New Reactions of γ-Halocarbanions: Simple Synthesis of Substituted Tetrahydrofurans

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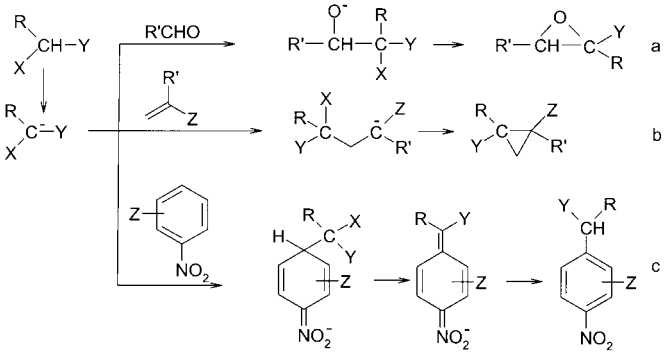
Dedicated to Professor Waldemar Adam on the occasion of his 65th birthday

Abstract: The treatment of 4-chlorobutyronitrile, 3-chloropropyl phenyl sulfone, and other related compounds with a base afforded γ-halocarbanions that undergo fast intramolecular substitution of the halogen to produce substituted cyclopropanes. We found that these short-lived carbanionic intermediates can be trapped with active external electrophilic partners, such as aldehydes, to give the aldol anions. These anions then undergo rapid intramolecular substitution of chloride to produce 2,3-disubstituted tetrahydrofurans. Under the right conditions, yields of tetrahydrofurans are excellent. Similar reactions with ketones gives 2,2,3-trisubstituted furans, but this process is usually less efficient. Ratios between the rates of intramolecular and intermolecular processes were qualitatively estimated by competitive experiments. It was shown that γ-halo and γ-trimethylammonium substituents substantially increase the kinetic CH acidity of alkane nitriles and sulfones.

Keywords: aldol reaction · carbanions · kinetics · ring formation · tetrahydrofurans

Introduction

Carbanions that contain halogen substitutents are interesting potential intermediates in organic synthesis. Thanks to the presence of a strongly nucleophilic carbanionic center as well as a leaving group in one molecule, such carbanions should be able to enter a variety of reactions. Indeed, α-halocarbanions have found wide application in organic synthesis as versatile active intermediates. The most important reactions of α-halocarbanions, namely the Darzens condensation,[1] additions to electrophilic alkenes producing cyclopropanes,[2] and reactions with nitroarenes resulting in vicarious nucleophilic substitution of hydrogen,[3] are shown in Scheme 1.



Scheme 1. Typical reactions of α-halocarbanions.

In contrast to α-halocarbanions, reactions of carbanions that contain halogen atoms in other positions with respect to the carbanionic center, namely β, γ, and δ, are practically limited to intramolecular processes, such as the base-induced β-elimination that proceeds with a E1cb mechanism[4] and cyclization to form cyclopropane derivatives.[5, 6] Intermolecular reactions of such halocarbanions are essentially unknown. It should be mentioned that the majority of examples of intramolecular substitution giving cyclopropanes are reported for γ-halocarbanions generated by the addition of α-halocarbanions to Michael acceptors[2] (Scheme 1b), or produced in the course of alkylation of methylenic carbanions with 1,2-dihaloalkanes.[6] An important group of processes that proceed with γ-halocarbanions are intramolecular substitution reactions, which are followed by further fast transformations of the initially formed three-membered carbocyclic or heterocyclic rings. The Favorski reaction of α-halodialkyl ketones[7] and the Ramberg–Bäcklund reaction of α-halodialkyl sulfones[8] belong to this category. The only reported intermolecular reactions of β- and δ-halocarbanions is reprotonation observed as isotope exchange during mechanistic studies of E1cb β-elimination[9] or formation of side-products in cycloalkylation of methylenic carbanions with 1,3-dihaloalkanes.[6, 10] In our literature search, we were not able

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to find any intermolecular reactions of γ-halocarbanions. In the only related paper, condensation of the tin enolate of γ-chlorobutyrophenone with aromatic aldehydes to give substituted tetrahydrofurans in moderate yields was reported; on the other hand, the lithium enolate of this ketone does not enter similar reaction with aldehydes.[11]

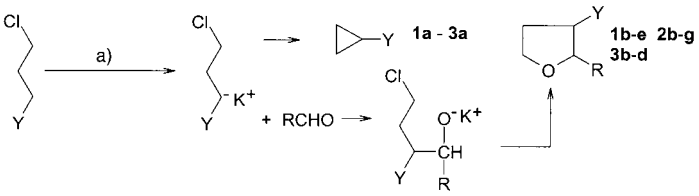
In our preceding short communication, we reported that the carbanion of γ-chlorobutyronitrile generated under PTC (phase-transfer catalytic) conditions can be trapped by external electrophilic reagents, aromatic aldehydes for example, to produce the corresponding aldol-type anions which enter further intramolecular reactions to give 2-aryl-3-cyanotetrahydrofurans.[12]

Substituted tetrahydrofuran rings are present in numerous natural products[13] and there is a great interest in methods of constructing such rings.[14] The most common strategies that have been used to construct tetrahydrofuran rings is the formation of carbon–oxygen bonds by means of acid-catalyzed cyclizations.[15] Recently, a variety of functionalized 2-alkylidenetetrahydrofuran derivatives were obtained by cyclization reactions of 1,3-dicarbonyl dianions and 1,3-bis-silyl enol ethers.[16] Di- and trisubstituted tetrahydrofurans can be produced by the oxidation of dienes,[17] and metal-catalyzed cycloisomerization of allyl propargyl ethers.[18] On the other hand, there are limited examples of cyclization to form 2,3-disubstituted tetrahydrofurans.

In this paper, we report a full account of our studies of reactions of γ-halocarbanions with aldehydes and ketones. This represents a new and general method for the synthesis of 2,3-substituted tetrahydrofurans.

Results and Discussion

Because of the rather low C–H acidity of γ-chlorobutyronitrile, its deprotonation with concentrated aqueous NaOH under PTC (phase-transfer catalytic) conditions is rather a slow process; thus the PTC reactions of this nitrile with aldehydes were accompanied by partial decomposition of the latter. As a consequence, the yields of the substituted cyanotetrahydrofurans reported in our communication,[12] although usually good, were far from being excellent. In order to improve the results and expand the scope of this new synthetic method, we have used stronger bases and also other precursors of γ-halocarbanions. In preliminary experiments, we found that *t*BuOK in THF is the most convenient and efficient base/solvent system for this reaction. Treatment of an equimolar mixture of 4-chlorobutyronitrile (**1**) and benzaldehyde in concentrated THF solution with *t*BuOK at −30 °C resulted in a fast reaction to give the expected 2-phenyl-3-cyanotetrahydrofuran in 78% yield of isolated product. A similar reaction proceeded with other aromatic aldehydes and also cinnamaldehyde. In all cases, yields of the substituted tetrahydrofurans exceeded 76%. The reaction was equally efficient when 3-chloropropyl phenyl sulfone (**2**) and aldehydes in THF were treated with *t*BuOK. The expected 2-aryl-3-phenylsulfonyltetrahydrofurans were obtained in yields exceeding 82%. Also *tert*-butyl-4-chlorobutyrate (**3**) enters this reaction to give 2-aryl-3-carbo-*tert*-butoxytetrahydrofurans (Scheme 2). Yields of these products were somewhat lower than the 3-cyano- and 3-phenylsulfonyl derivatives, but were still of preparative value.



Y = CN **1**, SO_2Ph **2**, COO*t*Bu **3**,

Scheme 2. Synthesis of cyclopropanes and tetrahydrofurans through intramolecular and intermolecular reactions of γ-chlorocarbanions. a) *t*BuOK, −30 °C, 0.5 M solution of **1**, **2**, **3** in THF.

Under identical conditions, but without aldehydes, all of these carbanion precursors cyclized to the corresponding cyclopropanes **1a**–**3a** in high yields. The reaction and results are presented in Scheme 2 and Table 1.

Table 1. Reactions of γ-chlorocarbanions with aldehydes.[a]

Reactants Y		R	Cyclo-propane	%	Products Tetra-hydrofuran	%	*trans*/*cis* ratio
CN	**1**	–[b]	**1a**	89	–	–	–
CN	**1**	Ph	**1a**	21	**1b**	78	79/21
CN	**1**	*p*-ClPh	**1a**	16	**1c**	77	79/21
CN	**1**	*p*-MePh	**1a**	14	**1d**	82	81/19
CN	**1**	PhCH=CH	**1a**	15	**1e**	76	69/31
$PhSO_2$	**2**	–[b]	**2a**	94	–	–	–
$PhSO_2$	**2**	Ph	**2a**	0	**2b**	95	100/0
$PhSO_2$	**2**	*p*-ClPh	**2a**	15	**2c**	83	100/0
$PhSO_2$	**2**	*p*-MePh	**2a**	8	**2d**	88	100/0
$PhSO_2$	**2**	PhCH=CH	**2a**	15	**2e**	82	100/0
$PhSO_2$	**2**	Et(Me)CH	**2a**	62	**2f**	35	100/0
$PhSO_2$	**2**	$(Me_3)C$	**2a**	10	**2g**	76	100/0[c]
COO*t*Bu	**3**	–[b]	**3a**	76	–	–	–
COO*t*Bu	**3**	Ph	**3a**	15	**3b**	61	100/0
COO*t*Bu	**3**	*p*-ClPh	**3a**	28	**3c**	44	100/0
COO*t*Bu	**3**	*p*-MePh	**3a**	32	**3d**	61	100/0

[a] Notations as in Scheme 2, all reactions, except with aliphatic aldehydes, were carried out with 0.5 M solutions of **1**, **2**, and **3** in THF. [b] Experiments without aldehydes. [c] Only one isomer, apparently the *trans* isomer, was produced; its geometry was not determined unambiguously.

Since there are two competing processes in the reaction system, namely monomolecular reaction of intramolecular nucleophilic substitution producing cyclopropanes and bimolecular intermolecular addition as a step in the formation of tetrahydrofurans, the outcome of this competition should be affected, inter alia, by concentration and ratio of the reacting partners.

The results presented in Table1 1 were obtained under standard conditions: the carbanion precursors and aldehydes were used in a ratio close to equimolar (1:1.2), whereas the concentration of the carbanion precursor in the THF solution was 0.5 M. Under such conditions, the reaction of **2** with benzaldehyde gave the corresponding substituted tetrahydrofuran **2b** exclusively with a yield of 95%. When the concentration of the reacting species was lower, for example,

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the concentration of **2** was 0.1M and 0.05M, the competing process of intramolecular cyclization become important: yields of **2b** and **2a** were 79%, 17% and 74%, 22%, respectively. Thus, the ratio of the cyclopropanes to tetrahydrofurans can be changed in favor of the latter when aldehydes were used in substantial excess and the reaction was carried out in more concentrated solutions. For example, in the reaction of **1** with benzaldehyde, when the concentration of **1** in THF was 1.14M and the ratio **1**:benzaldehyde was 1:2.4, **1a** was produced with a high yield of 90%.

The successful synthesis of substituted tetrahydrofurans, as shown in Scheme 2, indicates that potassium salts of the corresponding γ-chlorocarbanions stabilized with CN, SO_2Ph, and COO*t*Bu groups enter fast intermolecular reactions with active external electrophilic partners, such as aromatic aldehydes, to produce aldol anions that subsequently undergo an intramolecular substitution of the chloride to produce tetrahydrofurans. In the case of carbanions of **1** and **2**, the rate of intermolecular addition under the standard conditions was much faster than intramolecular substitution, so substituted tetrahydrofurans were the dominant products, whereas cyclopropanes **1a** and **2a** were formed in small quantities. On the other hand, under these conditions, the rate of addition of the carbanion of **3** to aldehydes was only somewhat higher than its intramolecular cyclization.

Thus the base-promoted reactions of γ-chlorobutyronitrile, γ-chloropropyl phenyl sulfone, and *tert*-butyl γ-chlorobutyrate with aromatic aldehydes is an efficient way of synthesizing 2-aryl-3-substituted tetrahydrofurans. The reaction is less efficient with aliphatic aldehydes. For instance, in the reaction of **2** with butyraldehyde under the standard conditions, the expected substituted tetrahydrofuran was formed in low yield. A somewhat better result was obtained in the reaction of **2** with 2-methylbutyraldehyde carried out in a more concentrated system, namely a 1M solution of **2** in THF with a 35% yield of **2f**. It appears that the reason for this is the high CH acidity of the CH_2 and CH groups α to the carbonyl group of the aldehydes. Thus, their deprotonation followed by transformations of the produced enolates dominated compared to the desired reactions. Indeed, the reaction of **2** with pivalyl aldehyde gave the expected tetrahydrofuran **2g** in a yield similar to that obtained with aromatic aldehydes.

In the reaction of the γ-chlorocarbanions with aldehydes, the substituted tetrahydrofurans can be formed as two geometrical isomers. Indeed, in our preliminary communication, we reported that the PTC reaction of γ-chlorobutyronitrile (**1**) with aldehyde gave mixtures of *cis* and *trans* isomers of 2-aryl-3-cyanotetrahydrofurans, the latter being the major products.[12] Under the conditions used in the present studies, the reaction of **1** with aldehydes also produced mixtures of *cis* and *trans* tetrahydrofurans in ratios of approximately 4:1, whereas the other carbanion precursors, **2** and **3**, practically only gave *trans* isomers of the tetrahydrofurans. There are two possibilities concerning the factors which control the stereochemical outcome of these reactions: 1) substituted tetrahydrofurans, which are still C–H acids, can undergo epimerization under the reaction conditions so the composition of the products reflects their thermodynamic stability. 2) Epimerization does not proceed so that the ratio of stereoisomers is decided by the addition step, which can produce *threo* and *erythro* isomers of the aldol anions that cyclize to *trans*- and *cis*-disubstituted tetrahydrofurans, respectively. In both of these cases, steric interactions of the aryl groups of aldehydes and Z groups promote the formation of the less hindered isomer of the tetrahydrofuran or the aldol. Since this interaction is the smallest in the case of **1**, in which Z is a small cyano group, substantial amounts of the *cis* isomers were formed only in these cases. To clarify which step is decisive for the stereochemical outcome of the reaction, pure *trans* **1b** was subjected to the reaction conditions. It gave a mixture of *trans*- and *cis*-**1b** identical to that produced in the reaction between **1** and benzaldehyde. Therefore, it appears that the composition of the product mixture reflects the thermodynamic stabilities of the isomers. This conclusion is supported by the observation that the composition of the mixture of *cis*- and *trans*-**1b** produced according to Scheme 2 is not affected by the reaction time.

The possibility of synthesizing tetrahydrofurans by the reaction of γ-chlorocarbanions with aldehydes depends upon a delicate balance between intramolecular substitution producing cyclopropane ring, which is known to be a very fast process, and intermolecular addition to the carbonyl groups. To estimate the relationship between the rates of the processes involved and the lifetime of the γ-chlorocarbanions, a solution of **1** in THF at low temperature was first treated with base in THF, and then benzaldehyde was added after a short time. Even when the base was added at $-70\,^{\circ}C$ and the mixture treated immediately with benzaldehyde, only the cyclopropane **1b** was produced. A similar result was obtained in an identical experiment with **2**. These observations indicate that deprotonation and intramolecular cyclization are really very fast processes that cannot be studied by simple methods. On the other hand, when γ-chlorocarbanion precursor **1** or **2** was treated with base in the presence of benzaldehyde, practically only the tetrahydrofurans were produced. This indicates that rate of the addition of these carbanions to benzaldehyde is much higher than rate of the cyclization. To estimate the rate of intramolecular substitution of the halogen with the aldol anion, which leads to a five-membered tetrahydrofuran ring, the reaction mixture of **2** and benzaldehyde upon addition of *t*BuOK was immediately treated with MeI, a very active alkylating agent. No traces of the *O*-methylated aldol product were observed indicating that this intramolecular substitution is also a very fast process. The same results were obtained when trimethylsilyl chloride was used instead of the MeI. Even when a mixture of **2**, benzaldehyde, and MeI were treated with *t*BuOK, the reaction gave exclusively tetrahydrofuran **2b**. Thus, intramolecular substitution of a moderately active leaving group, such as chloride, by the alkoxide anion of the aldol to form the five-membered ring of tetrahydrofuran proceeds much faster than its intermolecular reaction with very active alkylating and silylating agents (Scheme 3). Surprisingly, the rate of cyclization to produce a five-membered ring by intramolecular substitution of the chloro substituent which is a moderately active leaving group, was very high.

Any changes that favor intramolecular substitution or disfavor the addition should shift the reaction towards the

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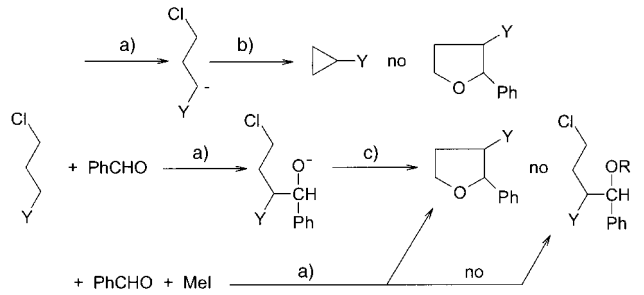
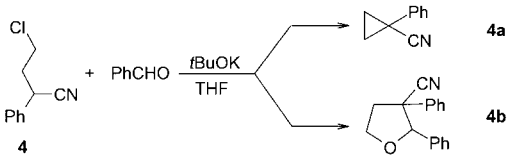


Scheme 3. Competition between intermolecular and intramolecular reactions in THF solutions. a) *t*BuOK, −70 °C; b) PhCHO, c) MeI or Me_3SiCl.

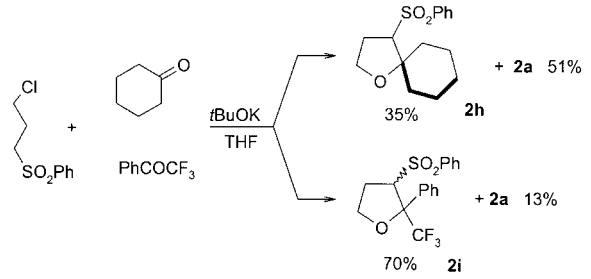
formation of cyclopropanes, at the expense of the formation of tetrahydrofurans. Thus, one can expect that the corresponding γ-bromocarbanions, generated from 4-bromobutyronitrile and 3-bromopropyl phenyl sulfone, should cyclize faster than their chloro analogues. Indeed, the reaction of these compounds with benzaldehyde in the presence of *t*BuOK under the standard conditions (0.5 M concentration of **1** and **2** in THF) gave exclusively the corresponding cyclopropanes **1a** and **2a**, while formation of the tetrahydrofurans was not observed. One should stress that under the same conditions, the reaction of chlorosulfone **2** with benzaldehyde gives the tetrahydrofuran derivative **2b** in 95% yield. When the reaction of these bromocarbanion precursors was carried out in a more concentrated solution (0.91 M) and 50% excess of benzaldehyde (ratio 1:1.5) was used, namely conditions that should favor the intermolecular reaction, compounds **1b** and **2b** were obtained in a small, but essential, yield of 25% and 27%, respectively.

The rate of addition of carbanions to the carbonyl group is strongly affected by steric effects. Usually, additional substituents at the carbanionic center decelerate this process. Indeed, the reaction of an equimolar mixture of 4-chloro-2-phenylbutyronitrile (**4**) and benzaldehyde under the standard conditions gave only 1-cyano-1-phenylcyclopropane (**4a**), while the formation of the tetrahydrofuran derivative was not observed. The substituted tetrahydrofuran **4b** was only formed when benzaldehyde was used in a substantial excess, albeit still in low yield of 9% (Scheme 4).



Scheme 4.

It is known that nucleophilic addition to the carbonyl group of ketones proceeds more slowly than that to the carbonyl group of aldehydes. Indeed, attempts to use ketones in the reaction with γ-chlorocarbanions to produce 2,2,3-trisubstituted tetrahydrofurans were less successful. The reaction of **2** with cyclohexanone, carried out under the standard conditions, which in the reaction with benzaldehyde assures a high yield 95% of the tetrahydrofuran **2b**, gave mostly cyclopropane **2a** in 84% yield and only 5% of the expected spiro derivative of cyanophenylsulfonylotetrahydrofuran (**2h**). When cyclohexanone was used in a substantial excess, fivefold relative to **2**, and in a concentrated system (concentration of **2** = 0.9 M), the addition was favored and the yield of **2h** improved to 35%. Under similar conditions and threefold excess of the ketone, the reaction of **2** with the more electrophilic α,α,α-trifluoroacetophenone proceeded satisfactorily to give 2-trifluoromethyl-2-phenyl-3-phenylsulfonyltetrahydrofuran (**2i**) in 70% yield as a mixture of two geometrical isomers, whereas **2a** was formed in 13% yield (Scheme 5). The mixture was separated by chromatography to give two products with melting points of 96 °C and 102 °C in a 1:3.4 ratio. The steric structures of these isomers were not determined.



Scheme 5.

These results confirm that nucleophilic addition to the carbonyl group of ketones proceeded more slowly than that to the aromatic aldehydes, whereas the highly electrophilic ketone α,α,α-trifluoroacetophenone is almost as active as aldehydes.

Halogen substituents provide stabilizing effects in α-halocarbanions and facilitate their generation, hence many reactions of such carbanions can be carried out in the presence of concentrated aqueous NaOH and phase-transfer catalysts (PTC conditions). However, nothing is known about carbanion-stabilizing effects of halogens in the γ-position to the carbanionic center. The observation that γ-chlorobutyronitrile reacts via its carbanion under the PTC conditions,[12, 19] being deprotonated by concentrated aqueous NaOH in the presence of Q^+X^-, whereas butyronitrile does not, suggests that Cl in the γ position to the CH_2 group exerts a noticeable carbanion-stabilizing effect. To make a qualitative estimation of how strong this effect of Cl and some other γ substituents is on the CH acidity of the CH_2 group α to CN and SO_2Ph, we measured the rate of base-catalyzed deuterium exchange in $XCH_2CH_2CH_2Y$ compounds. When Y is CN or SO_2Ph, the exchange takes place at the CH_2 group α to Y. For reasons of simplicity, the time to 50% conversion was measured (Table 2).

The exchange was carried out in protic media assuring rapid reprotonation of the generated carbanions so that the observed rate of deuterium incorporation was limited by the rate of deprotonation, hence it reflects the kinetic CH acidity. The results indicate that γ-halo substituents do indeed substantially accelerate the deprotonation rate of butyronitrile and propyl phenyl sulfone, hence they exert a strong carbanion-stabilizing effect. In this series of measurements,

Table 2. Deuterium exchange of γ-substituted butyronitriles and propyl phenyl sulfones.

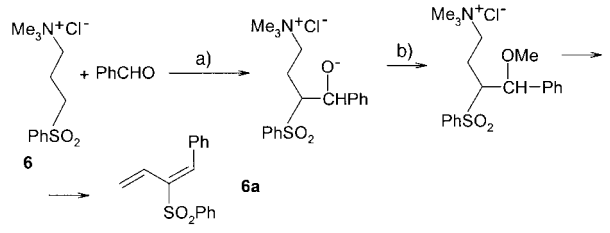
$XCH_2CH_2CH_2Y \xrightarrow{[a]} XCH_2CH_2CD_2Y$

Y	X	$t^1/_2$ [s]
CN	H	64800
CN	Cl	324
CN	Br	254
CN	Me_3N^+[b]	13[c]
SO_2Ph	H	900
SO_2Ph	F	43
SO_2Ph	Cl	22
SO_2Ph	Br	17
SO_2Ph	Me_3N^+[b]	1.2[c]

[a] 10% NaOD/D_2O (1 part), EtOD (1.4 parts) DMSO (1 part), 21 °C. [b] In the form of chlorides. [c] Value recalculated from experiments without DMSO.

we have also included the corresponding tetraalkylammonium salts: γ-trimethylammonia-butyronitrile chloride, $Cl^-Me_3N^+CH_2CH_2CH_2CN$ (**5**), and 3-trimethylammoniapropyl phenyl sulfone chloride, $Cl^-Me_3N^+CH_2CH_2CH_2SO_2Ph$ (**6**). Interestingly, the deuterium exchange in these compounds was much faster than for X = Cl, Br, and F. Thus, measurements were made under milder conditions and the corresponding data in Table 2 was recalculated for the general conditions. The nature of the carbanion-stabilizing action of the electron-withdrawing substituents in the γ-position is presently unclear.

The observation that the acidity of 3-trimethylammonia propyl phenyl sulfone chloride (**6**) is substantially higher than that of the chlorosulfone **2**, whereas the trimethylammonium substituent is a less efficient leaving group than chloride, suggested the possibility of obtaining the aldol produced by addition of the carbanion of **6** to aldehydes. The reaction of **6** with benzaldehyde in the presence of *t*BuOK under the standard conditions produced a complicated mixture of compounds, which was not separated. Attempts to trap the intermediate aldol with MeI resulted in the formation of 1-phenyl-2-phenylsulfonyl butadiene (**6a**) in moderate yield. This diene was obtained as the main product, in 62% yield when a mixture of **6**, benzaldehyde, and MeI was treated with excess *t*BuOK. Apparently, the methyl ether produced by methylation of the aldol undergoes E1cb elimination followed by the Hofmann elimination of trimethyl amine (Scheme 6).



Scheme 6. Reaction of the carbanion of 3-trimethylammoniapropyl phenyl sulfone with benzaldehyde and methyl iodide. a) *t*BuOK, b) MeI.

The observation that active electrophiles, such as aldehydes, can efficiently trap short-lived γ-halocarbanions to produce substituted tetrahydrofurans have substantial value for synthesis and open new possibilities that are presently being explored. Strong effects of halogen and trimethylammonium substituents in the γ-position that increase the CH acidity needs further study and rationalization.

Experimental Section

All reactions were performed under argon in oven-dried glassware. THF was freshly distilled from sodium/benzophenone. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini 200 MHz and Varian Mercury 400 MHz.

General procedure for the reaction of 1–3 with aldehydes—synthesis of tetrahydrofurans: A solution of the carbanion precursor **1**–**3** (2.5 mmol) and aldehyde (3 mmol) in THF (5 mL) was cooled to −30 °C, and commercial (99%) potassium *tert*-butoxide (0.505 g, 4.5 mmol) was added in 3–4 portions at this temperature. The mixture was stirred for 20 min, quenched with aqueous NH_4Cl (20 mL), and extracted with CH_2Cl_2. The organic phase was dried ($MgSO_4$), and the solvent evaporated. The residue was purified by column chromatography on silica gel or preparative TLC (hexane/ethyl acetate). Ratio of cyclopropanes **1a**–**3a** to tetrahydrofurans was determined by gas-chromatographic analyses of the mixtures formed in analogous experiments carried out with diphenyl as an internal standard.

Isotope-exchange experiments: A solution of 10% NaOD in D_2O (prepared by dissolution of Na_2O (0.75 g) in D_2O (9.2 g)), EtOD (14 g), and DMSO (10 g) was used. The carbanion precursor (0.5 mmol) was dissolved in this solution (1.7 g) and stirred at 21 °C for a given time. The mixture was acidified with dilute HCl, extracted with Et_2O, and the product analyzed by ^{1}H NMR spectroscopy. In the case of the ammonium salts **5** and **6**, the acidified mixture was evaporated to dryness, the solid extracted with DMSO, and the solution analyzed by ^{1}H NMR spectroscopy.

Cyclopropyl cyanide (1a):[20] ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.98–1.18 (m, 4H), 1.30–1.42 ppm (m, 1H).

2-Phenyl-3-cyanotetrahydrofuran (1b):[12] *trans Isomer*: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.32–2.63 (m, 2H), 2.74–2.97 (m, 1H), 4.06–4.33 (m, 2H) , 4.99 (d, ^3J(H,H) = 7.70 Hz, 1H), 7.34–7.48 ppm (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.71, 37.67, 68.57, 84.25, 120.40, 126.01, 129.14, 129.32, 139.20 ppm.

cis Isomer: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.37–2.60 (m, 2H), 3.39–3.48 (m, 1H), 3.97–4.09 (m, 1H), 4.32–4.43 (m, 1H), 5.01 (d, ^3J(H,H) = 6.08 Hz, 1H), 7.34–7.47 ppm (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.96, 37.22, 67.91, 82.10, 119.55, 126.63, 129.03, 129.13, 137.65 ppm.

2-(4-Chlorophenyl)-3-cyanotetrahydrofuran (1c):[12]

trans Isomer: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.37–2.52 (m, 2H), 2.74–2.86 (m, 1H), 4.01–4.27 (m, 2H), 4.90 (d, ^3J(H,H) = 7.74 Hz, 1H), 7.26–7.47 ppm (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.63, 37.70, 68.59, 83.56, 120.06, 127.40, 129.50, 134.92, 137.68 ppm.

cis Isomer: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.42–2.54 (m, 2H), 3.35–3.45 (m, 1H), 3.97–4.09 (m, 1H), 4.31–4.42 (m, 1H), 4.98 (d, ^3J(H,H) = 6.04 Hz, 1H), 7.32–7.46 ppm (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.93, 37.17, 67.97, 81.48, 119.29, 128.05, 129.26, 134.89, 136.17 ppm.

2-(4-Methylphenyl)-3-cyanotetrahydrofuran (1d):[12]

trans Isomer: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.40 (s, 3H), 2.31–2.60 (m, 2H), 3.38 (m, 1H), 4.04–4.32 (m, 2H), 4.96 (d, ^3J(H,H) = 7.90 Hz, 1H), 7.20–7.36 ppm (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.83, 31.69, 37.66, 68.47, 84.23, 120.47, 126.01, 129.97, 136.17, 138.94 ppm.

cis isomer: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.41 (s, 3H), 2.40–2.53 (m, 2H), 3.35–3.45 (m, 1H), 3.94–4.07 (m, 1H), 4.27–4.42 (m, 1H), 4.97 (d, ^3J(H,H) = 6.22 Hz, 1H), 7.18–7.36 ppm (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.82, 31.93, 37.23, 67.83, 82.06, 119.55, 126.57, 129.72, 134.52, 138.82 ppm.

2-(2-Phenylvinyl)-3-cyanotetrahydrofuran (1e):[12]

trans Isomer: oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.21–2.56 (m, 2H), 2.84 (dt, ^3J(H,H) = 8.92 , 7.69 Hz, 1H), 3.97–4.20 (m, 2H), 4.56–4.64 (m, 1H), 6.20 (dd, J = 6.70, 15.88 Hz, 1H), 6.81 (dd, ^3J(H,H) = 15.81, 1.12 Hz, 1H), 7.30–7.49 ppm (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.46, 35.54, 68.18, 83.52, 120.28, 125.99, 127.30, 128.88, 129.21, 134.15, 136.24 ppm.

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cis Isomer: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.37-2.49$ (m, 2H), 3.24–3.34 (m, 1H), 3.89–4.01 (m, 1H), 4.17–4.30 (m, 1H), 4.57–4.64 (m, 1H), 6.34 (dd, $^3J(H,H) = 6.96$, 15.79 Hz ,1H), 6.80 (dd, $^3J(H,H) = 1.02$, 15.88 Hz, 1H), 7.30–7.52 ppm (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 31.70$, 35.37, 67.66, 80.64, 119.53, 124.99, 127.45, 128.85, 129.16, 135.06, 136.39 ppm.

Cyclopropyl phenylsulfone (2a):[21, 22] M.p. 33 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.98-1.09$ (m, 2H), 1.31–1.40 (m, 2H), 2.41–2.54 (m, 1H), 7.52–7.70 (m, 2H), 7.89–7.94 ppm (m, 3H).

***trans*-2-Phenyl-3-phenylsulfonyl tetrahydrofuran (2b)**: M.p. 84 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.18-2.38$ (m, 1H), 2.46–2.60 (m, 1H). 3.65–3.74 (m, 1H), 4.02 (dt, $^3J(H,H) = 6.62$, 8.75 Hz, 1H), 4.12–4.23 (m, 1H), 5.33 (d, $^3J(H,H) = 5.24$ Hz, 1H), 7.11–7.28 (m, 5H), 7.49–7.70 (m, 3H), 7.87–7.93 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 28.50$, 68.36, 71.10, 80.03, 125.65, 127.92, 128.47, 128.59, 129.35, 133.96, 138.09, 140.27 ppm; elemental analysis calcd (%) for $C_{16}H_{16}O_3S$ (288.36): C 66.64, H 5.59, S 11.12; found: C 66.48, H 5.54, S 11.15.

***trans*-2-(4-Chlorophenyl)-3-phenylsulfonyl tetrahydrofuran (2c)**: M.p. 88 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.15-2.35$ (m, 1H), 2.43–2.52 (m, 1H), 3.57–3.62 (m, 1H), 4.00 (dt, $^3J(H,H) = 6.41$, 8.75 Hz, 1H), 5.31 (d, $^3J(H,H) = 5.34$ Hz, 1H), 7.09–7.27 (m, 4H), 7.51–7.72 (m, 3H), 7.87–7.93 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 28.69$, 68.40, 71.09, 79.34, 127.15, 128.59, 128.64, 129.44, 133.73, 134.10, 138.02, 138.85 ppm; elemental analysis calcd (%) for $C_{16}H_{15}ClO_3S$ (322.81): C 59.53, H 4.68, S 9.93, Cl 10.98; found: C 59.29, H 4.68, S 9.73, Cl 10.71.

***trans*-2-(4-Methylphenyl)-3-phenylsulfonyl tetrahydrofuran (2d)**: M.p. 94 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.30$ (s, 3H), 2.18–2.38 (m, 1H), 2.46–2.61 (m, 1H), 3.63–3.72 (m, 1H), 4.00 (dt, $^3J(H,H) = 6.51$, 8.81 Hz, 1H), 4.11–4.21 (m, 1H), 5.29 (d, $^3J(H,H) = 5.13$, 1H), 6.99–7.09 (m, 4H) 7.49–7.70 (m, 3H), 7.86–7.92 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.03$, 28.51, 68.27, 71.11, 79.99, 125.59, 128.60, 129.14, 129.33, 133.91, 137. 28, 137.67, 138.16 ppm; elemental analysis calcd (%) for $C_{17}H_{18}O_3S$ (302.39): C 67.52, H 6.00, S 10.60, found: C 67.26, H 5.99, S 10.59.

***trans*-2-(2-Phenylvinyl)-3-phenylsulfonyl tetrahydrofuran (2e)**: M.p. 71 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.19-2.38$ (m, 1H), 2.47–2.63 (m, 1H), 3.51–3.62 (m, 1H), 3.87–4.11 (m, 1H), 4.81 (dt, $^3J(H,H) = 1.04$, 6.24 Hz, 1H), 5.92 (dd, $^3J(H,H) = 6.29$, 15.86 Hz, 1H), 6.36 (dd, $^3J(H,H) = 1.02$, 15.86 Hz, 1H), 7.17–7.32 (m, 5H), 7.52–7.69 (m, 3H), 7.91–7.97 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 28.18$, 67.73, 68.86, 79.37, 126.49, 126.63, 127.95, 128.46, 128.60, 129.38, 131.99, 134.03, 135.84, 138.18 ppm; elemental analysis calcd (%) for $C_{18}H_{18}O_3S$ (314.40): C 68.77, H 5.77, S 10.20; found: C 68.49, H 5.79, S 10.17.

Synthesis of 2-alkyl-3-phenylsulfonyl tetrahydrofuran (2f, 2g): The procedure above was followed with **2** (1 mmol), THF (1 mL), and aliphatic aldehyde (1.2 mmol).

***trans*-2-(1-Methylpropyl)-3-phenylsulfonyl tetrahydrofuran (2f)**: Oil; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.76-0.88$ (m, 9H), 0.99–1.48 (m, 3H), 1.97–2.17 (m, 1H), 2.31–2.47 (m, 1H), 3.41–3.51 (m, 1H), 3.70–3.96 (m, 1H), 4.20–4.26 (m, 1H), 7.54–7.72 (m, 3H), 7.88–7.94 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 11.76$, 13.10, 26.39, 28.80, 38.53, 66.37, 67.62, 81.59, 128.68, 128.75, 129.33, 133.88 ppm; elemental analysis calcd (%) for $C_{14}H_{20}O_3S$ (268.37): C 62.66, H 7.51, S 11.95; found: C 62.42, H 7.44, S 11.76.

2-*tert*-Butyl-3-phenylsulfonyl tetrahydrofuran (2g): M.p. 116 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.84$ (s, 9H), 1.95–2.17 (m, 1H), 2.36–2.48 (m, 1H), 3.49 (ddd, $^3J(H,H) = 1.43$, 3.63, 9.48 Hz, 1H), 3.79–3.92 (m, 1H), 4.02 (dt, $^3J(H,H) = 1.47$, 8.06 Hz, 1H), 4.18 (d, $^3J(H,H) = 3.52$ Hz, 1H), 7.58–7.75 (m, 3H), 7.94–8.01 ppm (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.11$, 29.82, 35.24, 66.31, 68.67, 86.41, 129.49, 129.91, 134.47, 138.82 ppm; elemental analysis calcd (%) for $C_{14}H_{20}O_3S$ (268.37): C 62.66, H 7.51, S 11.95; found: C 62.50, H 7.63, S, 12.09.

***tert*-Butyl cyclopropylcarboxylate (3a)**: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.68-0.80$ (m, 2H), 0.83–0.91 (m, 2H), 1.41 (s, 9H), 1.43–1.51 ppm (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 7.83$, 13.98, 28.02, 79.90, 173.92 ppm.

***trans*-2-Phenyl-3-*tert*-butoxycarbonyl tetrahydrofuran (3b)**: Oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.44$ (s, 9H), 2.22–2.35 (m,2H), 2.87 (dt, $^3J(H,H) = 7.01$, 8.94 Hz, 1H), 3.99–4.05 (m, 1H), 4.11–4.17 (m, 1H), 4.98 (d, $^3J(H,H) = 7.15$ Hz, 1H), 7.22–7.40 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.00, 30.50, 53.32, 68.39, 80.99, 83.46, 125.76, 127.55, 128.30, 141.65, 172.49 ppm; elemental analysis calcd (%) for $C_{15}H_{20}O_3$ (248.32): C 72.55, H 8.12; found: C 72.43, H 8.15.

***trans*-2-(4-Chlorophenyl)-3-*tert*-butoxycarbonyl tetrahydrofuran (3c)**: Oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.44$ (s, 9H), 2.20–2.35 (m, 2H), 2.77–2.83 (m, 1H), 3.99–4.04 (m, 1H), 4.11–4.16 (m, 1H), 4.95 (d, $^3J(H,H) = 7.42$ Hz, 1H), 7.30 ppm (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 28.02$, 30.49, 53.40, 68.42, 81.24, 82.76, 127.18, 128.47, 133.26, 140.17, 172.21 ppm; elemental analysis calcd (%) for $C_{15}H_{19}ClO_3$ (282.77): C 63.71, H 6.77, Cl 12.54; found: C 63.52, H 6.82, Cl 12.60.

***trans*-2-(4-Methylphenyl)-3-*tert*-butoxycarbonyl tetrahydrofuran (3d)**: Oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.44$ (s, 9H), 2.18–2.35 (m, 2H), 2.33 (s, 3H), 2.85 (dt, $^3J(H,H) = 8.97$, 7.32 Hz, 1H), 3.97–4.03 (m, 1H), 4.10–4.16 (m, 1H), 4.95 (d, $^3J(H,H) = 7.32$ Hz, 1H), 7.14 (d, $^3J(H,H) = 7.86$Hz, 2H), 7.24–7.26 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 21.09, 28.01, 30.53, 53.27, 68.29, 80.93, 83.41, 125.71, 128.98, 137.16, 172.59 ppm; elemental analysis calcd (%) for $C_{16}H_{22}O_3$ (262.35): C 73.25, H 8.15; found: C 73.20, H 8.57.

The reaction of 2 with cyclohexanone—synthesis of 2,2-pentamethylene-3-phenylsulfonyl tetrahydrofuran (2h): The procedure given above was followed with **2** (1.5 mmol), THF (1 mL), and cyclohexanone (0.735 g, 7.5 mmol). Yield of **2h** 35%, m.p. 97 °C (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.19-1.31$ (m, 1H), 1.52–1.70 (m, 6H), 1.86–2.13 (m, 4H), 2.45–2.54 (m, 1H), 3.20 (t, $^3J(H,H) = 9.33$ Hz, 1H), 3.73–3.79 (m, 1H), 3.96 (dt, $^3J(H,H) = 4.20$, 8.97 Hz, 1H), 7.55–7.67 (m, 3H), 7.88–7.92 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.60$, 22.96, 25.21, 28.61, 30.45, 37.34, 63.43, 71.26, 83.78, 128.03, 129.23, 133.58, 140. 59 ppm; elemental analysis calcd (%) for $C_{15}H_{20}O_3S$ (280.38): C 64.26, H 7.19, S 11.43; found: C 64.40, H 7.02, S 11.43.

Synthesis of 2-trifluoromethyl-2-phenyl-3-phenylsulfonyl tetrahydrofuran (2i) and 2,3-diphenyl-3-cyano tetrahydrofuran (4b): The procedure given above was used with the precursors of carbanion **2** or **4** (1 mmol), THF (0.6 mL), and the carbonyl compound (3 mmol).

2-Trifluoromethyl-2-phenyl-3-phenylsulfonyltetrahydrofuran (2i): Yield 70%

Isomer 1: M.p. 96 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.39-2.56$ (m, 1H), 2.72–2.91 (m, 1H), 4.20 (q, $^3J(H,H) = 7.69$ Hz, 1H), 4.34 (t, $^3J(H,H) = 7.69$ Hz, 1H), 4.43–4.54 (m, 1H), 7.27–7.64 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 29.61$, 67.78, 68.71, 76.49, 86.58, 127.63, 127.98, 128.00, 128.04, 129.12, 129.14, 133.60, 138.90 ppm; elemental analysis calcd (%) for $C_{17}H_{15}F_3O_3S$ (356.36): C 57.30, H 4.24; found: C 57.40, H 4.29.

Isomer 2: M.p. 102 °C (EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.93-2.08$ (m, 1H), 2.66–2.87 (m, 1H), 3.89–4.07 (m, 2H), 4.42 (dt, $^3J(H,H) = 3.41$, 8.33 Hz, 1H), 7.41–7.74 (m, 6H), 7.87–8.02 ppm (m, 4H); C^1 NMR (100 MHz, $CDCl_3$): $\delta = 31.80$, 67.69, 73.30, 87.47, 127.34, 128.97, 129.11, 129.62, 129.95, 134.66, 137.66, 140.71 ppm; elemental analysis calcd (%) for $C_{17}H_{15}F_3O_3S$ (356.36): C 57.30, H 4.24; found: C 57.53, H 4.44.

1-Cyano-1-phenylcyclopropane (4a):[23] ^{1}H NMH (200 MHz, $CDCl_3$): $\delta =$ 1.41–1.48 (m, 2H), 1.73–1.60 ppm (m, 5H).

2,3-Diphenyl-3-cyano tetrahydrofuran (4b): M.p. 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.87-3.02$ (m, 2H), 4.34–4.45 (m, 1H), 4.52–4.65 (m, 1H), 5.00 (s, 1H), 7.11–7.49 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 41.13$, 55.58, 67.00, 90.04, 119.94, 126.31, 126.54, 127.92, 128.04, 128.51, 128.73, 129.10, 129.37 ppm; HRMS calcd for $C_{17}H_{15}NO$: 249.11536; found: 249.11635

1-Phenyl-2-phenylsulfonyl-1,3-butadiene (6a): Potassium *tert*-butoxide (0.448 g, 4 mmol) was added in 4 portions to a solution of **6** (0.194 g, 0.7 mmol), benzaldehyde (0.106 g, 1 mmol), and MeI (0.312 g, 2.2 mmol) in DMF (5 mL) cooled to −30 °C. The mixture was stirred for 2 min, quenched with aqueous NH_4Cl (5 mL), and water (30 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL), the organic solution was dried, and the solvent was evaporated. The product was purified by preparative TLC (hexane/ethyl acetate 3:1). Yield of **6a**: 0.116 g, 62%; m.p. 83 °C (EtOH); H^1 NMR (200 MHz, $CDCl_3$): $\delta = 5.50$ (td, $^3J(H,H) = 1.24$, 11.72 Hz, 1H), 5.95 (dd, $^3J(H,H) = 1.28$, 17.91 Hz, 1H), 6.42 (ddd, $^3J(H,H) = 1.20$, 11.71, 17.84 Hz, 1H), 7.39–7.68 (m, 8H), 7.90–7.96 ppm (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 124.43$, 126.94, 128.63, 129.16, 129.47, 130.52, 130.95, 133.68, 133.78, 138.60, 139.18, 140.38 ppm; elemental analysis calcd (%) for $C_{16}H_{14}O_2S$ (270.35): C 71.03, H 5.18, S 11.84; found: C 70.97, H 5.26, S 11.70.

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