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An Improved Reductive Demercuration of Organomercurials Using Triethylborane

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Abstract : Organomercurials, which were generated by intra- and inter-molecular mercury(II)-promoted electrophilic additions, have been reductively demercurated *in situ* efficiently using sodium borohydride in the presence of triethylborane at low temperature. Under these conditions, the frequently accompanying side reactions such as reductive elimination and oxidative demercuration have not been detected.

Intra- and inter-molecular electrophile-promoted addition reactions of alkenes evidently belong to one of the most useful functionalization methods in organic synthesis. While the intramolecular cyclizations can provide various heterocycles stereoselectively,[1] the intermolecular additions follow the Markownikoff rule.[2] The mercury(II)-mediated electrophilic additions have the prime merit of the versatile functionalization of the resulting organomercurials.[3] Their reductive demercuration is the most widely employed transformation, which can be carried out with basic sodium borohydride,[4] tri-*n*-butyltin hydride,[5] diethylaluminum hydride,[5] hydrido(tri-*n*-butylphosphine)copper(I),[5] sodium amalgam,[6] lithium aluminum hydride,[6b] basic sodium borohydride in the presence of phase transfer catalyst (PTC)[7] and so on. It is not unusual to observe the skeletal rearrangement and the reductive elimination in the reductive demercuration under the above reaction conditions.[8] Furthermore, since the organomercurials produced by solvomercuration often revert to the original starting alkenes during work-up, it is desirable to accomplish the transformation *in situ*.

On studying one of our on-going research projects, the aforementioned problems were confronted in the intramolecular solvomercuration and reductive demercuration process. Our alkylmercury hydride generated during the process was survived for a long time at room temperature to decompose into various products. This observation led us to discover a chemical to induce a rapid decomposition of organomercury hydride via a free radical intermediate at low temperature. We have now established an efficient reductive demercuration by making use of triethylborane, which was previously employed as a free radical initiator.[9] In this paper the results of reductive demercuration under our developed conditions are described and compared with those under the best known method using basic sodium borohydride in the presence of PTC.

The intramolecular mercuriocyclization was conducted with mercuric trifluoroacetate in THF in the presence of potassium carbonate for the 5-membered heterocycles and mercuric oxide for the 6-membered. Then the resulting organomercurials were reductively demercurated *in situ*

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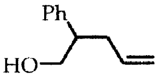
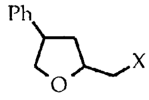
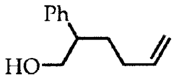
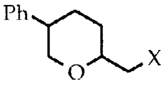
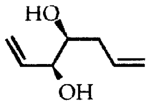
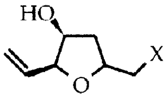
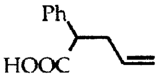
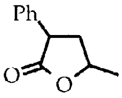
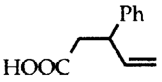
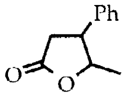
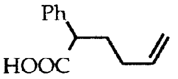
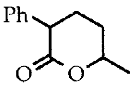
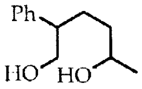
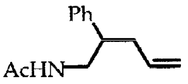
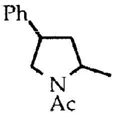
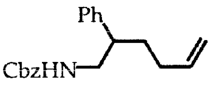
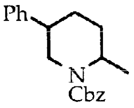
Table I. Reductive demercuration of organomercurials from intramolecular cyclization

$$\text{Substrate} \xrightarrow[K_2CO_3 \text{ or HgO, rt}]{Hg(OOCCF_3)_2\text{, THF}} \xrightarrow[\text{method A or B}]{NaBH_4} \text{Product(s)}$$

method A	method B
Et_3B, - 78°C ⟶ rt	$BnNEt_3Cl$, 10% aq. NaOH, rt

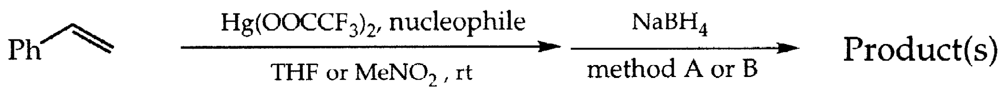
entry	substrate	% yield			
		products		method A	method B
1			X = H	90	70
			X = OH	-	18
		S. M.		-	5
2			X = H	90	75
			X = OH	-	15
3			X = H	83	34
			X = OH	-	10
		S. M.		-	7
4				93	39
		S. M.		-	48
5[10]				91	71
		S. M.		-	23
6				71	34
				21	-
		S. M.		-	57
7				93	89
8				93	78

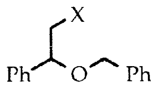
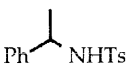
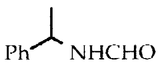
with sodium borohydride in the presence of triethylborane (method A) and in the presence of benzyltriethylammonium chloride (method B). The experimental results are summarized in Table I. While the intramolecular etherification of olefinic alcohols by method B afforded the reductively demercurated products in moderate to good yields along with significant amounts of the oxidatively demercurated alcohols, only the desired cyclic ethers were obtained in excellent yields by method A(entry 1-3). Even the application of the reductive demercuration method B under the strictly deoxygenated conditions could not avoid the formation of alcohols. In lactonization of olefinic carboxylic acids, considerable amounts of the starting carboxylic acids were recovered by method B, which were certainly generated from the corresponding organomercury hydrides via reductive elimination (entry 4-6). In contrast any starting carboxylic acids could not be isolated under the conditions of method A. It is noted that 21% of the overreduced diol was yielded by method A in the case of entry 6. Although the intramolecular amidation of amide and carbamate proceeded smoothly by both methods, somewhat better yields were attained with triethylborane (entry 7-8).

The intermolecular mercurioetherification and mercurioamidation of styrene were performed using mercuric trifluoroacetate in THF and in nitromethane in the absence of base, respectively. The subsequent *in situ* reductive demercurations were carried out under the aforementioned conditions. The experimental data are described in Table II. The etherification was efficiently achieved by both methods, albeit the oxidatively demercurated alcohol was produced to some extent under the conditions of method B (entry 1). In the formation of amides, the electrophilic additions generated the expected organomercurials without difficulty. The ensuing reductive demercurations were cleanly effected by method A, however the desired amides could not be prepared at all using method B (entry 2-3). Alternatively, method B was applicable to the purified amidomercurials.[13, 14]

To sum up, the improved reductive demercuration has been developed using sodium borohydride in the presence of triethylborane at low temperature, during which the troublesome

Table II. Reductive demercuration of organomercurials from intermolecular addition



entry	substrate	% yield			
		products		method A	method B
1	$PhCH_2OH$		X = H	97	82
			X = OH	-	6
2[11]	$TsNH_2$			91	-
3[12]	H_2NCHO			90	-

reductive elimination and oxidative demercuration have been suppressed completely.

General procedure : Mercuric trifluoroacetate(169mg, 0.40mmol) and potassium carbonate (55mg, 0.40mmol) were added to a stirred solution of 2-phenyl-4-pentenoic acid (58mg, 0.33mmol) in THF (3ml) at room temperature. After 0.5h, the reaction mixture was cooled down to -78°C, and then triethylborane (0.33ml, 1M in THF, 0.33mmol) and sodium borohydride (25mg, 0.66mmol) were added in sequence. After 1h at -78°C, the mixture was allowed to warm to room temperature and subsequently subjected to aqueous work-up with ethyl acetate. The organic layer was dried over sodium sulfate and evaporated *in vacuo*. The residue was purified on a silica gel column (n-hexane:ether = 2:1) to afford 3-phenyl-5-methyl-γ-butyrolactone as a colorless oil (54mg, 93%).

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9 Nozaki, K.; Oshima, K.; Utimoto, K. *Tetrahedron*, **1989**, *45*, 923-933.
10. 5-Methyl-4-phenyl-γ-butyrolactones had been prepared in 45% yield using basic sodium borohydride.[8b]
11. Barluenga, J.; Jiménez, C.; Nájera, C.; Yus, M. *J. Chem. Soc., Perkin Trans. I*, **1984**, 721-725. N-(1-Phenylethyl)tosylamide had been obtained in 31% yield from styrene.
12. Barluenga, J.; Jiménez, C.; Nájera, C.; Yus, M. *J. Chem. Soc., Perkin Trans. I*, **1983**, 591-593. N-(1-Phenylethyl)formamide had been produced in 35% yield from styrene.
13. The reductive demercuration of the purified organomercurials by method B furnished tosylamine in 71% yield along with 20% of oxidatively demercurated alcohol, and formamide in 40% yield, respectively.
14. All new compounds showed satisfactory spectral data.