

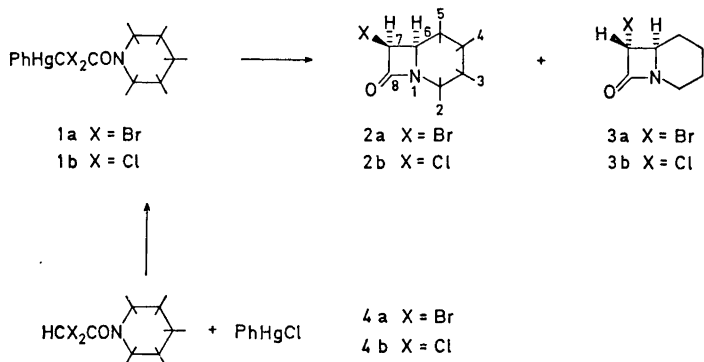
## The Synthesis of [Dihalo(*N,N*-pentamethylenecarbamoyl)-methyl]phenylmercury Compounds and Their Thermal Decomposition to Halo- $\beta$ -lactams\*

NILS GUNNAR JOHANSSON

*Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm 70, Sweden*

The base catalyzed condensation between phenylmercuric chloride and the *N*-(dihaloacetyl)piperidines *4a* and *4b* has been investigated. The yields are strongly influenced by the temperature and the state of the base. The thermal generation of  $\beta$ -lactam from the condensation product *1a* was quite facile whereas the compound *1b* reacted very sluggishly.

A novel synthesis of bromo- $\beta$ -lactams has recently been described.<sup>1</sup> In this synthesis [dibromo(*N,N*-pentamethylenecarbamoyl)methyl]phenylmercury (*1a*) was decomposed in refluxing bromobenzene to yield a mixture of the two isomeric bromo- $\beta$ -lactams *2a* and *3a*. The reaction is an extension of the mercury induced dihalocarbene synthesis introduced by Seyferth and his coworkers.<sup>2</sup>



Mercury compound *1a* was synthesized in 50 % yield by stirring a benzene solution of *N*-(dibromoacetyl)piperidine (*4a*), potassium *t*-butoxide (*t*-BuOK)

\* Synthesis of Strained Heterocyclic Compounds, 4. Part 3. Johansson, N. G. and Åkermark, B. *Tetrahedron Letters* 1971 4785.

and phenylmercuric chloride with a high-speed stirrer at 5–10°. The yield can be increased to 70–80% (*cf.* Ref. 4) by the use of tetrahydrofuran (THF) in place of benzene. Two different *t*-BuOK preparations have been used, the solid 1/1 complex *t*-BuOK/*t*-BuOH<sup>5</sup> (referred to as complexed *t*-BuOK) and noncomplexed *t*-BuOK made from equimolar amounts of potassium metal and *t*-BuOH in THF.

The yields of the mercury compounds *Ia* and *Ib* obtained at different reaction conditions are listed in Table 1. The yields are highest when noncomplexed

Table 1. Yields of [dihalo(*N,N*-pentamethylenecarbamoyl)methyl]phenylmercury (*Ia*, *Ib*) from *N*-(dihaloacetyl)piperidine (*4a*, *4b*), phenylmercuric chloride, and *t*-BuOK for variations of the condensation method.

Method	Solvent	Base	Temp. °C	Yield <i>Ia</i>	Yield <i>Ib</i>
A. High-speed stirring <sup>1,3</sup>	Benzene	1/1 complex <i>t</i> -BuOK/ <i>t</i> -BuOH <sup>5</sup>	5–10	50	35
B. Base added to a mixture of PhHgCl and <i>4</i>	THF	1/1 complex <i>t</i> -BuOK/ <i>t</i> -BuOH	–20 to –30	75	60
C. Base added to a mixture of PhHgCl and <i>4</i>	THF	1/1 complex <i>t</i> -BuOK/BuOH	–70 to –75	~10	–
D. Base added to a mixture of PhHgCl and <i>4</i>	THF	Noncomplexed <i>t</i> -BuOK (see text)	–20 to –30	80	60
E. Base added to a mixture of PhHgCl and <i>4</i>	THF	Noncomplexed <i>t</i> -BuOK	–70 to –75	50	–
F. <i>4</i> and PhHgCl consecutively added to the base		Noncomplexed <i>t</i> -BuOK	–70 to –75	70	60

*t*-BuOK is used at –25° or –75° (methods D and F) and when complexed *t*-BuOK is used at –25° (method B). The order in which the reagents are added is also important (*cf.* Experimental, methods E and F). It is noteworthy that the dichloro compound *Ib* is obtained in 10–20% lower yield than the dibromo compound *Ia*. Since the THF solution of noncomplexed *t*-BuOK is easier to make and handle than the 1/1 complex, method D appears to be the most convenient.

These findings are contrary to the results of Seyferth and Lambert concerning the condensation between phenylmercuric chloride and haloforms in THF.<sup>4</sup> They found that complexed *t*-BuOK gave high yields of phenyl-(trihalomethyl)mercury compounds at –25° as well as at –75° whereas the noncomplexed commercial *t*-BuOK they used was not very effective at these temperatures. The reason for these discrepancies may be the different nature of the dihaloacetyl piperidines and the haloforms. Also the noncomplexed commercial product may be less pure than that freshly prepared from *t*-butyl alcohol and potassium.

[Dichloro(*N,N*-pentamethylenecarbamoyl)methyl]phenylmercury (*Ib*) was decomposed by refluxing a solution in bromobenzene for a 22 h period. Phenylmercuric chloride and two isomeric chloro- $\beta$ -lactams were obtained. The IR, NMR, and mass spectra of these were quite analogous to those of the *cis*- and *trans*-bromo- $\beta$ -lactams *2a* and *3a*.<sup>1</sup> Consequently the chloro- $\beta$ -lactams are assigned the *cis*- and *trans*-structures *2b* and *3b*, respectively. Some *N*-(dichloroacetyl)piperidine (*4b*) was also isolated.

Dichloro compound *Ib* is considerably more stable than dibromo compound *Ia*. This is shown by the fact that heating in refluxing bromobenzene for 22 h was required to decompose compound *Ib* while only 1.7 h was required for compound *Ia*. This is analogous to the findings of Seyferth *et al.* that the dihalocarbene is formed much more rapidly from phenyl(tribromomethyl)mercury than from phenyl(trichloromethyl)mercury.<sup>6</sup>

A synthesis of the diiodo- and bromochloroanalogues of [dibromo(*N,N*-pentamethylenecarbamoyl)methyl]phenylmercury is under way.

#### EXPERIMENTAL

Melting points were determined on a micro hot stage and are uncorrected. Elemental analyses were carried out by A. Bernhardt, Elbach über Engelskirchen, West Germany. Infrared spectra were recorded on a Perkin Elmer No. 421, nuclear magnetic resonance spectra on a Varian A-60, and mass spectra on an LKB 2000 spectrometer. All THF used was freshly distilled from potassium metal under a nitrogen atmosphere.

*Noncomplexed t-BuOK.* *t*-BuOH (60.0 g, 0.81 mol), freshly distilled from sodium metal, and potassium metal (31.3 g, 0.80 mol) were heated in refluxing THF (700 ml) under an atmosphere of purified nitrogen until the reaction was complete (approximately 3 days). The solution was stored under nitrogen in the refrigerator. The concentration of *t*-BuOK was determined by titration of an aliquot of the solution; samples were removed with a pipette under nitrogen flushing.

[*Dibromo(N,N-pentamethylenecarbamoyl)methyl]phenylmercury* (*Ia*). The apparatus was dried in an oven prior to use and was assembled and flushed with nitrogen while still hot.

The compositions of the crude reaction products were determined by quantitative IR spectroscopy and TLC.

*Method A*, see Refs. 1 and 3.

*Method B* (*cf.* Ref. 4). A magnetically stirred solution of *N*-(dibromoacetyl)piperidine (2.8 g, 10 mmol) and phenylmercuric chloride (3.1 g, 10 mmol) in THF was maintained at  $-30^{\circ}$  to  $-20^{\circ}$  by the use of an acetone bath to which dry ice was added as needed. A suspension of complexed *t*-BuOK<sup>5</sup> (1.9 g, 10 mmol) in THF (100 ml) was added to the reaction mixture over a 15 min period from a pressure equalizing addition funnel equipped with a magnetic stirrer. When the addition was complete the reaction mixture was stirred an additional 30 min at about  $-25^{\circ}$ . The temperature was quickly raised to  $+10^{\circ}$ , the solution was then transferred to a one-necked flask and the solvent evaporated on a rotary evaporator at room temperature. The residue was dissolved in benzene (250 ml), washed with distilled water (40 ml) and dried ( $\text{MgSO}_4$ ).

Crystallization from dry diethyl ether gave [dibromo(*N,N*-pentamethylenecarbamoyl)methyl]phenylmercury<sup>1</sup> (*Ia*) (4.1 g, 75%), m.p.  $126-128^{\circ}$ .

*Method C.* As method B but performed at  $-75^{\circ}$ . IR analysis of the crude product indicated that the yield of *Ia* was *ca.* 10%.

*Method D.* As method B except that the 1/1 *t*-BuOK/*t*-BuOH complex was replaced with noncomplexed *t*-BuOK (10 mmol in 50 ml of THF). Yield 4.4 g (80%), m.p.  $126-128^{\circ}$ .

*Method E.* As method D but performed at  $-75^{\circ}$ . Yield 50% (from IR).

*Method F.* A magnetically stirred solution of noncomplexed *t*-BuOK (10 mmol) in THF (100 ml) was cooled to  $-75^{\circ}$ . To this was added *N*-(dibromoacetyl)piperidine (2.8 g,

10 mmol) in THF (50 ml) over a 10 min period, immediately followed by a solution of phenylmercuric chloride (3.1 g, 10 mmol) in THF (50 ml), also over a 10 min period. The solution was stirred at  $-75^{\circ}$  an additional 30 min. The reaction mixture was worked up as usual. Yield 70 % (from IR).

*N*-(Dichloroacetyl)piperidine (4b). The title compound was synthesized like the dibromo analogue,<sup>1</sup> m.p.  $61-62^{\circ}$ . (Found: C 44.1; H 5.9; Cl 35.1. Calc. for  $C_7H_{11}NOCl_2$ : C 42.9; H 5.7; Cl 36.1.) NMR ( $CDCl_3$ ,  $\delta$  units relative to TMS as internal standard): 1.65 (s,  $CH_2$ ), 3.60 (s,  $N-CH_2$ ), 6.2–6.5 (s,  $CHCl_2$ ,  $\delta$  depended on concentration). IR: (KBr) CO  $1645\text{ cm}^{-1}$ .

[Dichloro(*N,N*-pentamethylenecarbamoyl)methyl]phenylmercury (1b). The yields of the different synthetic variations are listed in Table 1. M.p.  $103-104^{\circ}$ . (Found: C 33.1; H 3.1; Cl 14.9; Hg 42.7. Calc. for  $C_{13}H_{15}NOCl_2Hg$ : C 33.0; H 3.2; Cl 15.0; Hg 42.4.) NMR: 1.65 (s,  $CH_2$ ), 3.70 (s,  $N-CH_2$ ), 7.25 (s, aromatic protons). IR: (KBr) CO  $1625\text{ cm}^{-1}$ .

*Thermal decomposition of [dichloro(N,N-pentamethylenecarbamoyl)methyl]phenylmercury (1b)*. A solution of 1b (18.5 g, 0.039 mol) in freshly distilled bromobenzene was refluxed for 22 h. The solvent was removed *in vacuo*, ether was added and the insoluble phenylmercuric chloride (10.3 g, 0.033 mol, 85 %) was filtered off. Separation of the ether soluble products was accomplished by chromatography on a short column of thin layer grade silica gel.<sup>7</sup> Elution with increasing amounts of diethyl ether in light petrol ether afforded *cis*-7-chloro-8-oxo-1-azabicyclo[4.2.0]octane(2b) (0.5 g, 8 %) and *trans*-7-chloro-8-oxo-1-azabicyclo[4.2.0]octane (3b), (2.7 g, 45 %). *cis*-7-Chloro-8-oxo-1-azabicyclo[4.2.0]octane (2b). (Found: C 52.5; H 6.3; Cl 22.0. Calc. for  $C_8H_{10}ClNO$ : C 52.7; H 6.3; Cl 22.2.) NMR: 1.1–2.1 (m, H-3, H-4 and H-5), 2.5–4.0 (m, H-2, H-6), 4.95 (two d,  $J$  1.4 and 4.4 cps, H-7). IR (KBr) CO  $1760\text{ cm}^{-1}$ . MS: 161, 159 (M, 14), 124 (M–Cl, 100). *trans*-7-Chloro-8-oxo-1-azabicyclo[4.2.0]octane (3b), m.p.  $58-60^{\circ}$ . (Found: C 52.3; H 6.5; Cl 22.1. Calc. for  $C_8H_{10}ClNO$ : C 52.7; H 6.3; Cl 22.2.) NMR: 1.1–2.2 (m, H-3, H-4 and H-5), 2.5–4.0 (m, H-2, H-6), 4.30 (d,  $J$  1.3 cps, H-7). IR (KBr): CO  $1760\text{ cm}^{-1}$ . MS: 161, 159 (M, 30) 124 (M–Cl, 100).

*Acknowledgements*. I thank Drs. B. Åkermark and B. Sjöberg for their interest and for stimulating discussions. The work has been supported by the *Swedish Board for Technical Development* and *AB Astra*. Miss G. Hammarberg recorded the spectra.

#### REFERENCES

1. Johansson, N. G. and Åkermark, B. *Acta Chem. Scand.* **25** (1971) 1927.
2. Seyferth, D., Burlitch, J. M., Minasz, R. J., Yick-Pui Mui, J., Simmarns, Jr., H. D. Treiber, A. J. and Dowd, S. R. *J. Am. Chem. Soc.* **87** (1965) 4259.
3. Seyferth, D. and Burlitch, J. M. *J. Organometal. Chem.* **4** (1965) 127.
4. Seyferth, D. and Lambert, Jr., R. L. *J. Organometal. Chem.* **16** (1969) 21.
5. Speziale, A. J. and Ratts, K. W. *J. Am. Chem. Soc.* **84** (1962) 854.
6. Seyferth, D., Burlitch, J. M. and Heeren, J. K. *J. Org. Chem.* **27** (1962) 1491.
7. Hunt, B. J. and Rigby, W. *Chem. Ind. (London)* **1967** 1868.

Received November 17, 1972.