

Microwave-Assisted Group-Transfer Cyclization of Organotellurium Compounds

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Abstract: Primary- and secondary-alkyl aryl tellurides, prepared by arenetellurolate ring-opening of epoxides/ O-allylation, were found to undergo rapid (3–10 min) grouptransfer cyclization to afford tetrahydrofuran derivatives in 60-74% yield when heated in a microwave cavity at 250 °C in ethylene glycol or at 180 °C in water. To go to completion, similar transformations had previously required extended photolysis in refluxing benzene containing a substantial amount of hexabutylditin. The only drawback of the microwave-assisted process was the loss in diastereoselectivity which is a consequence of the higher reaction temperature. Substitution in the Te-aryl moiety of the secondary-alkyl aryl tellurides (4-OMe, 4-H, 4-CF₃) did not affect the outcome of the group-transfer reaction in ethylene glycol. However, at lower temperature, using water as a solvent, the CF_3 derivative failed to react. The microwave-assisted grouptransfer cyclization was extended to benzylic but not to primary- and secondary-alkyl phenyl selenides.

Microwave-assisted chemistry has much to offer synthetic organic chemists.¹ Although there is probably no such phenomenon as a specific nonthermal "microwave effect", microwave dielectric heating causes an extremely rapid and uniform energy transfer to the reactants of chemical reactions. This will minimize formation of byproducts/decomposition products and increase product yields. In pressurized systems, it is possible to rapidly increase the temperature far above the boiling point of the solvent. Furthermore, the technique is energy efficient and the possibilities for applications in combinatorial/parallel and automated chemistry and environmental benign chemistry are obvious.² Microwaves have been recognized as an efficient means of heating organic reactions since the mid-1980s. Since then, dramatic rate accelerations have been demonstrated with a large variety of organic reactions.1 Today, the number of reports on microwave-assisted chemistry is well above one thousand. However, surprisingly few reports have appeared concerning microwave-assisted radical reactions.³

Curran and Hallberg showed a few years ago that hydrodebromination, reductive 5-*exo*-cyclization, and

intermolecular addition could be efficiently effected using fluorous tin hydride and short-time (5-10 min) microwave irradiation followed by three-phase extraction in the workup.^{3b} We thought it would be interesting to study the effect of microwave irradiation on atom- or grouptransfer reactions.^{3d} In such processes, a carbon-centered radical is initially produced by homolytic cleavage of a C-X bond (where X is commonly halogen or a chalcogen derivative).⁴ Following some type of radical transformation (for example, intra- or intermolecular addition), the heteroatom is transferred from the radical precursor to give the group- or atom-transfer product with regeneration of the initially formed carbon-centered radical. In contrast to products of reductive radical transformations, the functional group of the radical precursor is retained in the group-transfer product and is thus available for further synthetic manipulations.

Concerning radical precursors for group-transfer chemistry, a comparative study of halogen and chalcogen derivatives indicated similar rate constants for transfer of elements/groups in the same row of the periodic table (e.g., Br \approx PhSe; I \approx PhTe) and increased rates as one traverses a column (e.g., PhTe is transferred ${\sim}100$ times faster than PhSe).⁵

Since organotellurium compounds are often more robust than iodides when carried through synthetic sequences, substantial interest has focused to grouptransfer reactions of organotelluriums.⁶ So far, organotellurium group-transfer chemistry has been successfully applied for carbotelluration of alkynes,⁷ alkenes,⁸ isonitriles,⁹ and quinones¹⁰ and for the decarbonylation of aryltelluroformates.¹¹ Initiation of the above processes was brought about by various means. Often simple thermolysis or photolysis (or a combination of both) was sufficient. In a rare case, thermolysis of azo-bis(isobutyronitrile) (AIBN) was used to get a chain-reaction going.^{7a}

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R .

			$\xrightarrow{\text{ArTe}_2, \text{ NaBH}_4}_{\text{EtOH}} \xrightarrow{\text{R}_2}$	OH THF R2 O			
			1	2			
entry	R ₁	R_2	Ar	2-hydroxyalkyl aryl telluride, isolated yield (%)	2-allyloxyalkyl aryl telluride, isolated yield (%)		
1	-	(CH ₂) ₄ -	p-MeO-C ₆ H ₄	1a , 89	2a , 80		
2	_	$(CH_2)_4 -$	Ph	1b , 98	2b , 84		
3	_	$(CH_2)_4 -$	$p-CF_3-C_6H_4$	1c , 82 ^{<i>a</i>}	2c , 80 ^a		
4	Н	Bn	Ph	1d, 92	2d , 81		
5	Н	Bn	$p-CF_3-C_6H_4$	1e , 95	2e , 80		
6	Н	PhOCH ₂	Ph	1f , 91	2f , 72		
7	Н	$CH_2 = CH(CH_2)_2$	Ph	1 g, 80 ^a	-		
^a From ref 12.							

TοΔr

R.

TοΔr

R .

 TABLE 2.
 Influence of Aryl Substituents on Microwave-Assisted Group-Transfer Cyclization of Secondary-Alkyl Aryl

 Tellurides 2



entry	2-allyloxyalkyl aryl telluride	conditions ^a	additive	reaction time (min)	product, isolated yield (%), endo/exo ratio
1	2a , $Ar = p$ -MeO-C ₆ H ₄	А		3	3a , 65, 1/1.1
2	2b, Ar= Ph	Α		3	3b , 69, 1/1.1
3	2b, $Ar = Ph$	Α	(ArTe) ₂ (0.5 equiv)	3	3b , 73, 1/1.1
4	2c , $Ar = p - CF_3 - C_6H_4$	Α		3	3c , 67, 1/1.1
5	2c , $Ar = p - CF_3 - C_6H_4$	Α		5	3c , 61, 1/1.1
6	$2\mathbf{b}, \mathrm{Ar} = \mathrm{Ph}$	В		5	3b , 72, 1/1.3
7	$\mathbf{2b}, Ar = Ph$	В	$(ArTe)_2$ (0.5 eq)	5	3b , 74, 1/1.3
8	2c , $Ar = p - CF_3 - C_6H_4$	В		10	3c , <10, 1/1.3
^a A: et	hylene glycol, 250 °C; B: water,	180 °C.			

Some time ago we reported that *O*-allylated β -hydroxyalkyl aryl tellurides were induced to undergo intramolecular group-transfer cyclization by photolysis in refluxing benzene in the presence of hexabutylditin (eq 1).¹² In the present paper, we report a microwave-assisted version of this reaction which, as compared to the original procedure, is improved in several ways.



 β -Allyloxyalkyl aryl tellurides **2** were synthesized in two steps according to a protocol previously developed

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in our group.¹² Thus, epoxides were regioselectively ringopened with arenetellurolates in very good yields. The resulting alcohols **1** were then allylated using allyl bromide/NaH in THF (Table 1).

Group-transfer cyclization of compounds **2** was tried at various temperatures in solvents suitable for microwave heating (2-propanol at 200 °C, NMP at 250 °C, diethylene glycol dimethyl ether at 250 °C, ethylene glycol at 250 °C, water at 180 °C). It was found that short time (<5 min) microwave irradiation under an atmosphere of air in ethylene glycol at 250 °C afforded group transfer cyclization products in yields similar to those obtained previously by photolysis in refluxing benzene in the presence of 40 mol % hexabutylditin.

Initially, the influence of Te-aryl substituents in cyclohexene oxide-derived compounds **2** was examined (Table 2). The 4-methoxyphenyl, phenyl, and *p*-(trifluoromethyl)phenyl analogues, when reacted until the starting material was consumed, gave approximately the same yields (65, 69, and 67%, respectively) of group-transfer cyclization products (Table 2, entries 1, 2, and 4). It was noted, though, that compound **3a** was more sensitive to air-oxidation than the other analogues. Longer heating (5 min) at 250 °C seemed to lower the yield (Table 2, entry 5). This is probably due to decomposition of the group-transfer product. A striking difference in reactivity between secondary-alkyl aryl tellurides **2b** and **2c** was

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TABLE 3. Microwave-Assisted Group-Transfer Reactions of Primary-Alkyl Aryl Tellurides

$R \xrightarrow{TeAr} Microwaves R \xrightarrow{O} TeAr$							
entry	2-allyloxyalkyl aryl telluride	Ar	conditions ^a	reaction time (min)	product, isolated yield (%), <i>cis/trans</i> ratio		
1	$\mathbf{2d}, \mathbf{R} = \mathbf{Bn}$	Ph	В	10	3d , <10, 1/2.4		
2	$\mathbf{2d}, \mathbf{R} = \mathbf{Bn}$	Ph	А	6	3d , 74, 1/1.8		
3	2e, R = Bn	p-CF ₃ -C ₆ H ₄	А	10	3e, 60, 1/1.8		
4	2f , $R = PhOCH_2$	Ph	Α	6	3f, 63, 1/1.5		
^a A: ethylene glycol, 250 °C; B: water, 180 °C.							

observed when the reaction was attempted in water at 180 °C. Even after a prolonged reaction time (10 min) cyclization of telluride 2c failed to go to completion. When telluride 2b was heated at 180 °C, the reaction was complete in 5 min and a 72% yield of product 3b was isolated. With the hope to increase group-transfer yields, the corresponding diaryl ditelluride (0.5 equiv) was added to some of the reaction mixtures. As seen from Table 3 (entries 3 and 7), the additive did not cause any significant improvement in yields. Hexabutyldistannane was also tested as an additive. It caused a drop in product yields and increased reaction times.

We were also interested to see if primary-alkyl aryl tellurides could be induced by microwaves to undergo group transfer (Table 3). Heating at 180 °C for 10 min in water did not cause cyclization of telluride **2d** to go to completion. However, when the same reaction was performed at elevated temperature (250 °C) in ethylene glycol, it was complete in 6 min and a 74% yield of the desired group-transfer product **3d** was isolated. Telluride **2e** with an electron-withdrawing aryl group was more reluctant to undergo group transfer. The isolated yield of compound **3e** was 60% (Table 3, entry 3). As a final example of microwave-assisted formation of tetrahydrofuran derivatives from primary-alkyl phenyl tellurides, compound **3f** was prepared in 63% yield.

To demonstrate that the chemistry developed is not restricted only to heterocycle-construction, alcohol 1g was group-transfer cyclized to afford compound 4 in 58% yield as a 1/1.1 mixture of *cis* and trans isomers (eq 2).



Based on general knowledge of radical stability and our results with primary-alkyl- and secondary-alkyl aryl tellurides, one can predict that tertiary-alkyl aryl tellurides would be the most reactive substrates for grouptransfer cyclization. Unfortunately, the chemistry developed (Table 1) failed to produce the desired organotellurium radical precursors (1,1-dimethyloxirane was only ring-opened from the sterically least hindered side and ring-opened tetramethyloxirane could not be *O*-allylated).

Group-transfer cyclization products **3** were always formed as mixtures of *exo/endo* (Table 2) or *cis/trans* (Table 3) isomers. The stereochemistry of the products was determined by gNOESY-experiments. *Exolendo* ratios were in the range of 1/1.1-1/1.3 and *cis/trans* ratios in the range of 1/1.1-1/1.8. Thus, as compared with tin-promoted, light-induced group transfer in refluxing benzene,¹² selectivity is significantly reduced. The predominant formation of *exo* and *trans* isomers, respectively, is in accord with the Beckwith–Houk model for ring-closure of 5-hexenyl radicals assuming a chairlike transition state.¹³

Although group transfer of organoselenium compounds is known to proceed slower than those of the corresponding iodine and phenyltelluro analogues, a substantial number of inter- and intramolecular carboselenation reactions have been described in the literature.¹⁴ The key to success in these reactions seems related to the radical stability of the organic moiety attached to the PhSe group—at least one and often two stabilizing groups need to be present.

Spurred by the above results with organotelluriums, we also attempted some microwave-assisted grouptransfer reactions of related organoselenium compounds. Compound **5**, the selenium analogue of compound **2b**, failed to react even after 20 min of microwave heating at 250 °C in ethylene glycol. This was also true for the derivative carrying an electron releasing dimethylamino group *para* to selenium.



On the other hand, group-transfer cyclization of benzylic selenide **6** was complete in 5 min, affording tetrahydrofuran **7** (*cis/trans* = 1/2.1) in 75% yield along

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SCHEME 1



With 0.5 eq (PhSe)₂ (91%, *cis/trans*: 1/2.1) (4%, *cis/trans*: 1/2.1)

with 13% of cyclized but hydrodeselenated compound **8** (Scheme 1). When the reaction was carried out in the presence of 0.5 equiv of diphenyl diselenide, a 91% yield of compound **7** was isolated together with only 4% of the byproduct **8**. However, attempts to extend the group-transfer cyclization to α -phenylseleno esters and nitriles carrying a suitably positioned allyloxy group elsewhere in the molecule were met with failure.

In conclusion, we have demonstrated that group transfer chemistry can be substantially improved if performed in a microwave cavity. Not only does microwave heating cause a reduction in reaction time from a few hours to a few minutes. Group-transfer cyclization of primary- and secondary-alkyl aryl tellurides—reactions that could previously only be performed in the presence of toxic tin mediators using traditional methodology—could now be induced to occur without additives in environmentally benign solvents such as water. We foresee that other types of group-transfer reactions could be facilitated in a similar way by microwave heating. The only drawback we have experienced so far in the new methodology is a loss in diastereoselectivity. This could be accounted for by the higher than normal (up to 250 °C) temperatures required in the microwave-assisted reactions.

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Supporting Information Available: Experimental procedures, characterization data and copies of ¹³C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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