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# CONVERSION OF BROMO COMPOUNDS TO CHLORO COMPOUNDS

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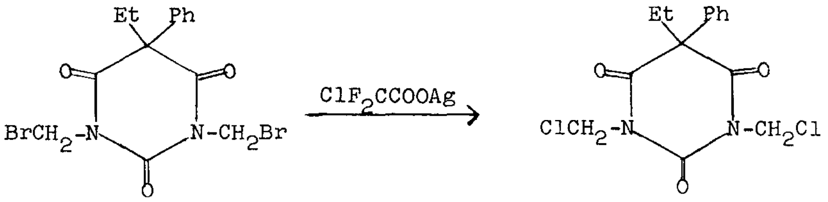
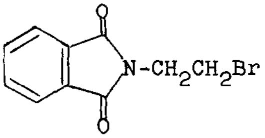
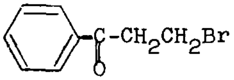
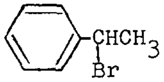
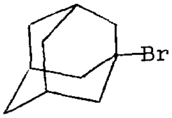
Several methods are known for the conversion of chloro-compounds to bromo-compounds[1] and bromo-compounds to iodo-compounds.[2] Only a few examples are known for the reverse procedure, i.e. conversion of bromo-compounds to chloro-compounds.[3]

It has now been found that transhalogenation of bromo derivatives takes place readily using silver difluorochloroacetate.[4] To a solution of 1,3-bis-(bromomethyl)-5-ethyl-5-phenyl-barbituric acid[5] (I), mp 160-161.5°, (Analysis: calculated for $C_{14}H_{14}O_3N_2Br_2$: C, 40.22; H, 3.37; N, 6.70; Br, 38.23. Found: C, 39.99; H, 3.23; N, 6.80; Br, 38.51.) in acetonitrile, silver difluorochloroacetate (two equivalents) was added, and the mixture was heated at reflux overnight. The precipitated silver salt was removed by filtration, and the solvent evaporated to yield a solid product. Crystallization from ethanol afforded pure 1,3-bis(chloromethyl)-5-ethyl-5-phenyl-barbituric acid (II), mp 154-156° in 70% yield. Analysis: calculated for $C_{14}H_{14}O_3N_2Cl_2$: C, 51.08; H, 4.29; N, 8.51; Cl, 21.54. Found: C, 51.17; H, 4.34; N, 8.50; Cl, 21.67.



In the other examples, which are summarized in the accompanying table, purification was achieved by column chromatography using E. Merck 70-325 mesh ASTM silica gel. Elution was carried out with benzene-ethyl acetate solvent mixtures. All starting materials and products were subjected to microanalyses and the values were within ±0.3% of the theoretical values.[6] All products gave satisfactory infrared spectra and TLC values which were identical to those of the corresponding authentic samples. (1-Chloroadamantane and N-(2-chloroethyl)-phthalimide samples were not available.)

| Compound | Solvent | Reaction Temperature | Reaction Time (Hours) | % Yield of Chloro-Compound |
|---|---|---|---|---|
|  | diglyme | 150° | 140 | 92 |
|  | $CH_3CN$ | 81° | 16 | 70 |
| $CH_3(CH_2)_6CH_2Br$ | glyme | 124° | 78 | 89 |
|  | glyme | 124° | 16 | 95 |
|  | glyme | 124° | 24 | 85 |

## REFERENCES

1. Houben-Weyl, Methoden der Organische Chemie, Vol. 5/4, p. 354, G. Thieme Verlag, Stuttgart, (1962).

2. ibid., p. 595.

3. ibid., p. 749.

4. Supplied by K & K Laboratories, Inc., Plainview, New York.

5. J. A. Vida, W. R. Wilber and J. F. Reinhard, J. Med. Chem., (submitted for publication).

6. Analyses by Galbraith Laboratories, Knoxville, Tenn. and S. M. Nagy Microchemical Laboratory, Belmont, Mass.