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HALOMETHYL–METAL COMPOUNDS
XX. AN IMPROVED SYNTHESIS OF PHENYL(TRIHALOMETHYL)-MERCURY COMPOUNDS*

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SUMMARY

The preparation of $PhHgCCl_nBr_{3-n}$ ($n=0$–2) in good yield can be accomplished by the reaction of phenylmercuric chloride, the respective haloform and the tert-butanol monosolvate of commercial, unsolvated potassium tert-butoxide in *ca.* 1/1.5/1.4 molar ratio in tetrahydrofuran solution at −25°. This represents a significant improvement over the previous procedure (ref. 7) in that a high speed stirring apparatus is not required, commercial potassium tert-butoxide may be used and large excesses of the haloform are not necessary.

INTRODUCTION

Phenyl(trihalomethyl)mercury compounds have proved to be useful dihalocarbene transfer reagents and in particular find unique application in the conversion of base-sensitive and/or weakly nucleophilic olefins to the respective dihalocyclopropanes[2–5]. During the first few years of our research on the chemistry of these mercurials we used a modified version of the original Reutov–Lovtsova procedure[6] to prepare the compounds $PhHgCCl_nBr_{3-n}$ ($n=0$–3)[7]. This procedure, when correctly practised, gave these mercurials in good yield and purity, as has been confirmed by other workers in the United States and Europe. However, this procedure has a number of drawbacks, some of them serious enough so as to render the preparation of these reagents rather difficult and tedious, and this has made the phenyl(trihalomethyl)mercurials somewhat less attractive as dihalocarbene precursors than they otherwise might have been. These drawbacks are the following: (*1*) A high-speed stirrer [used preferably in conjunction with a Morton (creased) flask] is an essential

$$PhHgY\ (Y=Cl \text{ or } Br) + CHX_3\ (X=Cl, Br) + \text{tert-BuOK} \xrightarrow{\text{benzene}} PhHgCX_3 + KY + \text{tert-BuOH} \quad (1)$$

* Part XIX: ref. 1.
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requirement*, since both the phenylmercuric halide and the potassium tert-butoxide (PTB) (in the form of its tert-butanol monosolvate) have very low solubility in the solvent system used. (2) All attempts to adapt the commercially available PTB to this synthesis failed; good yields of product were obtained only if the PTB–tert-butanol monosolvate, prepared as described by Speziale and Ratts[8], was used as base. Such butoxide preparation, while operationally simple, is tedious and time-consuming, and it was found that *ca.* three days were required for the synthesis of these phenyl(trihalomethyl)mercury reagents on a 0.25–0.5 mole scale, from starting material preparation (PhHgX, PTB) to isolation of purified product. (3) In our modified procedure[7], best results were obtained when a phenylmercuric halide/haloform/base ratio of *ca.* 1/4/2 was used. This was not a serious consideration when the most useful haloform for CCl_2 studies, $HCCl_2Br$, was available commercially relatively cheaply ($6.25 per U.S. pound). However, during the course of this work the commercial supplies of bromodichloromethane became depleted and were not renewed**. Thus the use of four moles of haloform to make at best one mole of $PhHgCX_3$ is wasteful and expensive.

In 1966 Finnish workers[9] reported carrying out reaction (1) in diethyl ether at $-20°$, but they gave no details concerning procedure or yields. We checked this variation in procedure and found that for phenyl(bromodichloromethyl)mercury it did indeed represent a somewhat more convenient procedure that gave this mercurial in somewhat better yield (70–85% recrystallized yields)[10]. [For the preparation of *p*-fluorophenyl(bromodichloromethyl)mercury by this procedure see ref. 1.] Due to the insolubility of both phenylmercuric halide and PTB in diethyl ether, high speed stirring still was required for good results. A new drawback was introduced by the replacement of benzene by diethyl ether, due to an apparent instability of the bromine-containing phenyl(trihalomethyl)mercury compounds in the latter solvent. Rapid removal of the ether solvent upon completion of the reaction was mandatory in order to obtain the yields of $PhHgCCl_2Br$ mentioned, and in the case of phenyl(tribromomethyl)mercury, the original procedure in which benzene was used as solvent actually seemed better.

RESULTS AND DISCUSSION

In view of the growing application of the phenyl(trihalomethyl)mercury reagents in *gem*-dihalocyclopropane synthesis[4,5], it seemed desirable to develop a method which was not burdened by the three drawbacks mentioned above. We report here an improved procedure for the high yield preparation of these mercurials in which high speed stirring is not essential, in which such large excesses of haloform are not required and in which commercial PTB may be used, and which, as a result, can be effected in much shorter time (less than one day for 0.25 to 0.5 mole preparations).

These improvements have been made possible by the use of tetrahydrofuran (THF) as reaction solvent. Phenylmercuric halides have appreciable solubility in

* Most of the cases of the unsuccessful application of this procedure, reported at various times to the senior author, appear to be due to the failure to use the recommended high-speed stirring apparatus.
** Bromodichloromethane is now available from research chemicals vendors, but a price of $122 for 500 g is typical.

THF, in contrast to their insolubility in benzene and diethyl ether. Thus one can prepare solutions of phenylmercuric chloride in THF that are ~0.26 *M* at 28°, ~0.2 *M* at 6° and ~0.14 *M* at −22°. Unsolvated PTB is quite soluble in THF (25 g/100 g of THF)[11], but the tert-butanol monosolvate is not very soluble in THF and precipitates out when one equivalent of tert-butanol is added to a solution of PTB in THF. However, it was found that it was sufficient that the phenylmercuric halide was reasonably soluble in the system : high speed stirring no longer was required; a simple paddle-type stirrer sufficed. A large number of reactions was carried out in order to delineate those factors which favor the production of phenyl(trihalomethyl)mercury compounds in good yield and purity. The principle variations in procedure involved the reaction temperature and the nature of the base used : "homemade" PTB (according to ref. 8), unsolvated, commercial PTB or the latter with one added equivalent of tert-butanol ("doped" commercial PTB). Some general comments may be made : (*1*) As we had found in the case of reactions carried out in benzene[7], the unsolvated, commercial PTB was not very effective in the mercurial synthesis. Using this base, in a reaction in THF at −78° with phenylmercuric chloride and bromodichloromethane, the $PhHgCCl_2Br$ yield was only 20%. In contrast, under identical conditions, use of "doped" commercial PTB resulted in a product yield of 55%. (*2*) Phenylmercuric chloride gave slightly better results than phenylmercuric bromide, probably because the latter was less soluble than the former. (*3*) Relatively slow addition of the suspension of base ("homemade" or "doped" commercial PTB) to the PhHgX/haloform/THF solution gave getter product yields than did rapid addition of the base. (*4*) With "homemade" PTB, a very nearly 1/1/1 PhHgX/haloform/base ratio produced good yields of product, but with "doped" commercial PTB, ratios of 1/1.5/1.4 seemed to give best results. (5) Reaction temperatures of *ca.* −25° gave good results when "doped" commercial PTB was used. The combination of "doped" commercial PTB and lower (−78°) reaction temperatures often resulted in reaction mixtures from which the product was difficult to isolate. The reaction solution in those cases appeared normal, but when only a part of the THF had been removed, it became noticeably thicker, and complete removal of THF usually was not possible. In many cases where such apparent gelation occurred, one could obtain product in moderately high-yield, but the difficulties of the work-up were such that these reaction conditions could not be considered satisfactory. For reasons unknown, the use of "homemade" PTB at −78° was not accompanied by such problems. The last two observations may reflect a difference between "homemade" and "doped" commercial PTB ; a difference in purity is conceivable and there will also be differences in particle size.

This improved procedure for the preparation of the $PhHgCCl_nBr_{3-n}$ mercurials can also be applied to the preparation of other halomethylmercury compounds, *e.g.*, $PhHgCBr_2H$ and $PhHgCCl_2F$. We recognize that further modifications of this procedure may lead to further improvements. Of particular interest would be a broad survey of other bases and perhaps more solvents. However, we present our new procedure at this time since it does represent a very significant improvement and thus makes phenyl(trihalomethyl)mercury compounds much more accessible and their CX_2 transfer reactions much more practical. In the Experimental Section we describe what we consider to be the optimum conditions for the preparation of $PhHgCCl_nBr_{3-n}$ compounds.

EXPERIMENTAL

Starting materials

Phenylmercuric chloride and bromide were prepared as described previously[7]. Unsolvated potassium tert-butoxide (PTB) was purchased from M.S.A. Research Corp., Callery, Pennsylvania. The PTB/tert-butanol monosolvate was prepared by the method of Speziale and Ratts[8]. Tetrahydrofuran (Fisher reagent grade) from freshly opened bottles could be used without further purification. (We advise drying over calcium hydride and distilling from lithium aluminum hydride if commercial THF with an appreciable water content is used.) Reagent grade bromoform was purchased (Eastman), while bromodichloromethane and dibromochloromethane were prepared as described in a Dow Chemical Co. patent[12]. Tert-butanol was distilled from sodium and stored under dry nitrogen and was transferred by means of a syringe.

General comments

All reactions were carried out under an atmosphere of prepurified nitrogen. The products were recrystallized as described previously[7] from reagent grade hexane and chloroform (3/1). All yields reported are for recrystallized products; the observed melting/decomposition points were no more than 3° below the melting points reported for highly purified samples in ref. 7.

Preparation of phenyl(trihalomethyl)mercury compounds

Into a dry (flamed out) one liter, three-necked flask equipped with a nitrogen inlet tube and a glass-sleeved Tru-Bore stirrer with Teflon paddle was transferred 50.0 g (0.16 mole) of phenylmercuric chloride. The material which remained in the weighing beaker was rinsed into the flask with 200 ml of THF. To this was added 0.24 mole of the haloform, followed by a 100 ml THF rinse. This mixture was stirred (using a standard laboratory stirring motor) and maintained at −25° during the entire reaction time by external cooling (limited Dry Ice in acetone). The contents of a 25 g bottle of commercial PTB (*ca.* 0.22 mole) were quickly transferred under nitrogen into a dry, 500 cc, single necked flask containing a magnetic stirring bar; 150 ml of THF was added and the PTB/THF mixture was stirred under nitrogen until all of the base had dissolved. To this solution was added under nitrogen with stirring, by means of a pressure-equalizing dropping funnel, 16.5 g (0.22 mole) of tert-butanol in 50 ml of THF over a 10 min period. The resulting yellowish suspension was cooled to room temperature and transferred to an addition funnel fixed to the third neck of the reaction flask. The PTB/tert-BuOH suspension was added to the cooled PhHgCl/haloform/THF solution over a 15–20 min period. Upon completion of the addition, the reaction mixture was stirred for 5 min at −25°, then was transferred into a two-liter, one-necked flask. The solvent was stripped off rapidly at reduced pressure using a rotary evaporator with a trap immersed in a −78° bath (water aspirator vacuum). No heating was applied until nearly all of the solvent had been removed; then the residue was warmed using a water bath whose temperature was below 25°. Reagent grade benzene (800 ml) was added to the dry residue and the mixture was shaken until the solid had partially dissolved. Subsequently, 100 ml of distilled water was added and the mixture shaken thoroughly. The phases were allowed

to settle and the benzene layer was decanted carefully through a filter into a two-liter, one-necked flask. The aqueous layer was washed with another 200 ml of benzene. The benzene extract and washings were evaporated at reduced pressure and the residue quickly dissolved in hot 3/1 hexane/chloroform; approximately 600 ml of 3/1 hexane/chloroform was heated to boiling and added in portions to the solid, with vigorous swirling after each addition, until nearly all of the solid had dissolved. Mild heating on the steam bath was at times necessary. The warm solution was filtered through filter paper into a one-liter Erlenmeyer flask (thus removing some phenylmercuric halide which had not dissolved) and *immediately* chilled in a freezer below 0°. The first crop was suction-filtered using a sintered glass funnel; usually a thin flaky mat of phenylmercuric halide covered the sintered glass disc and the dense, white needles of the $PhHgCX_3$ compound were on top. The latter could be easily separated from the mat of phenylmercuric halide. A wash with cold hexane followed the filtration. The mother liquor was evaporated to dryness at reduced pressure and the residue crystallized again as before from 3/1 hexane/chloroform to give a second crop of product. (About 60 ml of the hot 3/1 solvent mixture will dissolve *ca.* 10 g of $PhHgCX_3$.) A third crop of product usually was isolated by renewed concentration of the mother liquor and crystallization of the residue. The following yields obtained by this general procedure are typical:

$PhHgCCl_2Br$	50.4 g	72% yield	m.p. 108.0–110.0° (dec.)
$PhHgCClBr_2$	58.6 g	75% yield	m.p. 107.0–109.0° (dec.)
$PhHgCBr_3$	61.9 g	73% yield	m.p. 119.0–120.0° (dec.)

Melting (dec.) points reported previously[7] for these compounds are 110–111°, 110–112° and 119–120°, respectively.

As mentioned in the discussion, the "homemade", solid PTB/tert-BuOH complex[8] may be used in place of "doped" commercial PTB. In such reactions the required amount of complex, 41.0 g (0.22 mole) was first weighed (under dry nitrogen) into a 250 ml flask and subsequently added to the PhHgCl/haloform/THF solution via a flexible, 1" rubber tube. In one example, use of 0.1 mole of PhHgCl, 0.12 mole of bromodichloromethane and 0.1 mole of "homemade" PTB, in THF at −78°, resulted in the production of phenyl(bromodichloromethyl)mercury in 74% yield, using the general procedure outlined above. A similar preparation when dibromochloromethane was the haloform used gave $PhHgCClBr_2$ in 71% yield, while with bromoform $PhHgCBr_3$ was isolated in 70% yield.

We have no doubt that phenyl(trichloromethyl)mercury can be prepared by these procedures, but in view of the limited applicability of this mercurial as compared to the much more reactive $PhHgCCl_2Br$[2], this point was not investigated.

Additional recommendations

In view of the limited stability of the $PhHgCCl_nBr_{3-n}$ compounds in THF (note the rapid reaction of $PhHgCCl_2Br$ with THF at higher temperatures[2]), we strongly suggest that the reaction mixture be worked up immediately and rapidly after the reaction has been completed. Furthermore, since these mercurials are more stable as the solids than in solution, we recommend that the work-up not be interrupted until the chloroform/hexane solution has been placed in the freezer. These

mercurials have a longer shelf life as the solid reagents if they are stored in the freezing compartment of a refrigerator.

Preparation of phenyl(dibromomethyl)mercury

A reaction carried out in similar fashion in THF solution (400 ml) at *ca.* 5° using 0.2 mole of phenylmercuric chloride, 0.3 mole of dibromomethane (Eastman White Label) and 0.22 mole of "*undoped*", commercial PTB, followed by the work-up procedure described above, gave 58.7 g of $PhHgCBr_2H$ (65% yield), m.p. 67.0–68.5° (lit.[13] m.p. 69–70°). We have no explanation as to why the unsolvated PTB can be used successfully in this case; however, previous work in these laboratories[14] had shown that the preparation of $PhHgCBr_2H$ in benzene medium (*cf.* ref. 13) could be accomplished in good yield when commercial, unsolvated PTB was used.

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