Regioselectivity of the Base-Induced Ring Cleavage of 1-Oxygenated Derivatives of Cyclobutabenzene

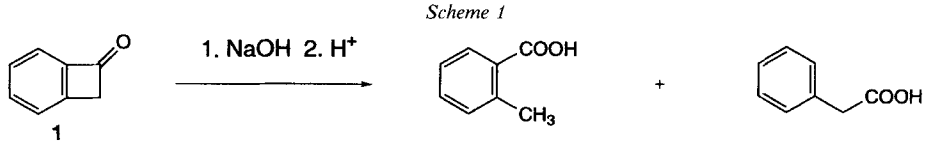
by **Abha Gokhale** and **Peter Schiess***

Institut für Organische Chemie der Universität, St. Johanns-Ring 19, CH-4056 Basel

Oxy anions **3** generated from 1,2-dihydrocyclobutabenzen-1-ones **1** through addition of a charged nucleophile or from 1-hydroxy-1,2-dihydrocyclobutabenzenes **2** by deprotonation with base lead to stable products through *distal* and/or *proximal* cleavage of the strained four-membered ring *via* benzyl carbanion **4** and/or aryl carbanion **5**. A systematic study of this process reveals the relative stability of the two isomeric carbanions **4** and **5** as a key factor in determining the course of the ring-cleavage reaction. While benzyl carbanions **4** can be trapped with carbon electrophiles, attempts at trapping aryl carbanions **5** with electrophiles other than H^+ failed. In protic solvents, the magnesium salt of the tertiary alcohol **2** shows an increased rate of *proximal* cleavage as compared to its alkali salts. From this, we conclude that, in contrast to benzyl carbanions **4**, free aryl carbanions **5** are of transient existence only. *Proximal* C,C-bond cleavage seems to occur either through protonation of **5** from a fast, reversible equilibrium **3**⇌**5** in which **3** strongly predominates, or in protic solvents possibly even through a rate-limiting protonation of **3** at the aromatic C-atom, bypassing free anion **5** altogether. Thus, additional factors other than just the relative stability of isomeric carbanions **4** and **5** are of importance in determining the regiochemistry of the base-induced C,C-bond cleavage in ketones **1** and in alcohols **2**.

Introduction. – As reported by *Cava* and *Muth* in 1960 [1] 1,2-dihydrocyclobutabenzen-1-one (**1**), when treated with aqueous NaOH, reacts through cleavage of the strained four-membered ring yielding a 1:1 mixture *ortho*-toluic acid/2-phenylacetic acid (*Scheme 1*). The two reaction modes of **1**, depending on the position of the reacting C,C-bond with respect to the aromatic ring, have been referred to as *distal* and *proximal* bond cleavage, respectively [2]. As inferred from literature [3][4], the regiochemical course of this C,C-bond cleavage depends strongly on the presence of substituents in the aromatic ring of **1**.

Scheme 1



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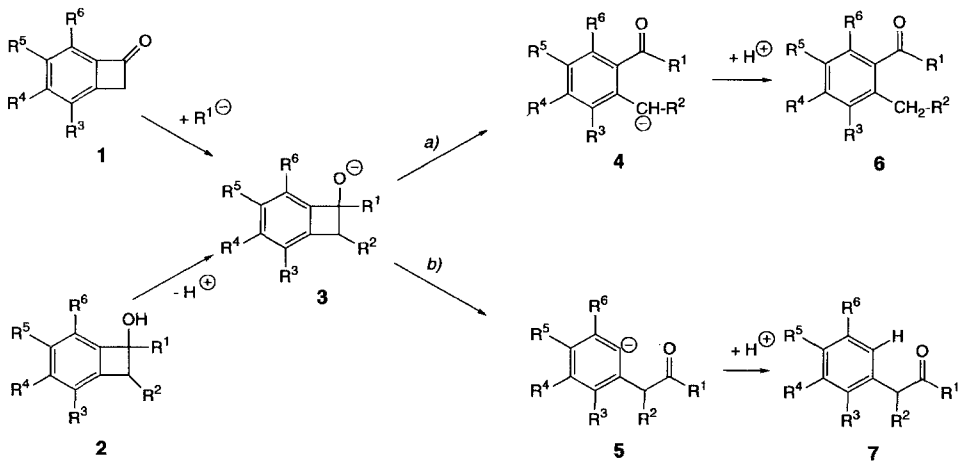
In contrast to ketone **1**, alcohols **2** (R^1 = H, alkyl, or aryl), which are readily accessible from **1** through reduction or *Grignard* addition, react with base through cleavage of the C,C-bond *distal* to the aromatic ring exclusively [1][5]. Derivatives of **2**, however, carrying more than one alkyl substituent on the four-membered ring have been reported by *Caubére et al.* to yield mixtures of both regioisomeric products through competing *proximal* and *distal* bond cleavage upon treatment with base [6–8].

The base-induced ring cleavage of 1-oxygenated derivatives of cyclobutabenzene such as **1** and **2** can be assumed to proceed *via* an oxy-anionic intermediate **3**, generated

either through reversible addition of a nucleophile to **1** or through deprotonation of the OH group from the preformed alcohol **2** by base (*Scheme 2*). Due to its ring strain, oxy anion **3** leads either to benzylic carbanion **4** through *distal* C,C-bond cleavage (path *a* in *Scheme 2*) or to aryl carbanion **5** through *proximal* C,C-bond cleavage (path *b* in *Scheme 1*).

Scheme 2

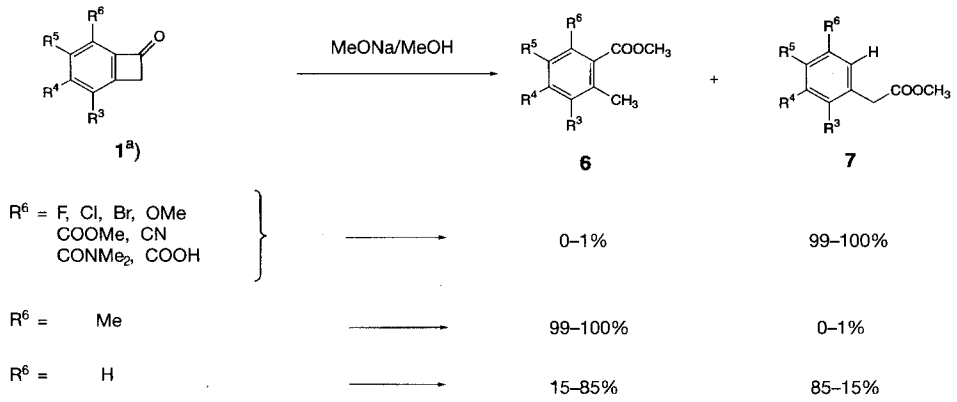


Benzyl carbanions **4** generated from **2** (R^1, R^2 = H) through base-induced *distal* bond cleavage (path *a* in *Scheme 1*) have been trapped in aprotic solvents with various carbon electrophiles [9–11]. The question arises as to whether aromatic carbanions **5** upon generation from appropriately substituted precursors **1** and/or **2** through *proximal* bond cleavage (path *b* in *Scheme 1*) could also be trapped with carbon electrophiles.

As we had a considerable number of ketones **1** and, therefrom, of alcohols **2** available in our laboratory [12], we considered it worthwile to embark on a systematic study of the factors influencing the regiochemistry of the base-induced C,C-bond-cleavage reactions described above. Our aim was to arrive at new procedures for the formation of C,C bonds *via* either benzylic carbanions **4** or aryl carbanions **5** generated through base-induced cleavage from appropriately substituted and readily available 1-oxygenated cyclobutabenzene derivatives such as **1** and/or **2**.

2. Results and Discussion. – 2.1. *Influence of Substituents on the Preferred C,C-Bond Cleavage Mode of 1-Oxygenated 1,2-Dihydrocyclobutabenzenes* **1** *and* **2**. The effect of aromatic substituents on the regiochemistry of the ring-cleavage reaction of oxy anions of general structure **3** was investigated by treating 1,2-dihydrocyclobutabenzen-1-ones **1**, carrying various substituents in the aromatic ring, with MeONa in MeOH under reflux. In each case, the expected esters **6** and/or **7** (R^1 = MeO) were the only products formed in quantitative yield as revealed by gas chromatography and by ^{1}H-NMR spectroscopy (*Scheme 3*). Furthermore, it was ascertained that the **6**/**7** product ratio did not change with time upon extended treatment with base.

Scheme 3. *Regioselectivity of the Base-Induced C,C-Bond Cleavage in MeOH*



[a]) For R^3 to R^5, see *Table 4*.

The experimental results as summarized in *Scheme 3* (for details, see *Table 4* in the *Exper. Part*) reveal that the regioselectivity of the MeONa-induced ring cleavage of the strained four-membered ring in ketones **1** is essentially determined by the nature of the aromatic substituent at C(6). If this substituent is an electronegative atom or functional group stabilizing an adjacent negative charge through induction or a neighboring carbon-metal ion pair through coordination, *proximal* C,C-bond cleavage to the phenylacetic-acid derivative **7** (R^1 = MeO) is strongly favored (see *Scheme 3*)[1]). If this substituent is an alkyl group, which, through its steric effect, would be expected to prevent efficient solvation of a neighboring negative charge, *distal* ring cleavage giving **6** is observed exclusively. From these findings, we conclude that it is the influence of the substituent R^6 on the stability of the aromatic carbanion **5** which determines the regiochemical course of the C,C-bond cleavage occurring from oxy anion **3**. In line with this reasoning, we found that ketones with an H-atom at C(6) yield mixtures of both isomeric methyl esters **6** and **7** through competing *proximal* and *distal* C,C-bond cleavage. Supporting this interpretation is the qualitative observation that the ketones reacting exclusively through *proximal* cleavage are at the same time the most reactive ones toward base as indicated by the lower reaction temperature required for the ring cleavage to proceed to completion (see *Table 4*). Thus, the stabilization of the negative charge in **5** through R^6 correlates with the increased rate of *proximal* bond cleavage **3** → **5**[2]).

The stability of benzylic carbanion **4** is not expected to be strongly influenced by polar substituents at C(6). Conjugating, electron-withdrawing substituents at C(3) and

[1]) Based on a limited number of observations, a similar conclusion has been arrived at by *Amupitan* and *Stansfield* [3].

[2]) Tricarbonylchromium complexes of **2** have been reported by *Butenschön* and coworkers [2] to show an increased tendency towards base-induced *proximal* C,C-bond cleavage as compared with uncomplexed **2**. Considering the electron-withdrawing effect of the $Cr(CO)_3$ group, it seems not surprising that the regioselectivity of the cleavage reaction is affected through complexation, even though it may not be clear *a priori* in which direction, since both aryl and benzyl C–H bonds are activated through complexation of the aromatic ring to the $Cr(CO)_3$ moiety [13].

Table 1. *Base-Induced Cleavage of the Four-Membered Ring in Cyclobutabenzen-1-ols* **2**: *Effect of Substituents on Product Ratio* **6**/**7**[a])

Reactant	Substituents				1N MeONa/MeOH, refl.			t-$C_5H_{11}ONa$ in THF[b])				t-BuLi in THF[b])			
	R^1	R^2	R^4	R^6	$t_{1/2}$[min]	**6**	**7**	[°C]/[min]	Conv. [%]	**6**	**7**	[°C]/[min]	Conv. [%]	**6**	**7**
2a	Me	H	H	H	7	99	1	−40/15	62	99	1	25/15	95	100	0
2b	Me	H	Me	Me	15	100	0	−20/15	80	100	0	25/15	100	100	0
2c	Me	H	H	Cl	1.5	69	31	−40/15	90	21	79	0/15	89	48	52
2d[c])	Et	Me	H	H	360	17	83	25/15	99	40	60	25/90	67	77	23
2e[d])	$CH_2CH_2CH_2$		H	H	76	92	8	25/15	97	100	0	50/60	90	100	0
2f[d])	$CH_2(CH_2)_2CH_2$		H	H	155	64	36	25/15	57	90	10	66/60	85	27	73
2g[d])	$CH_2(CH_2)_3CH_2$		H	H	70	93	7	0/60	87	100	0	50/15	61	97	3

[a]) Analysis of product ratio by GLC and ^{1}H-NMR spectroscopy.
[b]) 1.0 equiv. of base was used.
[c]) Substituents R^1, R^2: *trans*.
[d]) Substituents R^1, R^2: *cis*.

at C(5), however, should stabilize **4** through conjugation and, therefore, they would be expected to enhance specifically the rate of *distal* bond cleavage. Unfortunately, precursors **1** with such substituents have not been available to verify this hypothesis.

In contrast to the unsubstituted ketone **1** (R^2–R^6 = H, the alcohols **2** (R^1 = H, alkyl or aryl, R^2–R^6 = H), upon treatment with base, react through *distal* bond cleavage exclusively yielding the *ortho*-methylated product **6** (R^1 = H, alkyl, or aryl; R^2–R^6 = H) [1][5]. Compounds **2** with more than one alkyl substituent on the four-membered ring, however, according to *Caubère et al.*, yield mixtures of both isomeric cleavage products **6** and **7**, their ratio depending in a non-predictable way on the nature of R^1 and R^2, and on the polarity of the solvent as well [7][8]. To learn about the factors controlling the regioselectivity of this seemingly capricious C,C-bond cleavage reaction, we have compared the reaction with base of seven selected alcohols **2** differing in their substituents R^1 to R^6. The results are presented in *Table 1*.

The tertiary alcohols **2a** to **2g** differ widely in their reactivity toward MeONa in MeOH (see *Table 1*). Interestingly, the most reactive alcohol, **2c**, and the two least reactive alcohols, **2d** and **2f**, yield the highest ratio of *proximal* cleavage product **7**. As mentioned above, in **2c** the *proximal* cleavage mode is expected to be enhanced by Cl at C(6) through stabilization of the negative charge on the aromatic C-atom in **5**, this stabilization being partially effective already in the transition state leading from **3** to **5**. On the other hand, the high ratio of *proximal* cleavage in **2d**–**2g** cannot be due to stabilization of the aryl carbanion **5** but, on the contrary, has to be ascribed rather to *destabilization* of the isomeric benzyl carbanion **4**, and thus to a reduced rate of *distal* cleavage.

Benzyl carbanions **4** gain stability through conjugation of the negative charge on the benzyl C-atom with the *ortho*-carbonyl group. This conjugation is hindered in all four anions **4** derived from 1,2-dialkylated alcohols **2d** to **2g**. According to [14], a preferred *exo*-rotation of the ionic oxygen upon *distal* C,C-bond cleavage can be assumed for all oxy anions **3**. The alcohol **2d**, having both alkyl groups *trans*[3]), should give, *via* **3d** upon *distal* cleavage through *conrotation* (*Woodward-Hoffmann* rules), highly strained **4d** with both alkyl groups *endo*. For steric reasons, this anion cannot enjoy full stabilization through conjugation.

Similarly, anions **4** derived from **2e**–**2g** contain their four adjacent trigonal C-atoms as part of a nonplanar medium ring of size 7 to 9 and thus cannot gain full stabilization through conjugation either. The destabilization of the anions **4** through hindered conjugation should be felt already in the transition state leading from **3** to **4**. Therefore, for all four 1,2-disubstituted alcohols **2d**–**2g**, a reduced rate for the base-induced *distal* ring opening is to be expected in comparison to **2a**–**2c** which have only a single alkyl substituent on the four-membered ring.

Due to a lack of information on anion structure and solvation, a quantitative prediction of the relative rates of *proximal* to *distal* ring opening for anions **3** is not possible. The correlation observed between the rate of bond cleavage and its regioselectivity,

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[3]) The tertiary alcohol **2d** was obtained as a single stereoisomer by reaction of pentan-3-one and PhBr with $NaNH_2$ following *Caubère*'s procedure [15c]. The more stable configuration with both alkyl groups *trans* on the four-membered ring is corroborated by a NOE experiment (see *Exper. Part*).

however, seems of value as an empirical guide in understanding relative rates and selectivities in similar processes.

From this study, we conclude that the relative stability of isomeric anions **4** and **5**, being strongly influenced by polar and steric effects of substituents on the C-skeleton, is a key factor in determining the relative extent of *distal* and of *proximal* C,C-bond cleavage upon base treatment of ketones **1** and of alcohols **2**. It is not obvious, but simplifying the picture that alcohols **2**, under aprotic conditions in THF through treatment with Na and Li base (see *Table 1*), give similar results with respect to the regioselectivity of the bond-cleavage reaction as are found in MeOH.

2.2. *Influence of the Substituent R^1 at C(1) on the Preferred C,C-Bond-Cleavage Mode of the Oxy-anionic Intermediate* **3**. Oxy anions of general structure **3**, differing in the nature of the substituent R^1 at C(1), were generated in anhydrous THF either from fluoro ketone **1** (R^6 = F) through reversible addition of ionic nucleophiles R^{1-} or from various fluoro alcohols **2** (R^6 = F) by deprotonation with base[4]).

The results presented in *Table 2* indicate an increasing tendency to *proximal* cleavage with functional groups R^1 being linked to C(1) through atoms of increasing electronegativity (*Entries 1–4*):

$H \approx RS < NR_2 < RO$: tendency to *proximal* cleavage increases.

Table 2. *C,C-Bond Cleavage of Oxy Anions* **3** *Generated in THF from Ketone* **1** (R^6 = F) *and from Alcohols,* **2** (R^6 = F): *Influence of Atom or Group R^1 in* **3** *on Product Ratio* **6**/**7**

Entry	R^1 in Oxy anion **3**	Generation of **3**[a]) [°C]/[min]		Products[b])	
				6	**7**
1	MeO	*A*	−20/25	<0.1	>99.9
2	Et_2N	*A*	−78/180	2	98
3	BuS	*A*	0/15	27	73
4	H	*B*	25/150[c])	23	77
5	Me	*B*	−20/20[c])	5	95
6	Ph	*B*	0/5	94	6
7	NO_2CH_2	*A*	25/150	>98	<2

[a]) Procedure *A*: Addition of **1** (R^6 = F) at −78° to LiR^1 in THF. Procedure *B*: Addition of **2** (R^1 = variable, R^6 = F) to BuLi or LDA in THF. [b]) Product ratios were determined by GLC analysis of crude reaction mixtures and were verified by inspection of ^{1}H-NMR spectra. [c]) Conversion not quantitative.

Electronegativity of the key atom in R^1, however, cannot be the only factor influencing the preferred cleavage mode of **3** as indicated by the high variance within the compounds having an organic functional group with the C-atom directly connected to C(1) (*Entries 5–7* in *Table 2*). A simple explanation for the influence of the groups R^1 on the preferred C,C-bond cleavage mode from **3** cannot be provided on the basis of anion stability alone.

[4]) Reactants **1** and **2** having a strong bias toward *proximal* cleavage through the halogen at C(6) were chosen as substrates in order to find *proximal* cleavage product of structure **7** in the reaction mixtures even with substitution at C(1) strongly favoring *distal* cleavage.

A similar conclusion can be drawn from a recent report on the base-induced ring opening of various 1-oxygenated derivatives of 2-benzylidenecyclobutabenzene by *Bradley* and *Durst* [16]. No simple correlation between the reported ratios of *proximal* to *distal* C,C-bond cleavage for these compounds with electronegativity of R^1 or with relative anion stability can be arrived at from the given data.

2.3. *Influence of the Metal Counterion in the Base and of the Solvent on the Direction of C,C-Bond Cleavage from Oxy Anion* **3**. The 6-chloro alcohol **2** (R^1 = Me, R^6 = Cl)[4]), was treated in anhydrous THF and in protic solvents with bases differing in the nature of the metal cation. In each case, the reaction products were isolated after acid quenching at low temperature followed by aqueous workup. The ratio of the isomeric cleavage products **6**/**7** (R^1 = Me, R^6 = Cl) as a function of solvent and base is presented in *Table 3*.

Table 3. *Base-Induced C,C-Bond Cleavage in Alcohol* **2** (R^1 = Me, R^6 = Cl): *Influence of the Metal Counterion and of the Solvent on the Product Ratio* **6**/**7**

					Products[c][d]	
Entry[a]	Solvent	Base[b]	[°C]/[min]	Conv. [%]	**6**	**7**
1	THF	*t*-$C_5H_{11}OK$	−78/15	100	1	99
2	THF	*t*-$C_5H_{11}ONa$	−40/15	90	21	79
3	THF	BuLi	0/15	90	48	52
4	THF	MeMgBr	56/180	11	100	0
5	MeOH	MeOLi	65/15	90	72	28
6	MeOH	MeONa	65/15	100	69	31
7	MeOH	MeOK	65/15	100	50	50
8	MeOH	$(MeO)_2Mg$	65/10	100	2	98
9	*t*-BuOH	$(t\text{-BuO})_2Mg$	80/200	70	16	84
10	EtOH	$(EtO)_2Ca$	78/330	100	23	77
11	*t*-BuOH	$(t\text{-BuO})_3Al$	80/300	30	55	45

[a]) Reactant concentration: 0.05M. [b]) In THF, 1.0 equiv. of base was added, in protic solvents an excess was used. [c]) Product ratio determined by GLC integration and verified by ^{1}H-NMR spectroscopy. [d]) The fluoro alcohol **2** (R^1 = Me, R^6 = F) gave analogous results but a much lower ratio of **6**/**7** (*e.g.*, < 5: > 95 for *Entries 5–11*).

Not unexpectedly, in the aprotic solvent (anhydrous THF) the rate of bond cleavage increases dramatically in the sequence $Mg^{2+} < Li^+ < Na^+ < K^+$ as shown qualitatively by the reaction temperature necessary to reach quantitative conversion to products **6** and/or **7** (see *Table 3*). With the Mg salt of **3**, *distal*-cleavage product **6** forms exclusively, but only slowly even under reflux. The highly reactive K salt, in contrast, is reacting rapidly even at −78° and yieds only **7**, the product of *proximal* cleavage[5]).

The observed change in regioselectivity in going from a strongly coordinated and unreactive to a weakly coordinated and, therefore, highly reactive oxy anion **3** is not obvious. In **2f** (R^1–R^2 = –$(CH_2)_4$–; see *Table 1*), for instance, the opposite trend is found in going from the Li salt (which yields **6**/**7** 27:73) to the K salt (which yields **6**/**7**

[5]) For a recent discussion of charge-accelerated rearrangements in organic synthesis, see [17].

95:5). This latter result, while confirming similar conflicting observations of *Caubère et al.* [7][8], leaves us without a simple, rational explanation.

In MeOH, as expected, the three alkali bases, with Li^+, Na^+, and K^+, react at similar rates and yield the two isomeric products **6** and **7** in approximately the same ratio. In this solvent of high ionizing power, reaction *via* dissociated ions can be assumed, the reaction of the organic anion **3** being independent of the nature of its alkali counterion. Quite unexpected, however, is the result of treating alcohol **2** with $(MeO)_2Mg$ in MeOH. At a similar rate as with the alkali methoxides, almost exclusive formation of the *proximal* cleavage product **7** is observed. As shown in *Table 3* this change in regioselectivity holds too, however less pronounced, with higher and, therefore, less polar alcohols than MeOH, and with other coordinating cations such as Ca^{2+} but not with Al^{3+}. The increased selectivity toward *proximal* cleavage with Mg base in protic solvents must be a consequence of the much stronger coordinating power of the Mg^{2+} cation as compared with the alkali cations. As suggested in *Scheme 4*, the Mg salt of **2** through solvent molecules in its tight coordination sphere may guide a proton directly to the aromatic C-atom. Such a reaction path would bring about *proximal* C,C-bond cleavage bypassing a free aryl carbanion **5** altogether. The seemingly capricious behavior of substituents R^1 at C(1) in oxy anions **3** in directing the base-induced C,C-bond cleavage may well be a consequence of carbon protonation being intimately coupled to C,C-bond breaking for the *proximal* cleavage pathway in protic solvents[6]) and the substituents R^1 having an influence on the rate of protonation both by their steric and electronic effects.

Scheme 4

2.4. *Attempts at Trapping Aryl Carbanion* **5** *with Electrophiles.* As has been shown recently [9–11], alcohols **2** (R^1, R^2 = H) having no further substituents on the four-membered ring, upon base treatment, yield benzyl carbanions **4** through *distal* C,C-bond cleavage which can be trapped in aprotic solvents with various carbon electrophiles. In the course of the present study, we have learned that 6-fluoro alcohol **2** (R^1 = Me, R^6 = F), due to the F substituent at C(6), upon treatment with base, reacts through *proximal* C,C-bond cleavage almost exclusively (> 95%) both in protic solvents (MeONa in MeOH) and in aprotic solvents (BuLi in THF). In these reactions, carbanion

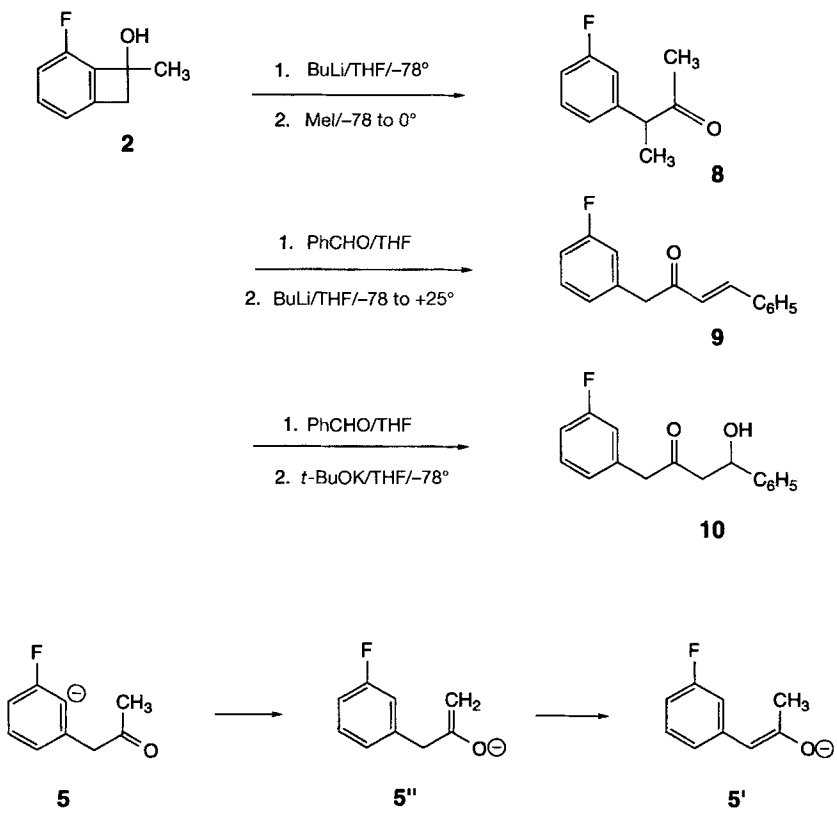
[6]) A similar mechanism has been proposed by *DePuy* and *Breitbeil* [18] for the base-induced cleavage of cyclopropanols. The regiochemistry of the cleavage of the strained three-membered ring in these compounds is determined by relative carbanion stability. Carbanions, however, are not generated as free intermediates, the reaction rate being limited by the rate of carbon protonation of the cyclopropoxy anion through the protic solvent.

5 (R^1 = Me, R^6 = F) is supposed to be an intermediate. Attempts at trapping **5** are described below.

Treating fluoro alcohol **2** (R^1 = Me, R^6 = F) with MeONa in MeOD yielded 3'-fluorophenylpropan-2-one (**7**, R^1 = Me; R^6 = F) containing 5 to 6 D-atoms. Through an additional treatment of this sample with MeONa in MeOH, all the D-atoms in aliphatic positions were washed out. The material recovered from this process contained still one D-atom in the aromatic ring *ortho* to the F-atom as revealed by its ^{1}H- and ^{13}C-NMR spectrum (see *Exper. Part*). From this, we conclude that the product of base-induced *proximal* C,C-bond cleavage indeed is formed through a heterolytic process, protonation through the protic solvent having occurred at one of the aryl C-atoms *ortho* to the F substituent, as expected if anion **5** (R^1 = Me, R^6 = F) were an intermediate.

All attempts, however, to trap carbanion **5** (R^1 = Me, R^6 = F) with carbon electrophiles in aprotic solvents failed (see *Scheme 5*).

Scheme 5



Treating fluoro alcohol **2** (R^1 = Me, R^6 = F) with BuLi in THF followed by MeI at 0° led to **8** formed through methylation in the benzylic position of the *proximal* ring cleavage product **7** but not on the aromatic ring. Attempted *in situ* reaction of the anion **5** with PhCHO by treating a mixture of **2** (R^1 = Me, R^6 = F) and PhCHO with

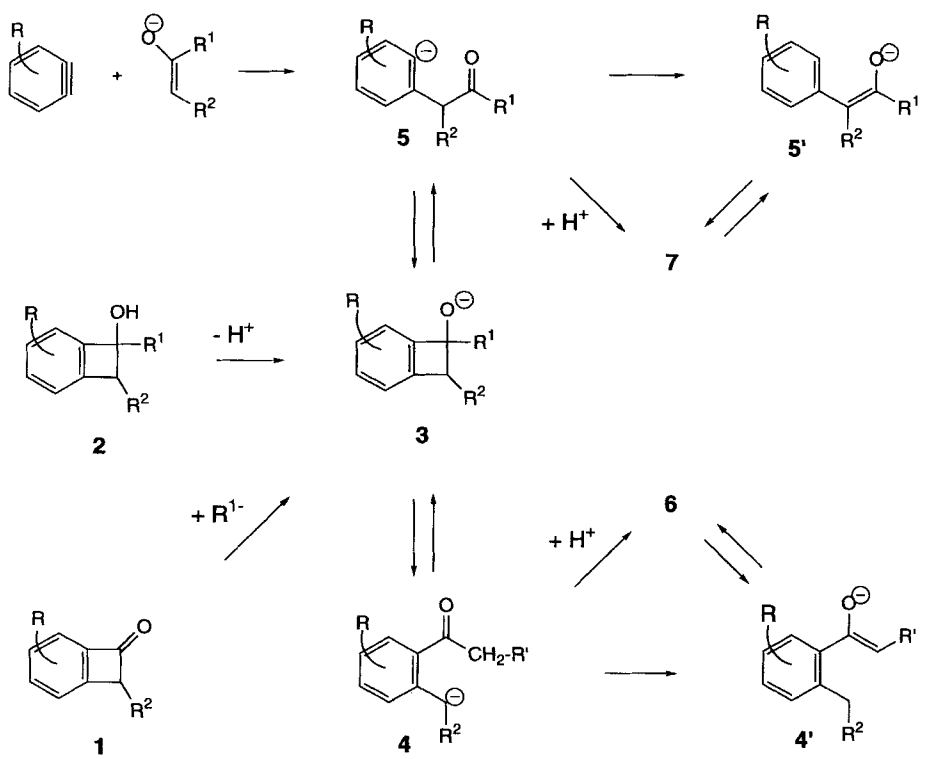
BuLi in THF at −40° and warming to room temperature led to the aldol condensation product **9** (see *Scheme 4*). Performing the same reaction with *t*-BuOK in THF at −78° led to the aldol addition product **10** instead. In no experiment could an isomeric product of addition of PhCHO and **2** be detected, even in the crude reaction mixture.

From these negative experiments, the conclusion is drawn that aryl carbanion **5** (R^1 = Me, R^6 = F), if generated as a distinct intermediate, reacts faster under proton transfer to the thermodynamically more stable enolate anion **5'** and/or **5''**. Thus, we conclude that isomerization of **5** either through an intramolecular process to **5''** or by an intermolecular proton transfer to **5'** *via* **7** is faster than *in situ* addition to a reactive electrophile such as PhCHO.

The failure to trap **5**, even if generated from **2** (R^1 = Me, R^6 = F) in the presence of PhCHO, can be taken as an indication that **5**, in contrast to benzylic carbanion **4** (R^1, R^2 = H), may only be of transient existence in the course of the base induced *proximal* bond-cleavage reaction.

In this respect it should be recalled that aryl carbanions **5** can be generated not only through *proximal* C,C-bond cleavage from **2** after deprotonation *via* **3**, but also by addition of enolate anions to benzyne generated *in situ* [19–22]. This latter process can lead to carbonyl compounds **7** through protonation of **5**. Frequently, however, under the strongly basic reaction conditions, products of type **6** are formed through ring closure to oxy anion **3** followed by *distal* C,C-bond cleavage *via* **4** (see *Scheme 6*). From this

Scheme 6



it becomes clear that aryl carbanions **5** must be in equilibrium with the bicyclic oxy anions **3**. The failure of trapping **5** is an indication that, in this equilibrium, **3** is strongly favored over **5**. Benzyl carbanions **4** can be trapped by carbon electrophiles as long as generated from **2** carrying no substituents on the four-membered ring [9–11]. In this case, **4** seems favored in the equilibrium with **3** and furthermore, bearing no α-H-atom to the carbonyl group, cannot isomerize to a more stable enolate anion **4'**. Highly substituted anions **4** (R^1, R^2 = alkyl), however, could not be trapped with electrophiles as reported by *Caubère* and *Lallot* [8], but isomerized in the strongly basic reaction medium to the more stable enolate anions **4'**. It is likely, therefore, that also in this case an equilibrium **3** ⇌ **4** exists, in which **3** is favored over **4**, and that escape to a stable product occurs from this equilibrium through rate-limiting isomerization **4** → **4'**. As for the isomerization **5** → **5''**, both an intramolecular reaction path and an intermolecular proton transfer *via* **6** is conceivable for the isomerization **4** → **4'**.

The ratio of *proximal* to *distal* CC-bond cleavage observed upon base treatment of 1-oxygenated cyclobutabenzenes such as **1** and **2** according to *Scheme 6* depends on the rates describing the two coupled equilibria **3** ⇌ **4** and **3** ⇌ **5**, and of the competing protonation or isomerization reactions therefrom[7]). From this complex situation, it becomes clear why the regioselectivity of the C,C-bond-cleavage process cannot be predicted *a priori* from substituent effects unless substrates of very similar structure are to be compared.

Conclusion. – Upon treatment with base or with nucleophiles 1-oxygenated cyclobutabenzenes such as ketones **1** and alcohols **2** proceed to products *via* an oxyanionic intermediate **3** through *distal* or through *proximal* cleavage of a C,C bond

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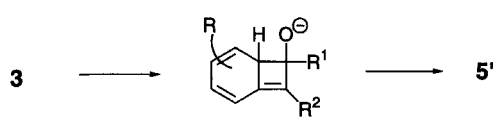
[7]) As suggested by a referee, an alternate mechanism for the base-induced proximal C,C-bond cleavage of oxy anion **3** bypassing the elusive aryl carbanion **5** could be envisaged. This mechanism, involving a base-catalyzed isomerization **3** → **3'**, followed by a fast electrocyclic ring opening to **5'**, should be assessed on the following experimental facts: *1*) As amply documented in *Table 4* (*Exper. Part*) and by others [3][4], *proximal* cleavage of **3** is strongly enhanced through electronegative substituents at C(6). This substituent effect is hard to rationalize by a reaction pathway involving **3'** but not **5** as an intermediate. *2*) Ketones **1** and alcohols **2** with appropriate substitution in the aromatic ring yield products of *proximal* C,C-bond cleavage *via* oxy anion **3**. This cleavage proceeds with base both in aprotic as well as in protic solvents (see *Tables 3* and *4*). A pathway involving a highly endothermic double-bond shift **3** to **3'** *via* proton abstraction from carbon under the influence of dilute base in protic solvents such as H_2O or MeOH would be without precedence. *3*) The fluoro alcohol **2** (R^1 = Me, R^6 = F), which reacts by proximal cleavage almost exclusively with any solvent-base combination (see *Table 3*), has been found to yield the unconjugated enolate **5''** under kinetic control, and not the conjugated enolate **5'** as required if **3'** were an intermediate (see *Scheme 5*). *4*) Alcohols **2** fully substituted at C(2), for which an isomerization **3** → **3'** is precluded, still react through *proximal* cleavage as reported by *Caubère et al.* [7][8].



3'

On account of these experimental findings, a mechanism for base-catalyzed *proximal* C,C-bond cleavage of **3** *via* **3'** seems highly unlikely and, therefore, is not included in the above discussion (see *Scheme 6*).

in the strained four-membered ring. Benzyl carbanions **4** are stable if not highly substituted. Therefore, they can be trapped with electrophiles upon being formed through *distal* C,C-bond cleavage from **3**. All efforts to trap aryl carbanions **5** with carbon electrophiles, even *in situ*, proved unsuccessful. Therefore, it seems that *proximal* cleavage proceeds from an equilibrium **3** ⇌ **5** in which **3** strongly predominates. In aprotic and strongly basic medium, rate-limiting isomerization of **5** to a more stable anion **5′/5″** is occurring from this equilibrium either through an intramolecular process (**5** → **5″**) or through intermolecular proton transfer (**5** → **5′**) *via* **7**. In less basic, protic media or upon acid workup, the product of carbon protonation **7** is formed either directly from the equilibrium **3** ⇌ **5** or from **5′/5″**. The chances for C,C-bond formation *via* aryl anions **5** generated from appropriately substituted ketones **1** or alcohols **2** thus seem remote at best.

We wish to thank Mr. *A. Pfiffner* for technical assistance. The financial support of this work through the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

1. *General.* Air- and moisture-sensitive reactions were carried out under Ar or N_2 in flame-dried reaction vessels. Dry solvents were prepared according to standard procedures. THF was freshly distilled from K and MeOH from Mg before use. Normal workup means distribution of reaction crude between Et_2O and H_2O, washing the org. layer with sat. aq. $NaHCO_3$ and with brine, followed by drying (Na_2SO_4) and evaporation on a rotary evaporator at reduced pressure below 40°. The following reagents were used as obtained from the suppliers (*Aldrich*, *Fluka*, or *Merck*): BuLi (1.6M in hexane), *t*-BuLi (1.5M in pentane), MeLi (1.5M in Et_2O), MeMgBr (1.4M in toluene/THF 3:1). For TLC, ready-made plates silica gel *Merck 60 F 254* were used. For column chromatography, (CC) silica gel (60–200 μm) supplied by *Chemische Fabrik Uetikon was used.* M.p.: *Kofler* hot stage, corrected. UV Spectra: *Varian-Cary-219*, λ_{max} in nm (log ε). IR Spectra: *Perkin-Elmer-781* and *Perkin-Elmer-1600 FTIR* spectrophotometer. Absorptions in cm^{-1}. NMR Spectra: *Varian Gemini-300* at 300 MHz for ^1H and at 75 MHz for ^{13}C, $CDCl_3$ as solvent except where mentioned otherwise; chemical shifts in δ [ppm] relative to TMS (δ = 0); coupling constants *J* in Hz. MS: *VG-70-250*. GC-MS: *Hewlett-Packard HP 5790/5970*. GLC: *HP 5890* with integrator *HP 3392A*. A fused silica capillary column (25 m × 0.3 mm) with 0.17 μ cross linked *OV 1* as stationary phase was used. A standard program for GLC analysis was used with injection at 100° and a linear temp. gradient of 10° min^{-1} up to 300°.

2. *Synthesis of Dihydrocyclobutabenzen-1-ones* **1** (*cf. Scheme 3* and *Table 4*). Compounds **1a**–**1o** were obtained through gas-phase pyrolysis according to [12]. Compounds **1p**–**1r** were synthesized according to [4].

2.1. *6-Bromo-1,2-dihydrocyclobutabenzen-1-one* (**1p**). From 1,3-dibromobenzene (10.0 g, 42.3 mmol) and 1,1-dimethoxyethene (7.45 g, 84.6 mmol), following the procedure [4], 6-bromo-1,1-dimethoxy-1,2-dihydrocyclobutabenzene (7.75 g) was obtained as a colorless liquid of b.p. 120–140°/15 Torr. Hydrolysis according to [4] and crystallization from Et_2O gave **1p** (4.60 g, 55%). Colorless prisms. M.p. 80–82°. IR (KBr): 1760, 1570, 1450, 1390, 1120, 960, 780. ^1H-NMR: 4.00 (*s*, 2 H–C(2)); 7.51–7.36 (*m*, H–C(3), H–C(4), H–C(5)). ^{13}C-NMR: 52.8 (CH_2); 112.7 (C); 122.2, 131.9, 136.2 (CH); 147.1, 153.0, 185.3 (C). EI-MS (70 eV): 198 (37, $[M + 2]^+$), 196 (38, M^+), 170 (25), 168 (27), 89 (100). Anal. calc. for C_8H_5BrO (197.03): C 48.77, H 2.56, O 8.12, Br 40.55; found: C 48.90, H 2.49, O 7.82, Br 40.40.

2.2. *6-Chloro-1,2-dihydrocyclobutabenzen-1-one* (**1q**)[8]. From 1-chloro-3-bromobenzene (7.0 g, 35.9 mmol) following the procedure *2.1*, **1q** (5.02 g, 57%) was obtained as prisms from Et_2O. M.p. 65–66°. IR (KBr): 1765, 1580, 1120, 785. ^1H-NMR: 4.00 (*s*, 2 H–C(2)); 7.33 (*d*, *J* = 7.4, H–C(3)); 7.41–7.50 (*m*, H–C(4), H–C(5)). ^{13}C-NMR: 52.6 (CH_2); 121.7 (CH); 125.3 (C); 128.9, 136.3 (CH); 144.7, 152.4, 184.7 (C). EI-MS (70 eV): 154 (18, $[M + 2]^+$), 152 (57, M^+), 124 (45), 89 (100), 63 (25). Anal. calc. for C_8H_5ClO (152.58): C 62.98, H 3.30, O 10.49, Cl 23.24; found: C 62.77, H 3.34, O 10.38, Cl 23.08.

2.3. *1-Oxo-1,2-dihydrocyclobutabenzene-6-carboxylic Acid* (**1s**). To a sample of 6-bromo-1,1-dimethoxy-1,2-dihydrocyclobutabenzene (7.5 g, 30.8 mmol), prepared as described in *2.1*, dissolved in THF (10 ml) at −78°, BuLi (23 ml, 37 mmol) was added within 40 min. The mixture was stirred at −78° for another 10 min. Then, CO_2 gas was bubbled through the soln. for 40 min at the same temp. The mixture was quenched with EtOH/conc. HCl

[8]) Anal. data for **1q** are given since not reported in [4].

(10 ml, 1:1) and was stirred for 15 min at −78°. Upon warming to r.t., a precipitate formed, yielding 3.5 g white solid upon filtration. Recrystallization from acetone gave **1s** (3.2 g, 48%). Colorless prisms. M.p. 216.8–218°. IR (KBr): 3400–2600, 1810, 1710, 1690, 1575, 1495, 1300, 1125, 750. ^{1}H-NMR ((D$_6$)acetone): 4.04 (br. *s*, 2 H–C(2)); 7.72 (*t*, *J* = 7.4, H–C(4)); 7.87 (*d*, *J* = 7.4, H–C(3)); 8.02 (*d*, *J* = 7.4, H–C(5)). ^{13}C-NMR ((D$_6$)acetone): 53.3 (CH_2); 125.3 (C); 128.6, 130.9, 135.7 (CH); 148.7, 152.8, 165.2, 185.1 (C). EI-MS (70 eV): 162 (13, M^+), 134 (100), 118 (56), 105 (60), 89 (48), 78 (76), 63 (82), CI-MS (NH_3): 180 (100, $[M + NH_4]^+$). Anal. calc. for $C_9H_6O_3$ (162.14): C 66.67, H 3.73, O 29.60; found: C 66.64, H 3.78, O 29.64.

2.4. *Methyl 1-Oxo-1,2-dihydrocyclobutabenzene-6-carboxylate* (**1t**). To a suspension of **1s** (371 mg, 2.3 mmol) in abs. MeOH (5 ml) conc. H_2SO_4 (6 drops) was added. The mixture was refluxed for 2 h under Ar. Upon cooling, a precipitate formed which was filtered and recrystallized from Et_2O yielding **1t** (300 mg, 75%). Colorless prisms. M.p. 122–124°. IR (KBr): 1765, 1720, 1570, 1425, 1290, 1120–1110, 755. ^{1}H-NMR: 3.98 (*s*, $MeCO_2$); 4.05 (*s*, 2H–C(2)); 7.62 (*t*, *J* = 7.6, H–C(4)); 7.73 (*d*, *J* = 7.6, H–C(3)); 8.03 (*d*, *J* = 7.6, H–C(5)). ^{13}C-NMR: 52.5 (CH_2); 52.8 ($MeCO_2$); 124.0 (C); 127.6, 130.1, 134.8 (CH); 147.6, 151.5, 164.6, 185.2 (C). EI-MS (70 eV): 176 (28, M^+), 145 (24), 118 (100), 90 (92), CI-MS (NH_3): 194 (100, $[M + NH_4]^+$). Anal. calc. for $C_{10}H_8O_3$ (176.16): C 68.17, H 4.57, O 27.24; found: C 67.94, H 4.51, O 27.27.

2.5. N,N-*Diethyl-1-oxo-1,2-dihydrocyclobutabenzene-6-carboxamide* (**1u**). To a suspension of **1s** (1.00 g, 6.1 mmol) in toluene (10 ml), $SOCl_2$ (0.73 g, 6.1 mmol) was added. The mixture was heated at 100° for 1 h under N_2. Removal of the toluene and bulb-to-bulb distillation of the residue gave acid chloride (1.02 g) as a colorless oil (b.p. 172–180°/15 Torr), which solidified upon standing. This material was dissolved in THF (4 ml), and soln. of Et_2NH (3.88 g, 54.6 mmol) in Et_2O (4 ml) was added at 0°. The suspension was stirred for 30 min at 0° and then warmed to r.t. H_2O was added and the mixture extracted twice with Et_2O. The org. layers were washed with 2N HCl, H_2O, and brine, and were dried (Na_2SO_4). Removal of the solvent and bulb-to-bulb distillation of the residue gave a light yellow liquid (0.61 g; b.p. 172-186/0.03 Torr), which solidified upon standing. Recrystallization from petroleum ether gave **1u** (0.54 g, 40%). Colorless crystals. M.p. 56–58°. IR (KBr): 2973, 2934, 1769, 1618, 1573, 1428, 1290, 1117, 802, 763. ^{1}H-NMR: 1.16, 1.27 (2 *t*, *J* = 6.8, $(MeCH_2)_2NCO$); 3.30, 3.58 (2 br. *q*, *J* = 6.8, $(MeCH_2)_2NCO$); 4.00 (*s*, CH_2); 7.42 (br. *s*, H–C(4)); 7.56–7.60 (*m*, H–C(3), H–C(5)). ^{13}C-NMR: 12.7, 13.9 ($(MeCH_2)_2NCO$); 39.2, 42.8 ($(MeCH_2)_2NCO$); 52.4 (CH_2); 124.1, 127.1 (CH); 130.4 (C); 135.5 (CH); 143.8, 150.6, 166.4, 186.4 (C). EI-MS (70 eV): 217 (7, M^+), 188 (24), 145 (40), 118 (82), 72 (100). CI-MS (NH_3): 235 (4, $[M + NH_4]^+$), 218 (100, $[M + 1]^+$). Anal. calc. for $C_{13}H_{15}NO_2$ (217.27): C 71.87, H 6.96, N 6.45, O 14.73; found: C 71.72, H 6.98, N 6.35, O 14.73.

2.6. *1-Oxo-1,2-dihydrocyclobutabenzene-6-carbonitrile* (**1v**). A sample of the acid **1s** (1.0 g, 6.1 mmol) was transformed into acid chloride as described in *2.5*. The crystalline material obtained was dissolved in THF (5 ml), and a soln. of NH_3 (28%, 10 ml) was added at 0°. After stirring at 0° for 30 min, the mixture was warmed to r.t., and H_2O was added. The solid which had separated was filtered and dried yielding 0.80 g of colorless crystals. To this material, $POCl_3$ (8 ml) was added and the mixture heated at 100° for 40 min. The mixture was hydrolyzed with ice-H_2O. Filtration of the precipitate and sublimation (80–90°/0.01 Torr) gave 0.54 g of a colorless solid, which yielded **1v** (0.50 g, 57%). Colorless crystals from MeOH. M.p. 125.5–127.5°. IR (KBr): 2234, 1771, 1569, 1329, 1139, 934, 797. ^{1}H-NMR: 4.11 (*s*, H–C(2)); 7.65–7.81 (*m*, H–C(3), H–C(4)); 7.83 (*d*, *J* = 7.6, H–C(5)). ^{13}C-NMR: 53.3 (CH_2); 103.5, 114.6 (C); 128.1, 132.8, 135.1 (CH); 148.5, 152.3, 183.7 (C). EI-MS (70 eV): 143 (59, M^+), 115 (100), 88 (24), 62 (15). Anal. calc. for C_9H_5NO (143.14): C 75.52, H 3.52, N 9.79, O 11.18; found: C 75.19, H 3.56, N 9.72, O 11.31.

3. *General Procedure for the Base-Induced Ring Cleavage of Cyclobutabenzene-1-ones* **1** (*cf. Table 4*). To a soln. of $NaOCH_3$ (0.5N) in MeOH (5 ml) under N_2, a soln. of the cyclobutabenzen-1-one (3.8 mmol) in MeOH (5 ml) was added. This mixture was kept under reflux or was stirred at the appropriate temp. (*cf. Table 4*). The soln. was quenched with 2N HCl, and H_2O was added. Workup as usual followed by bulb-to-bulb distillation of the org. product gave mixtures of methyl esters **6** and **7** (80–92%) which were analyzed by ^{1}H-NMR and GLC.

4. *Synthesis of 1,2-Dihydrocyclobutabenzen-1-ols* **2** (*cf. Tables 1* and *2*). The following compounds were obtained according to published procedues: **2a**, **2b**: [5]; **2e**–**2g**: [15].

4.1. *6-Chloro-1-methyl-1,2-dihydrocyclobutabenzen-1-ol* (**2c**). To a soln. of **1q** (1.51 g, 9.89 mmol) in THF (35 ml) at −78° under N_2, 33 ml of MeLi (1.5M in Et_2O, 49.4 mmol) was added. The suspension was stirred for 1 h at −78° and then quenched with NH_4Cl soln. Workup as usual and crystallization from Et_2O gave **2c** (1.36 g, 82%). Colorless crystals. M.p. 93–94°. IR (KBr): 3296, 2974, 2923, 1585, 1419, 1367, 1231, 1171, 1055, 947, 924, 770. ^{1}H-NMR: 1.75 (*s*, Me); 2.41 (*s*, OH exchanges with D_2O); 3.23 (*d*, *J* = 14.2, H–C(2)); 3.31 (*d*, *J* = 14.2, H–C(2)); 7.09–7.25 (*m*, H–C(3), H–C(4), H–C(5)). ^{13}C-NMR: 24.7 (Me); 47.9 (CH_2); 77.9 (C); 122.3 (CH); 126.2 (C); 127.3, 130.6 (CH); 143.3, 146.9 (C). CI-MS (NH_3): 186 (20, $[M + NH_4]^+$), 168 (100, M^+), 153 (13). Anal. calc. for C_9H_9ClO (168.61): C 64.11, H 5.38, O 9.49, Cl 21.02; found: C 63.90, H 5.32, O 9.55, Cl 20.85.

Table 4. *Cleavage of the Four-Membered Ring in Cyclobutabenzen-1-ones* (**1**) *through the Action of 0.5*N *MeONa in MeOH*[a])

Reactant	Substituents				[°C]/[h]	Products		**6**	**7**		
	R^6	R^5	R^4	R^3		**6**	**7**	t_R[b]) [min]	$\delta(CH_3)$	t_R[b]) [min]	$\delta(CH_2)$
1a	Me	Me	Me	Me	65/20	100	0	10.50	2.20	10.30	3.61
1b	Me	H	Me	Me	65/7	99	1	8.02	2.25	8.19	3.68
1c	Me	H	Me	H	65/6	99	1	6.24	2.26	6.45	3.63
1d	H	H	H	Me	65/2	72	28	5.83	2.43	5.27	3.60
1e	H	H	Me	H	65/2	71	29	5.64	2.32	5.26	3.57
1f	H	Me	H	H	65/2	64	36	5.53	2.53	5.37	3.60
1g	H	H	H	H	65/6	65	35	4.30	2.59	4.16	3.61
1h	CH=CH–CH=CH		H	H	65/36	84	16	10.43	2.45	10.75	3.72
1i	H	i-Pr	MeO	H	65/6	88	12	9.93	2.59	9.35	3.58
1j	H	H	MeO	H	65/6	82	18	7.59	2.60	6.97	3.60
1k	H	MeO	MeO	H	65/4	56	44	9.96	2.57	9.48	3.60
1n	H	H	NO_2	H	65/6	13	87	8.57	2.68	9.04	3.75
1m	MeO	H	H	H	65/2	1	99	6.55	2.28	6.90	3.59
1n	MeO	Br	H	H	65/3	0	100	8.68	2.25	10.41	3.58
1o	MeO	Me	Me	MeO	65/3	1	99	10.67	2.19	11.12	3.65
1p	Br	H	H	H	−20/3	tr	100	6.75	2.32	7.38	3.59
1q	Cl	H	H	H	−20/2	0	100	5.69	2.32	6.16	3.59
1r	F	H	H	H	−20/2	0	100	3.95	2.39	4.10	3.61
1s	COOH	H	H	H	65/2	4	96	9.31	2.36	9.72	3.71
1t	COOMe	H	H	H	−20/0.5	0	100	–	–	9.07	3.67
1u	Et_2NCO	H	H	H	0/1	0	100	–	–	13.02	3.64
1y	CN	H	H	H	−20/0.5	0	100	–	–	7.34	3.67

[a]) Analysis of product mixtures was performed by GLC and by ^{1}H-NMR spectroscopy. [b]) See *General* in *Exper. Part* for GLC conditions used.

4.2. *1-Ethyl-2-methyl-1,2-dihydrocyclobutabenzen-1-ol* (**2d**). This product was obtained following the procedure for **2e–g** [15]. To a suspension of $NaNH_2$ (17.6 g, 0.40 mol) in 1,2-dimethoxyethane (DME; 100 ml), pentan-3-one (8.6 g, 0.10 mol) in DME (20 ml) was added at −30°. After stirring for 2 h at 35° the mixture was cooled to −40°, and PhBr (8.0 g, 0.050 mol) was rapidly added by syringe. Stirring at −40° was continued overnight. The mixture was hydrolyzed with ice 2N HCl and worked up as usual yielding 7.4 g of an oil (b.p. 80–120°/0.2 Torr). This oil was poured into a warm soln. of *Girard-T* reagent (11.5 g, 70 mmol) in 130 ml of EtOH/glacial AcOH 10:1. After reflux for 2 h, the mixture was cooled and neutralized with excess aq. $NaHCO_3$. Extraction by CH_2Cl_2 and workup as usual gave, after evaporative distillation, an oil which solidified (4.4 g; b.p. 60–80°/0.02 Torr). Crystallization from pentane yielded **2d** (2.95 g, 35%). Colorless prisms. M.p. 51–52°. IR: 3300, 3067, 2976, 2961, 2933, 2888, 1595, 1455, 1412, 1194, 1172, 1144, 986, 755, 742. ^{1}H-NMR: 1.09 (*t*, *J* = 7.4, Me); 1.32 (*d*, *J* = 7.2, Me); 1.89 (*q*, *J* = 7.4, CH_2); 2.22 (*s*, OH); 3.50 (*q*, *J* = 7.2, H–C(2)); 7.15 (*d*, *J* = 6.8, H–C(3)); 7.2–7.3 (*m*, H–C(4), H–C(5), H–C(6)). NOE: Irradiation at 3.51 (H–C(2)): enhancement at 1.09 (2.1%), 1.32 (5.6%), 1.89 (4.6%), 7.15 (2.4%); irradiation at 1.89 (MeCH_2): enhancement at 1.09 (5.0%), 3.51 (3.1%). ^{13}C-NMR: 9.0 (Me); 14.7 (Me); 32.1 (CH_2); 49.3 (CH); 82.2 (C–OH); 121.6, 122.6, 127.3, 129.1 (CH); 147.8, 149 (C). GC-MS: 162 (1, M^+), 133 (100), 115 (10), 105 (20), 91 (10). Anal. calc. for $C_{11}H_{14}O$ (162.23): C 81.44, H 8.70; found: C 81.47, H 8.83.

4.3. *6-Fluoro-1,2-dihydrocyclobutabenzen-1-ol* (**2**; R^1 = H, R^6 = F). To a suspension of $LiAlH_4$ (416 mg, 15.9 mmol) in THF (50 ml) at −78°, **1r** (600 mg, 4.4 mmol) in THF (10 ml) was added. After 2 h at −78°, the reaction was quenched with NH_4Cl soln. H_2O was added and the mixture worked up as usual yielding **2** (R^1 = H, R^6 = F; 500 mg, 86%). Colorless prisms from Et_2O. M.p. 55.5–56.5°. IR (KBr): 3279, 1596, 1472, 1236, 1201, 1236, 1201, 1107, 1065, 1006, 772. ^{1}H-NMR: 2.96 (*dd*, *J* = 14.5, H–C(2)); 3.47 (*dd*, *J* = 14.2, 4.0, H–C(2)); 3.74 (br. *s*, OH); 5.25 (*d*, *J* = 4.0, H–C(1)); 6.79–6.90 (*m*, H–C(3), H–C(5)); 7.19–7.26 (*m*, H–C(4)). ^{13}C-NMR: 41.9 (C(2)); 68.5 (C(1)); 113.8 (*d*, *J* = 20, C(5)); 119.6 (*d*, *J* = 4.3, C(3)); 131.5 (*d*, *J* = 5.8, C(4)); 132.0 (*d*, *J* = 16.1, C(6a)); 144.9 (*d*, *J* = 9, C (2a)); 155.5 (*d*, *J* = 254, C(6)). EI-MS (70 eV): 138 (51, M^+), 137 (100), 109 (73), 83 (35), 63 (25). Anal. calc. for C_8H_7FO (138.14): C 69.56, H 5.11, F 13.75; found: C 69.48, H 5.13, F 13.76.

4.4. *6-Fluoro-1-methyl-1,2-dihydrocyclobutabenzen-1-ol* (**2**; R^1 = Me, R^6 = F). Compound **1r** (780 mg, 5.74 mmol), as described in *4.1*, yielded **2** (R^1 = Me, R^6 = F; 650 mg, 75%). Colorless crystals. M.p. 57–58.6°. IR (KBr): 3313, 2923, 1608, 1473, 1419, 1367, 1242, 1172, 1069, 1001, 943, 776. ^{1}H-NMR: 1.73 (*s*, Me); 2.57 (*s*, OH exchanges with D_2O); 3.22 (*d*, *J* = 14.1, H–C(2)); 3.31 (*d*, *J* = 14.2, H–C(2)); 6.85 (*t*, *J* = 7.3, H–C(5)); 6.93 (*dd*, *J* = 2.2, 7.3, H–C(3)); 7.21–7.28 (*m*, H–C(4)). ^{13}C-NMR: 25.8 (Me); 48.4 (CH_2); 77.2 (C); 114.0 (*d*, *J* = 20, C(5)); 120.0 (*d*, *J* = 4.5, C(3)); 131.2 (*d*, *J* = 5.8, C(4)); 134.9 (*d*, *J* = 16, C(6a)); 143.6 (*d*, *J* = 9, C(2a)); 155.8 (*d*, *J* = 254, C(6)). EI-MS (70 eV): 137 (100), 109 (47), 83 (18), 43 (44). CI-MS (NH_3): 152 (100, M^+), 135 (47). Anal. calc. for C_9H_9FO (152.17): C 71.04, H 5.96, F 12.49; found: C 70.72, H 5.92, F 12.49.

4.5. *6-Fluoro-1-phenyl-1,2-dihydrocyclobutabenzen-1-ol* (**2**; R^1 = Ph, R^6 = F). Following procedure in *4.1*, **1r** (300 mg, 2.20 mmol), upon treatment with PhLi (2.2 ml, 4.4 mmol) in THF (15 ml), gave a yellowish oil, which was chromatographed on silica (15 g). With CH_2Cl_2, a light-yellow oil was eluted, which solidified upon standing. Crystallization from petroleum ether gave **2** (R^1 = Ph, R^6 = F; 290 mg, 61%). Colorless crystals. M.p. 53–55°. IR (KBr): 3320, 1600, 1472, 1239, 1201, 1149, 1058, 1004, 776, 697. ^{1}H-NMR: 3.09 (*s*, OH); 3.52 (*d*, *J* = 14.2, H–C(2)); 3.59 (*d*, *J* = 14.2, H–C(2)); 6.89–6.97 (*m*, 2 H); 7.26–7.47 (*m*, 4 H); 7.49 (*d*, *J* = 8.2, H–C(2′), H–C(6′)). ^{13}C-NMR: 48.8 (CH_2); 81.0 (C); 114.3 (*d*, *J* = 20, C(5)); 120.2 (*J* = 4.2, C(3)); 125.8, 127.9, 128.4 (CH); 131.6 (*J* = 5.8, C(4)); 132.9 (*d*, *J* = 16, C(6a)); 142.7 (C); 144.5 (*J* = 8.4, C(2a)); 156.4 (*J* = 255, C(6)). EI-MS (70 eV): 214 (23, M^+), 213 (100), 193 (16), 165 (13), 137 (19), 105 (34), 77 (36). Anal. calc. for $C_{14}H_{11}FO$ (214.24): C 78.49, H 5.18, F 8.87; found: C 78.37, H 5.31, F 8.90.

5. *Representative Procedure from* Table 2. 5.1. *2-Fluoro-6-methyl-α-nitroacetophenone* (**6**; R^1 = NO_2CH_2, R^6 = F; procedure *A*). To a soln. of LDA (2.5 mmol) in THF (20 ml), $MeNO_2$ (1.0 ml, 18.5 mmol) was added. After stirring for 1 h at r.t., ketone **1r** (250 mg, 1.83 mmol) in THF (10 ml) was added. After 2.5 h at r.t., the reaction was quenched with 2N HCl (5 ml) and H_2O. Workup as usual gave, after bulb-to-bulb distillation, 280 mg of an oil (b.p. 90–92°/0.01 Torr), which solidified upon standing. Recrystallization from MeOH yielded **6** (R^1 = NO_2CH_2, R^6 = F; 250 mg, 70%). Colorless crystals. M.p. 65–66°. IR (KBr): 3093, 2982, 2933, 1690, 1609, 1563, 1466, 1381, 1256, 1200, 799, 676. ^{1}H-NMR: 2.47 (*s*, Me); 5.67 (*d*, *J* = 2.8, CH_2NO_2); 6.98–7.05 (*m*, H–C(3)); 7.12 (*d*, *J* = 6.8, H–C(5)); 7.40–7.43 (*m*, H–C(4)). ^{13}C-NMR: 20.6 (Me); 84.7 (*d*, *J* = 11.5, CH_2NO_2); 110 (C); 113.6 (*d*, *J* = 23, C(3)); 128 (*d*, *J* = 3.1, C(5)); 133.8 (*d*, *J* = 9.9, C(4)); 141.8 (*d*, *J* = 2.3, C(1)); 161.6 (*d*, *J* = 245, C(2)); 187.1 (CO). EI-MS (70 eV): 197 (1, M^+), 151 (34), 137 (100), 109 (39), 82 (23). CI-MS (NH_3): 215 (27, $[M + NH_4]^+$), 170 (100). Anal. calc. for $C_9H_8FNO_3$ (197.17): C 54.83, H 4.09, N 7.10; found: C 54.84, H 3.99, N 7.46.

6. *Attempts at Trapping of Carbanion* **5** (R^1 = Me, R^6 = F). 6.1. *Deuteration Experiment.* Consecutive treatment of **2** (R^1 = Me, R^6 = F) with 0.5N MeONa in MeOD (20 min, 65°) and, after isolation as usual, with 0.5N MeONa in MeOH gave deuterated 3′-fluorophenylpropan-2-one as colorless oil of b.p. 95–110°/15 Torr. ^{1}H-NMR: 2.17 (*s*, 3 H); 3.69 (*s*, 2 H); 6.92–7.00 (*m*, 2 H instead of 3 H in non-deuterated sample); 7.25–7.32 (*m*, 1 H). ^{13}C-NMR: 29.4 (Me); 50.4 (CH_2); 114.0 (*d*, *J* = 21, C(4′)); 116.0 (*dt*, *J* = 21, 24, of low intensity instead of *d*, *J* = 21 in non-deuterated sample C(2′)); 125.0; 130.0 (C(6′)); 136.4 (*d*, *J* = 7.6, C(5′)); 163.9 (*d*, *J* = 247, C(3′)); 205.2 (CO).

6.2. *1-(3′-Fluorophenyl)-4-phenylbut-3-en-2-one* (**9**). To a soln. of **2** (R^1 = Me, R^6 = F; 150 mg, 1.0 mmol) and PhCHO (312 mg, 2.9 mmol) in THF (25 ml), BuLi (1.3 mmol) was added at −78°. The soln. was kept at −20° for 20 min and at r.t. for 3 h. Then, it was quenched with 2N HCl (5 ml) and worked up as usual yielding a yellow oil (196 mg), which was chromatographed on silica (8 g). Elution with toluene and crystallization from petroleum ether gave **9** (102 mg, 43%). Colorless crystals. M.p. 52–53°. IR (KBr): 1660, 1440, 1245, 1165, 1165, 740. ^{1}H-NMR: 3.93 (*s*, CH_2); 6.77 (*d*, *J* = 16, H–C(3)); 6.92–7.06 (*m*, 3 H); 7.25–7.34 (*m*, 1 H); 7.36–7.42 (*m*, 3 H); 7.49–7.56 (*m*, 2 H); 7.63 (*d*, *J* = 16, H–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 47.7 (CH_2); 113.9 (*d*, *J* = 20.5, C(4′)); 116.5 (*d*, *J* = 21, C(2′)); 125.0 (CH); 125.2 (*d*, *J* = 2.9, C(6′)); 128.4, 128.9 (CH); 130.1 (*d*, *J* = 8, C(5′)); 130.7 (CH); 134.3 (C); 136.7 (*d*, *J* = 7.7, C(1′)); 143.7 (CH); 162.2 (*d*, *J* = 245, C(3′)); 196.4 (CO). EI-MS (70 eV): 51 (6), 131 (100), 103 (34), 77 (20), 51 (6). CI-MS (NH_3): 258 (38, $[M + NH_4]^+$), 241 (100, $[M + H]^+$), 131 (9). Anal. calc. for $C_{16}H_{13}FO$ (240.28): C 79.98, H 5.45, F 7.91; found: C 79.94, H 5.46, F 7.89.

6.3. *1-(3′-Fluorophenyl)-4-hydroxy-4-phenylbutan-2-one* (**10**). To a soln. of *t*-BuOK (105 mg, 0.94 mmol) in THF (12 ml) at −78°, **2** (R^1 = Me, R^6 = F; 120 mg, 0.8 mmol) and PhCHO (167 mg, 1.6 mmol) in THF (8 ml) were added. After stirring for 2 h at −78°, the reaction was quenched with 2N HCl (5 ml) and worked up as usual yielding 125 mg of an oil (b.p. 120–150°/15 Torr). Chromatography on silica (10 g) with toluene led to **10** (78 mg, 38%). Colorless crystals from pentane. M.p. 47.5–49.5°. IR (KBr): 3475, 1700, 1440, 1055, 735. ^{1}H-NMR: 2.78 (*dd*, *J* = 17.2, 3.5), 2.90 (*dd*, *J* = 17.2, 8.8) (H–C(3)); 3.24 (br. *s*, OH); 3.68 (*s*, 2 H–C(1)); 5.12 (*dd*, *J* = 8.8, 3.5, H–C(4)); 6.83–6.98 (*m*, 3 H); 7.23–7.34 (*m*, 6 H). ^{13}C-NMR: 50.2, 50.5 (CH_2); 69.9 (CH); 114.3 (*d*, *J* = 21, C(4′)); 116.3 (*d*, *J* = 21, C(2′)); 125.0 (*d*, *J* = 2.8, C(6′)); 125.5, 127.6, 128.4 (CH); 130.0 (*d*, *J* = 8.3, C(5′)); 135.6 (*d*, *J* = 7.2, C(1′)); 142.5 (C); 162.5 (*d*, *J* = 245, C(3′)); 207.4 (CO). EI-MS (70 eV): 258 (6, M^+), 107 (100), 77 (41), 43 (76). CI-MS (NH_3): 258 (54, M^+), 170 (100). Anal. calc. for $C_{16}H_{15}FO_2$ (258.27): C 74.40, H 5.85; found: C 74.15, H 5.95.

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