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Electrophilic Anti Addition of Bromine to 2-Methylbut-2-ene with the *N*-Methylpyrrolidin-2-one Hydrotribromide Complex

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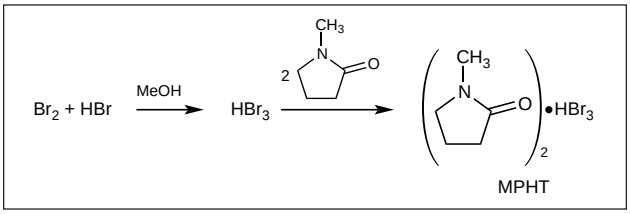
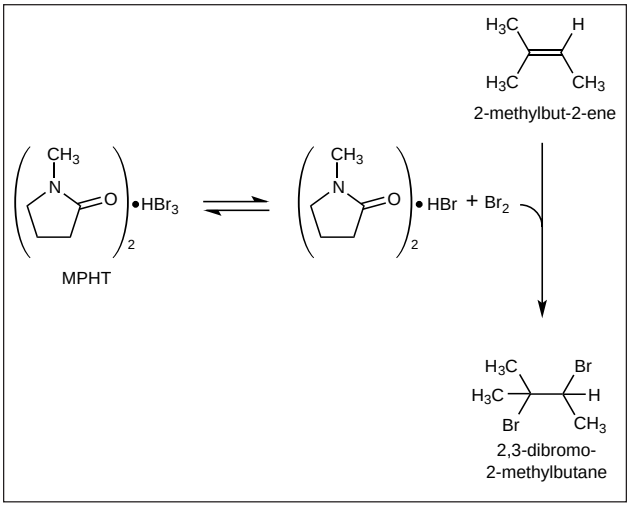
Despite the fact that bromine is very toxic by inhalation, highly corrosive, and may cause serious burns, its electrophilic addition reaction continued to be featured in the second-year laboratory course at Paris XI University. It had customarily been performed by the addition of a solution of bromine in chloroform to olefinic compounds such as 2-methylbut-2-ene *(1)*. The laboratory exercise also required two liquid purification techniques: liquid–liquid extraction followed by two kinds of distillation. Furthermore, preparation of the chloroform solution of bromine (8%) required manipulation of large quantities of bromine, and even the use of the resulting solution could not prevent bromine fumes. Moreover, the addition reaction of bromine to 2-methylbut-2-ene is an exothermic process, inducing evaporation of olefinic compound and therefore decreasing the overall reaction yield. For safety considerations, we proposed that bromine no longer be used and be replaced in the student laboratory by another brominating agent.



Scheme I. Reaction to prepare MPHT.



Scheme II. Reaction of MPHT with an olefin.

In our university, molecular bromine has been substituted by the *N*-methylpyrrolidin-2-one hydrotribromide complex (MPHT; ref *2*) whose crystalline data have been recently published *(3)*. This orange crystalline complex has been prepared by an experienced chemist in large quantities, following a slightly modified version of Daniels' procedure (ref *2*; Scheme I).

The MPHT complex is a stable solid that can be stored several months at room temperature; after a six-month storage test at room temperature no decrease in the free bromine titer could be detected. MPHT is not corrosive, not necrosing, less toxic, and easier to handle for students than molecular bromine. This complex smoothly liberates bromine in organic solvents according to Scheme II. The addition reaction was performed at room temperature in dichloromethane using 2-methylbut-2-ene. Discoloration of the resulting orange solution could be observed by students as long as MPHT is consumed. *N*-Methylpyrrolidin-2-one hydrobromide and *N*-methylpyrrolidin-2-one are byproducts of the reaction and are removed by washing the organic layer with water. Over a one-year period, the majority of the 230 students successfully completed this experiment with overall yields ranging from 35 to 80%.

Experimental Procedure

We simplified the Daniels, Chiddix, and Glickman procedure *(2)* to develop a reaction that could be easily performed in typical laboratory settings.

Synthesis of the MPHT Complex

To a 2-L round bottomed flask, cooled in an ice bath and equipped with a dropping funnel and a condenser, were added, successively, 200 mL of MeOH and 250 mL (one drop per second) of a commercial solution of HBr (30% in acetic acid) while maintaining the internal temperature between 10 °C and 15 °C. Molecular bromine, 60 mL, was then added by the dropping funnel (2 drops per second). The solution was stirred for 10 minutes and the crude brown mixture became orange. Commercial *N*-methylpyrrolid-2-one, 250 mL, was then added by the dropping funnel (2 drops per second). After 10 minutes, the MPHT complex started to precipitate in the media. The mixture was stirred for 1 hour at 10 °C and orange crystals were collected, dried, washed with Et_2O (4 × 50 mL), and dried under vacuum to give 440 g of MPHT as orange crystals (yield = 87%).

mp = 122–124 °C [lit *(2)* mp = 124 °C].

IR (cm^{-1}): 3339, 2935, 1640, 1420, 1228, 1011, 962, 850.

^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.25 (m, 4H), 2.90 (t, 4H, J = 8.0 Hz), 3.00 (s, 6H), 3.75 (t, 4H, J = 7.2 Hz), 14.6 (s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$, δ): 18.3, 31.4, 33.3, 52.8, 178.3.

Anal. Calcd for $(C_5H_9NO)_2 \cdot HBr_3$: C, 27.33; H, 4.33; N, 6.38. Found: C, 27.62; H, 4.32; N, 6.61.

Synthesis of 2,3-Dibromo-2-methylbutane

In a conical flask were mixed 4.95 g (7.5 mL) of 2-methylbut-2-ene (70 mmol) and 50 mL of CH_2Cl_2. To this solution 30.7 g of MPHT (70 mmol) was then added with a spatula. A discoloration of MPHT was observed after each addition. When the addition of the complex was complete, the crude organic layer was washed with water (3 × 150 mL). After each extraction, it was possible to observe reduction of the volume of the organic layer, indicating that *N*-methylpyrrolidin-2-one was transferred from the organic to the aqueous layer. After drying the organic layer with $CaCl_2$ (5 g), the crude mixture was distilled at room temperature to collect CH_2Cl_2. Then the 2,3-dibromo-2-methylbutane was distilled under reduced pressure.

bp = 50 °C (18 mm Hg) [lit *(4)* bp = 49–51°C (18 mm Hg)].

IR (cm^{-1}): 2979, 2934, 1450, 1377, 1098, 1051.

^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.90 (s, 3H), 2.05–2.20 (d, 3H, J = 6.7 Hz), 2.25 (s, 3H), 4.50–4.65 (q, 1H, J = 6.7 Hz).

^{13}C NMR (50 MHz, $CDCl_3$, δ): 23.5, 28.0, 34.9, 59.4, 68.2.

Hazards

Bromine is toxic by inhalation, very toxic for aqueous organisms, and may cause serious burns. Bromine *must* be used with gloves by an experienced chemist in a fume hood and in the presence of a saturated solution of sodium thiosulfate. Hydrobromic acid, *N*-methylpyrrolidone, methylene chloride, and MeOH are toxic and contact with the skin or eyes, ingestion, and inhalation should be avoided. Methylene chloride is a suspected carcinogen. The use of gloves should be encouraged and when possible all transformations should be carried out in a fume hood. For each manipulation of any chemical in the laboratory, eye protection is required. The toxicity level of MPHT is not actually known as it is a new synthetic complex. We suppose the MPHT toxicity is comparable to that of pyrrolidone hydrotri-bromide (PHT) (*5*), which is supposed to be very toxic by inhalation and in contact with skin, and irritating to eyes, respiratory system, and skin. So MPHT must be handled with the same care as PHT; that is, in case of contact with eyes, wash plentifully with water and call a doctor and take off immediately any soiled or splashed clothes.

Conclusion

The ease of MPHT use in bromination reactions together with its crystalline state make it less dangerous than the use of molecular bromine. This complex also proved to be effective for ketone bromination *(6)*.

Acknowledgments

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[W]Supplemental Material

Instructions for the students and notes for the instructor are available in this issue of *JCE Online*.

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