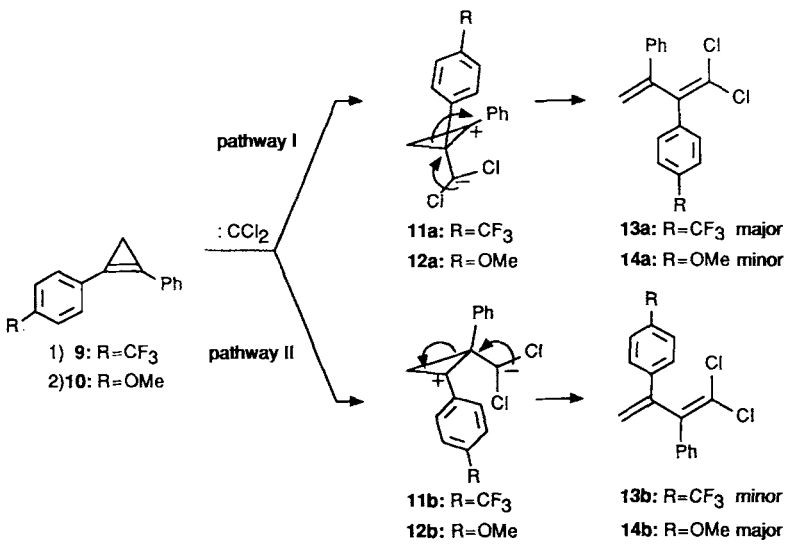


Scheme 3. Formation of cyclobutene **5b** by the ring-closing reaction of **8**.

Electrophilic attack of dichlorocarbene at the double bonds of **9** and **10** mainly gave **13a** and **14b**, which are derived from **11a** and **12b**, the intermediates that offer better charge stabilization (Scheme 4). Pathway I is more favorable for cyclopropene **9**, which has an electron-withdrawing trifluoromethyl substituent, due to better stabilization of the positive charge by the unsubstituted phenyl ring. On the other hand, for the reaction of **10** pathway II provides the better stabilization of the positive charge in **12b** through the electron-donating methoxy substituent. Comparison of the product ratios for both the butadienes substituted with *p*-methoxyphenyl or *p*-trifluoromethylphenyl shows a complete reversal of the ratios. This supports the proposed mechanism involving dipolar intermediates such as **7** (Scheme 2), **11**, and **12** (Scheme 4).[20, 21] For simplicity, however, fully developed charges (zwitterions) have been depicted to explain the behavior of the reactants, even though the extent of polarization has not yet been established. Furthermore,



Scheme 2. Three possible reaction pathways to dihalobutadienes **2**.



Scheme 4. Electrophilic attack of dihalocarbenes on cyclopropenes **9** and **10** followed by rearrangement. Ratios of the butadienes: a) Doering–Hoffmann method: **13a**:**13b** = 74:26 and **14a**:**14b** = 29:71; b) catalytic phase transfer method under ultrasound conditions: **13a**:**13b** = 69:31 and **14a**:**14b** = 30:70.

the reaction of **1** with dichlorocarbene gave an increased ratio of up to 50:50 of butadiene **2** to four-membered ring compounds[22] when performed in the more polar solvent acetonitrile. This also provides strong evidence for the involvement of a polar intermediate similar to **7** (Figure 2) in the addition of dichlorocarbene to the strained double bond of **1**.

The data from this study indicate that the butadienes in the reactions of cyclopropenes **1**, **9**, and **10** with dichlorocarbene are derived from zwitterionic species, whereas the cyclobutenes result from a CCA rearrangement of the intermediate geminal dihalobicyclobutanes.

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[12] Selected spectroscopic data: **2a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.51 (m, 4H, H-Ph), 7.25–7.37 (m, 6H, H-Ph), 5.87 (s, 1H, H-C4), 5.43 (s, 1H, H-C4); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 146.9 (s, C3), 140.2 (s, C2), 137.5 (s), 137.4 (s), 128.8 (d), 128.5 (d), 128.12 (d), 128.09 (d), 126.2 (d), 120.6 (s, C1), 117.3 (t, C4); MS (70 eV): *m/z* (%) = 279, 277, 275 ([(*M*+1)$^+$], 0.5, 2, 5), 278, 276, 274 ([*M*$^+$], 2, 14, 21), 242, 240 ([(*M*+1)$^+$ − Cl], 3, 11), 241, 239 ([*M*$^+$ − Cl], 15, 49), 240, 238([*M*$^+$ − HCl], 11, 9), 205 ([(*M*+1)$^+$ − 2Cl], 15), 204 ([*M*$^+$ − 2Cl], 52), 203 ([*M*$^+$ − Cl − HCl], 100), 202 ([*M*$^+$ − 2HCl], 55), 178 (12), 105 (16), 101 (41), 91 ($C_7H_7^+$, 18), 77 (Ph^+, 28), 51 (21); elemental analysis calcd for $C_{16}H_{12}Cl_2$ (275.18): C 69.84, H 4.40; found: C 69.96, H 4.40.

2b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.42 (m, 4H, H-Ph), 7.17–7.32 (m, 6H, H-Ph), 5.87 (t, 1H, ^5J(H,F) = 1 Hz, H-C4), 5.40("s", 1H, ^5J(H,F) ≤ 0.5 Hz, H-C4); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 154.3 (t, ^1J(C,F) = −293 Hz, C1), 140.9 (t, ^2J(C,F) = 10 Hz, C2), 138.7 (s, C3), 133.0 ("s", fine ^3J(C,F) coupling pattern, C_{Ph} at C2), 131.6 (s, C_{Ph} at C3), 128.6 (d), 128.3 (d), 127.9 (d), 127.3 (d), 126.4 (d), 118.9 (t, C4); MS (70 eV): *m/z* (%) = 243 ([*M*$^+$ + 1], 16), 242 ([*M*]$^+$, 16, 100), 241 ([*M*$^+$ − H], 33), 223 ([*M*$^+$ − F], 6), 222 ([*M*$^+$ − HF], 34), 221 ([*M*$^+$ − HF − H], 36), 220 (21), 192 (9), 178 (30), 165 ([*M*$^+$ − Ph], 19), 164 ([*M*$^+$ − PhH], 18), 127 (64), 115 (15), 112 (10), 95 (13), 77 (Ph^+, 21), 51 (16); elemental analysis calcd for $C_{16}H_{12}F_2$ (242.27): C 79.32, H 4.99; found: C 79.17, H 4.84.

5a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.75 (m, 4H, H-Ph), 7.36–7.50 (m, 6H, H-Ph), 3.58 (d, 1H, ^2J(H,H) = −11.5 Hz, H-C4), 3.44 (d, 1H, ^2J(H,H) = −11.5 Hz, H-C4); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 140.1 (s), 139.5 (s), 131.0 (s, Cl), 129.7 (d), 128.6 (d), 128.4 (d), 128.3 (d), 126.9 (d), 126.1 (d), 123.4 (s, C2), 71.8 (s, C3), 47.5 (t, C4); MS (70 eV): *m/z* (%) = 278, 276, 274 ([*M*$^+$], <0.5, 2, 3), 242, 240 ([(*M*+1)$^+$ − Cl], 6, 20), 241, 239 ([*M*$^+$ − Cl], 33, 100), 240, 238 ([*M*$^+$ − HCl], 20, 6), 205 ([(*M*+1)$^+$ − 2Cl], 15), 204 ([*M*$^+$ − 2Cl], 48), 203 ([*M*$^+$ − Cl − HCl], 84), 202 ([*M*$^+$ − 2HCl], 57), 105 (19), 101 (34), 89 (10), 77 (Ph^+, 28), 65 (13), 51 (18), 39 (13), 36 (29); elemental analysis calcd for $C_{16}H_{12}Cl_2$ (275.18): C 69.84, H 4.40; found: C 69.90, H 4.46.

5b: ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.25–7.60 (m, 10H, H-Ph), 2.96 (ddd, 1H, ^2J(H,H) = −9.8 Hz, ^4J(H,F) = 11.2 Hz, ^3J(H,F) = 6.4 Hz, H-C4), 2.80 (ddd, 1H, ^2J(H,H) = −9.8 Hz, ^4J(H,F) = 15.6 Hz, ^3J(H,F) = 3.8 Hz, H-C4); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 144.8 (dd, ^1J(C,F) = −350 Hz, ^2J(C,F) = 20 Hz, C2), 121.3 (dd, ^2J(C,F) = 17 Hz, ^3J(C,F) = 8 Hz, Cl), 97.7 (dd, ^1J(C,F) = −212 Hz, ^2J(C,F) = 24 Hz, C3), 37.6 (t"t", ^3J(C,F), ^4J(C,F) = 22 Hz, J(C,H) = 145 Hz, C4); ^{19}F NMR (282.4 MHz, $CDCl_3$ and $CFCl_3$): δ = −104.2 (ddd, 1F, ^3J(F,F) = 6.1 Hz, ^4J(H,F) = 15.6 Hz, ^3J(H,F) = 11.2 Hz, F-C2), −150.6 ("dd", 1F, ^3J(F,F) = 6.1 Hz, F-C3; from a ^{19}F–^{1}H decoupling experiment).

8: ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.27–7.24 (m, 4H), 7.13–7.00 (m, 6H), 2.58 (dd, 1H, ^2J(H,H) = −7.7 Hz, ^4J(H,F) = 3.4 Hz), 2.39 (d, 1H, ^2J(H,H) = −7.7 Hz); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 139.3 (s), 132.8 (s), 131.1 (br. d), 128.7 (d), 128.2 (t, ^1J(C,F) = −295 Hz), 128.1 (d), 128.0 (d), 127.9 (d), 127.8 (d), 45.3 (t, ^2J(C,F) = 25 Hz), 38.4 (s), 23.5 (t, ^1J(C,H) = 164 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$ and $CFCl_3$): δ = −51.1 (d, 1F, ^2J(F,F) = −160.4 Hz, ^4J(H,F) = 2.9 Hz), −44.3 (d, 1F, ^2J(F,F) = 160.0 Hz); MS (70 eV): *m/z* (%) = 358, 356 ([*M*$^+$], 3, 2), 279, 277 ([*M*$^+$ − Br], 22, 36), 242 ([*M*$^+$ − Br − Cl], 16), 241 ([*M*$^+$ − HBr − Cl), 79), 222 ([*M*$^+$ − HBr − Cl − F], 26), 221 ([*M*$^+$ − HBr − HCl − F], 71), 220 (44), 202, 200 ([*M*$^+$ − Br − Ph], 9, 11), 201, 199 ([*M*$^+$ − HBr − Ph], 37, 100), 192 (36), 191 (41), 189 (20), 165 (22), 164 (76), 127 (31), 115 (10), 111 (10), 110 (22), 103 (14), 95 (12), 89 (16), 77 (23), 63 (13), 51 (15); elemental analysis calcd for $C_{16}H_{12}BrClF_2$ (357.62): C 53.74, H 3.38; found: C 53.80, H 3.45.

9: ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.67–7.80 (m, 6H), 7.51–7.45 (m, 2H), 7.41–7.35 (m, 1H), 1.57 (s, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 133.6 (s), 130.0 (d), 129.8 (s), 129.6 (d), 129.0 (d), 128.8 (d), 125.6 (d"d", ^3J(C,F) = 5 Hz), 115.2 (s), 110.3 (s), 6.6 (t), the signal for the trifluoromethyl carbon atom was not found; MS (70 eV): *m/z*(%) = 261 ([*M*+1$^+$], 17), 260 ([*M*$^+$], 100), 259 ([*M*$^+$ − H], 43), 192 (16), 191 ([*M*$^+$ − CF_3], 91), 190 (22), 189 (48), 173 (18), 165 (14), 115 (14), 95 (10).

10: ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.62–7.70(m + "d", 4H, 2H on (*p*-methoxy)phenyl with J = 8.8 Hz and 2H on phenyl), 7.40–7.47 (m, 2H, H-Ph), 7.25–7.33 (m, 1H, H-Ph), 6.96–7.02 ("d", 2H, J = 8.8 Hz, other 2H on (*p*-methoxy)phenyl), 3.83 (s, 3H, H_3C-O), 1.50 (s, 2H, H_2-C3); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 159.8 (s, C_{Ar}-O), 131.2 (d), 130.5 (s), 129.3 (d), 128.6 (d), 127.7 (d), 123.1 (s), 114.2 (d), 111.4 (s, C1/C2), 108.7 (s, C2/C1), 55.3 (q, CH_3O), 6.3 (t, ^1J(C,H) = 165.7 Hz, C3); MS (70 eV): *m/z* (%) = 223 ([(*M*+1)$^+$], 19), 222 ([*M*$^+$], 100), 221 ([*M*$^+$ − H]18), 207 ([*M*$^+$ − Me], 47), 191 ([*M*$^+$ − OMe], 15), 179 (29), 178 ([*M*$^+$ − HOMe − CH_2] 79), 176 (14), 177 (13), 152 (18), 89 (13), 76 (13), 63 (11), 40 (46); HR-MS calcd for $C_{16}H_{14}O$: 222.1045; found: 222.1025.

13a (major) and **13b** (minor) as a mixture of isomers: ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.15–7.70 (m, 18H, H-Ar), 5.89 (s, 1H, *cis* H-C4 of **13b**), 5.50 (s, 1H, *trans* H-C4 of **13b**), 5.84 (s, 1H, *cis* H-C4 of **13a**), 5.40 (s, 1H, *trans* H-C4 of **13a**); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 119.6 (t, C4 of **13b**), 117.9 (t, C4 of **13a**).

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14a (minor) and **14b** (major) as a mixture of isomers: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.20-7.60$ (m, H-Ar), 6.80–7.00 (m, H-Ar, not assigned), 5.80 (s, 1H, H-C4 of **14a**), 5.35 (s, 1H, H-C4 of **14a**), 3.73 (s, 3H, H_3C-O); 5.70 (s, 1H, H-C4 of **14b**), 5.26 (s, 1H, H-C4 of **14b**), 3.75 (s, 3H, H_3C-O); ^{13}C NMR (90.6 MHz, $CDCl_3$): (signals of aromatic carbon atoms not assigned) **14a**: $\delta = 117.0$ (t, C4), 113.9 (d, C3′/C5′ of Ar), 55.2 (q, CH_3); **14b**: $\delta = 115.2$ (t, C4), 113.5 (d, C3′/C5′ of Ar), 55.2 (q, CH_3); MS (70 eV): m/z (%) = 306, 304 ([M^+], 16, 27), 271, 269 ([$M^+ - Cl$], 19, 52), 270 (13), 258 (20), 234 ([$M^+ - 2Cl$], 27), 233 (21), 224 (16), 223 (100), 219 (12), 208 (15), 203 (12), 192 (15), 190 (10), 189 (17), 178 (11), 145 (19), 122 (12), 116 (10), 115 (47), 91 (11); HR-MS calcd for $C_{17}H_{14}Cl_2O$: 304.0422; found: 304.0429. In addition, **14a** was independently prepared.

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[16] We thank Professor R. Boese, Universität Essen, Germany, for the X-ray structure determinination of **8**. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-179-179. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: int. code +(1223)336-033; e-mail: deposit@chemcrys.cam.ac.uk).

[17] Tetrahalocyclopropane **8** was synthesized from commercially available chlorodifluoroacetic acid: Treatment with sodium hydroxide gave the corresponding sodium salt, which reacted with phenylmagnesium bromide to afford chlorodifluoromethyl ketone [18] in 87% yield. Wittig reaction with methylenetriphenylphosphonium bromide produced α-(chlorodifluoromethyl)styrene (yield 71%). Addition of bromophenylcarbene, generated from treatment of benzal bromide with potassium *tert*-butoxide, afforded **8** and its *trans* isomer in very low yields. The isomers were purified in multiple steps and finally separated by HPLC.

[18] T. Ando, F. Namigata, M. Kataoka, K. Yachida, W. Funasaka, *Bull. Chem. Soc.* **1967**, *40*, 1275.

[19] The ratio of aryl-substituted butadienes to cyclobutenes was also found to be approximately 20:80, which is in good agreement with the previously determined ratio of **2** to **5**.

[20] Dipolar resonance structures have been proposed as intermediates in dihalocarbene additions to alkenes: P. S. Skell, A. Y. Garner, *J. Am. Chem. Soc.* **1956**, *78*, 5430; W. von E. Doering, W. A. Henderson, Jr., *J. Am. Chem. Soc.* **1958**, *80*, 5274.

[21] The strain energy probably has a major influence on the reaction of a dihalocarbene with cyclopropene **1**. Due to release of olefinic strain, an intermediate zwitterion should be lower in energy than **1**. Stabilization of the transition state can be achieved through ring opening and complete release of strain in the cyclopropane ring with concomitant formation of conjugated double bonds. On the other hand, ring closure of **7** to a geminal dichlorobicyclobutane leads to an initial increase in strain energy. However, once the bicyclic compound **3** has been formed, the CCA rearrangement inevitably proceeds, thereby releasing substantial amounts of strain energy.

[22] In addition to cyclobutene **5**, the coupling products *meso*- and (*R*,*S*)-2,2′-dichloro-1,1′,3,3′-tetraphenylbi[cyclobut-1-en-3-yl] were isolated.

Magnetization Studies of the Reduced Active Form of the Catalase from *Thermus thermophilus*

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Manganese-containing catalases[1, 2] are found in various bacteria such as *Thermus thermophilus* and *Lactobacillus plantarum*. Structural[3] and spectroscopic[4–6] evidence indicate that the enzyme from *T. thermophilus* possesses a dimanganese active site, which exists in four different redox forms. Mechanistic studies[7] have concluded that during catalysis the dimanganese center shuttles between a $Mn^{II}Mn^{II}$ and a $Mn^{III}Mn^{III}$ form. In vitro, mixed-valent forms $Mn^{II}Mn^{III}$ and $Mn^{III}Mn^{IV}$ can be generated. The latter two forms and the phosphate complex of the reduced enzyme exhibit characteristic EPR spectra, which have been extensively studied.[4–6] In particular, the temperature dependence of the EPR spectra has been used to estimate the magnetic exchange interaction J ($\mathcal{H} = -2J\boldsymbol{S}_1\boldsymbol{S}_2$) between the two manganese ions. This J value depends on the nature of the groups bridging these ions and therefore structural information may be derived from its estimation. A comparison of these values with those of structurally characterized model compounds supports the presence of a bis(μ-oxo)$Mn^{III}Mn^{IV}$ and a (μ-hydroxo)$Mn^{II}Mn^{III}$ unit in the two mixed-valent states.[5] Less conclusive results were obtained for the reduced catalase. For the phosphate derivative of the *T. thermophilus* enzyme, Khangulov et al. obtained a value of $J = -5.6\,cm^{-1}$ for the exchange interaction.[6] This value is intermediate between those observed for (μ-aqua)bis(μ-carboxylato)$Mn^{II}Mn^{II}$ centers ($-2.5\,cm^{-1} < J < -1.5\,cm^{-1}$)[8, 9] and for (μ-hydroxo)bis(μ-carboxylato)$Mn^{II}Mn^{II}$ centers ($J \approx -9\,cm^{-1}$).[10] No structural information is available for the unliganded $Mn^{II}Mn^{II}$ active form which does not have an EPR spectrum sufficiently resolved to investigate the temperature dependence.

In order to obtain structural information on the unliganded catalytically active site and on the phosphate complex of $Mn^{II}Mn^{II}$ catalase from *T. thermophilus*, we studied the field and temperature dependence of the saturation magnetization.[11] This technique is particularly suitable for evaluating the exchange interaction in dinuclear centers[12] and allowed us to get the first structural information on the active reduced state. From magnetostructural correlations we propose a (μ-aqua)(μ-carboxylato) bridging pattern in the unliganded $Mn^{II}Mn^{II}$ form of the enzyme. The same bridges are present in the phosphate derivative and the addition of a bridging phosphate is most consistent with all magnetic and biochemical observations—a fact that may have important mechanistic implications.

Figure 1 presents the magnetic properties of the reduced catalase in D_2O (curve a) and in a deuterated phosphate buffer

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