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Communications

Ultrasound in Organic Synthesis. 18.[1] Selective Oxymercuration via Sonochemically in Situ Generated Mercury Salts

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Summary: Selective mercuration of diolefins is favored by a proper choice of the mercuric salt, which can be generated in situ from mercuric oxide and the corresponding acid under sonochemical activation.

Sir: Oxymercuration–demercuration of olefins, first developed by Brown,[2] provides a very general and popular method for the Markovnikov hydration of carbon–carbon double bonds. Commercial mercuric acetate is used for the mercuration step in aqueous tetrahydrofuran (THF) followed by reductive demercuration with alkaline sodium borohydride, without isolation of the intermediate (β-hydroxyalkyl)mercurials. Under standard reaction conditions high yields are obtained from monoolefins, but mercuration of diolefins is frequently impaired by competitive reactions.[3,4] Higher degrees of selectivity are observed when diolefins are reacted under micellar conditions.[5] Better yields and selectivities are also obtained by using other mercuric salts, especially the trifluoroacetate, and the influence of the anion on the reaction course even if poorly investigated is suggested in some studies.[4,6] Asymmetric induction (although low) is observed with mercuric salts of chiral acids.[7] However the commercial availability of mercuric salts is restricted and their synthesis often impractical: oxidative reaction of metallic mercury with peracetic–acetic acids mixture,[8] anion exchange from the acetate to other carboxylates,[7c] reaction of anhydrides with mercuric oxide.[9]

Table I. Formation of Mercuric Salts in Dichloromethane[a,b]

acid	sonication time, min	entry
CH_3CO_2H	15	1
t-$C_4H_9CO_2H$	120	2
$CH_3(CH_2)_8CO_2H$	30	3
CBr_3CO_2H	15	4
$CF_3(CF_2)_2CO_2H$	2	5
$C_6H_5CO_2H$	30	6
	24 h	7[c]
	24 h	8[d]
p-$CH_3C_6H_4SO_3H$	30	9
dibenzoyltartaric acid	120	10

[a] A typical procedure follows: 2 mmol of acid and 0.216 g (1 mmol) of yellow HgO in 5 mL of CH_2Cl_2 are sonicated in a Sonoclean SHE 2500 cleaning bath until complete discoloration of the mixture. A white slurry is generally obtained except in entry 5 where the salt is soluble. [b] New compounds gave satisfactory analytical data. [c] With stirring, no sonication applied. [d] Under reflux (40 °C), no sonication applied.

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We have found that mercuric salts can be efficiently and rapidly prepared under sonochemical conditions. In the first attempts, stoichiometric amounts of yellow mercuric oxide and benzoic acid were sonicated in a common laboratory ultrasonic cleaner in various solvents.

$$2RCO_2H + HgO \xrightarrow{)))} (RCO_2)_2Hg \qquad (1)$$

Surprisingly the corresponding mercuric salt was readily formed in solvents of low polarity such as hexane, toluene, or tetrachloromethane as indicated by the fast discoloration of the mixture. Reactions were much slower in water, water–THF, or methanol, and no reaction occurs in other polar solvents like pure THF, ethyl acetate, or acetone. Several mercuric salts have been generated efficiently in the same way with dichloromethane as the solvent (Table I). Short sonication times (2–15 min) were sufficient in the case of strong acids (entries 4 and 5), but the reactions required up to 2 h in the case of less acidic or more bulky compounds (entries 2 and 10). Mercury sulfonates can be prepared by the same procedure (entry 9). The reaction proceeded much more slowly with stirring and/or reflux in the absence of sonic waves.

Cavitational erosion is generally considered as the basic phenomenon in sonochemical activation. Recent works have shown that interparticular collisions can lead, independently of cavitation, to an increased reactivity of solids.[10]

These findings suggested the possibility of preparing mercuric salts and using them simultaneously in oxymercuration reactions under ultrasonic activation. In contrast with the preparation of mercuric salts, the one-step preparation and reaction is better accomplished in the usual aqueous THF medium. Thus a stoichiometric mixture of 2-octene, mercuric oxide, and acetic acid (1/1/2) in aqueous THF was sonicated until the color of mercuric oxide completely disappeared (2 min). After the usual reductive treatment[2] 2-octanol was obtained in 85% yield (eq 2).

$$\underset{1}{C_6H_{13}CH{=}CH_2} \xrightarrow[\text{THF, H}_2\text{O,)))}]{\text{HgO, 2RCO}_2\text{H}} C_6H_{13}CH(OH)CH_2HgOCOR + RCO_2H \xrightarrow{\text{NaBH}_4\text{, NaOH}} \underset{2}{C_6H_{13}CH(OH)CH_3} \qquad (2)$$

In fact, the stoichiometric generation of the mercuric salt is not necessary as one molecule of acid is released in the mercuration step. The reaction is slower, but quite similar results are obtained with only 1.2 molar equiv of acid with respect to the olefin: after 45 min of sonication, 2-octanol was obtained in 88% yield.

This method allows the oxymercuration of olefins with virtually any mercuric salt in a very simple way. It was interesting to determine if the proper choice of the anion would increase the selectivity in a diolefin mercuration such as that of limonene **3**[4,5] (Scheme I, eq 3).

Scheme I

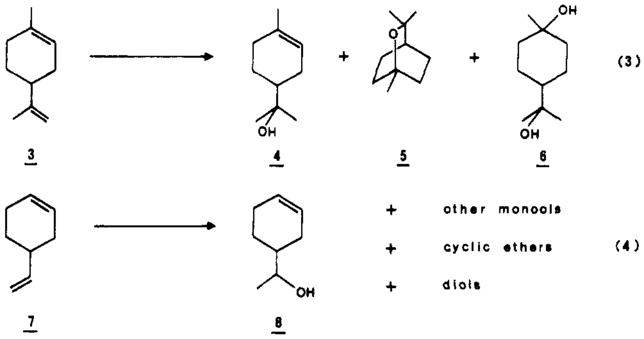

Table II. Oxymercuration of Limonene 3[a]

acid or salt	sonication time, min	yield,[b] % 4	5	6	entry
$Hg(OAc)_2$	*c*	48	7	17	1
CH_3CO_2H	30	47	6	18	2
$t\text{-}C_4H_9CO_2H$[d]	7	80	3	0	3
$Hg(CF_3COO)_2$	*c*	80	3	0	4
CF_3CO_2H	5	76	4	0	5
CBr_3CO_2H	30	70	3	0[e]	6
$CF_3(CF_2)_6CO_2H$	5	80	6	0	7
$C_6H_5CO_2H$	30	56	3	14	8
$C_6F_5CO_2H$	20	56	15	5	9
CF_3SO_3H	30	12	0	0	10
$p\text{-}CH_3C_6H_4SO_3H$	60	63	1	3[e]	11

[a] A typical procedure follows: 1.2 mmol of acid, 0.216 g (1 mmol) of yellow HgO and 0.136 g (1 mmol) of limonene in a mixture of 2.5 mL of THF and 2.5 mL of water are sonicated until complete discoloration. The mixture is then reduced and worked up as in ref 2. [b] GLPC analysis with *n*-tetradecane as an internal standard were effected with a Erba Science Fractovap chromatograph. Column: SE 30 (10% on Chromosorb W). Temperature: 140 °C. Peak areas were corrected for the response factor for every compound analyzed. Complement to 100% corresponds to starting material (±2%). [c] Commercial salt used under usual conditions (ref 2). [d] Accelerated by one drop of 70% perchloric acid. [e] Ca. 15% unidentified material.

Non selective dimercuration reactions produce compounds **5** and **6**, reducing the yield of monool **4** (eq 3). The results obtained by oxymercuration of limonene with in situ generation of various mercuric salts, along with two standard control reactions with commercial mercuric salts, are recorded in Table II. As shown with entries 1 and 2 the same product distributions were obtained from commercial or in situ generated mercuric acetate. The in situ prepared pivalate (entry 3) gave a much better selectivity, in agreement with earlier observations on reactions using this salt.[6] Other aliphatic acids with increasing chain length (decanoic and hexadecanoic acids) gave similar results, but the reaction time increases substantially. Lengthy reactions can, however, be accelerated by catalytic amounts of perchloric acid without changing the selectivity. The commercially available but expensive mercuric trifluoroacetate is a more selective reagent than the acetate[4] (entry 4). It is efficiently generated and reacted like other halogenated acids (entries 5–7) by our one-step process with comparable selectivity (entry 5). Aromatic acids are slightly more efficient than acetic acid (entries 8 and 9). Surprisingly, trifluoromethanesulfonic acid seems to be very unfavorable (entry 10), but *p*-toluenesulfonic acid (entry 11) gave even better results than acetic acid.

As these results appeared to be encouraging, the very difficult mono reaction of 4-vinylcyclohexene was studied under our conditions. The standard procedure using mercuric acetate gives a complex mixture of monools, diols, and cyclic ethers, the major monool product **8** never exceeding a 20–25% yield[4] (Scheme I, eq 4).

Much better selectivity is observed, however, when the mercuration is achieved with mercuric acetate in aqueous solutions under micellar conditions.[5] Data on the oxymercuration of 4-vinylcyclohexene are summarized in Table III. As in the case of limonene almost no difference is noted between the reaction with commercial and ul-

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Table III. Oxymercuration of 4-Vinylcyclohexene 7[a]

acid or salt/medium	sonication time, h	yield, %/selectivity[b]	entry
$Hg(OAc)_2$/50% aqueous THF	c	20-25/50	1
CH_3CO_2H/50% aqueous THF	0.5	23/50	2
$CH_3(CH_2)_8CO_2H$/ 50% aqueous THF[d]	4	47(40 isolated)/90	3
$Hg(OAc)_2$/0.3 M SDS	c	60/90	4
$CF_3(CF_2)_2CO_2H$/ 0.3 M SDS[e]	2	67/100	5

[a] Same procedure as in footnote a in Table II, replacing limonene by 4-vinylcyclohexene (0.108 g, 1 mmol). [b] By GLPC analysis with n-dodecane as an internal standard. Selectivity = [8]/[8] + monools + ethers + diols. [c] Commercial salt used under usual conditions (ref 2). [d] See corresponding footnote in Table II. [e] 0.257 g (1.2 mmol) of perfluorobutyric acid, 0.216 g (1 mmol) of mercuric oxide, and 0.108 g (1 mmol) of 4-vinylcyclohexene in 10 mL of distilled water containing 0.3 M SDS are sonicated until complete discoloration. The mixture is then worked up as in ref 11.

trasound-generated $Hg(OAc)_2$ (entries 1 and 2). The selectivity is improved by replacing acetic acid with n-decanoic acid (entry 3), and the product distribution is roughly the same as with mercuric acetate under micellar conditions (entry 4). It was of interest to try to combine both methods, i.e. in situ sonochemical generation of the salt and micellar conditions. Thus, perfluorobutyric acid, mercuric oxide, and 4-vinylcyclohexene were sonicated in a 0.3 M aqueous solution of sodium dodecyl sulfate (entry 5). Discoloration of the mixture, which indicates the consumption of the mercuric oxide, occurred after 2 h of sonication. Only monool 8 was obtained along with a small amount of starting material indicating a near 100% selectivity, with a 67% yield (VPC). This result can be put in parallel with that obtained in the same micellar medium without sonication, a "90% purity of compound 8"[5] (unfortunately without yield specification).

This work clearly illustrates the importance of the nature of the counteranion in selective oxymercuration with mercuric salts. It also demonstrates that the preliminary preparation of noncommercial or expensive mercuric salts is not necessary, with ultrasonic activation allowing the easy in situ generation of any salt directly from the acid. Further applications and extensions of this new procedure are presently under investigation.

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Reactions of Alkylthio-Substituted Chromium Carbene Complexes with Alkynes: Application to Synthesis of Visnagan

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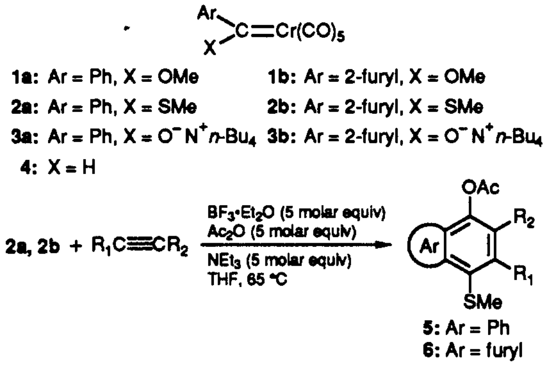
Summary: We report the first examples in which the reaction of the (methylthio)phenyl- or (methylthio)furylcarbene complexes with various alkynes in the presence of 5 molar equiv each of $BF_3{\cdot}Et_2O$, Ac_2O, and Et_3N in THF afford the acetate derivatives of 1,4-dihydrothionaphthoquinone and 4,7-dihydrothiobenzofuran.

Sir: Reaction between pentacarbonyl(phenylmethoxycarbene)chromium (**1a**) and alkynes is a direct method for preparation of substituted 1,4-dihydronaphthoquinones[1] and has been applied to the synthesis of natural products.[2] The process is efficient only with methoxy-substituted carbene ligands and therefore is applied only in the synthesis of 1,4-benzoquinone derivatives. Since the methoxy group of **1a** can be readily replaced by nitrogen,[3] sulfur,[4] and carbon nucleophiles,[5] a range of substituted carbene complexes is readily available. With amino-substituted arylcarbene ligands, a general formation of indenes is observed.[6] The carbene–alkyne reaction of the phenyl(alkylthio)carbene complex **2a** to afford 1,4-dihydrothionaphthoquinones has not been described. Such a process would have the advantage in that the alkylthio group can

Scheme I



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