An Improved Synthesis of 2,7-Dihydroxytropone (3-Hydroxytropolone)

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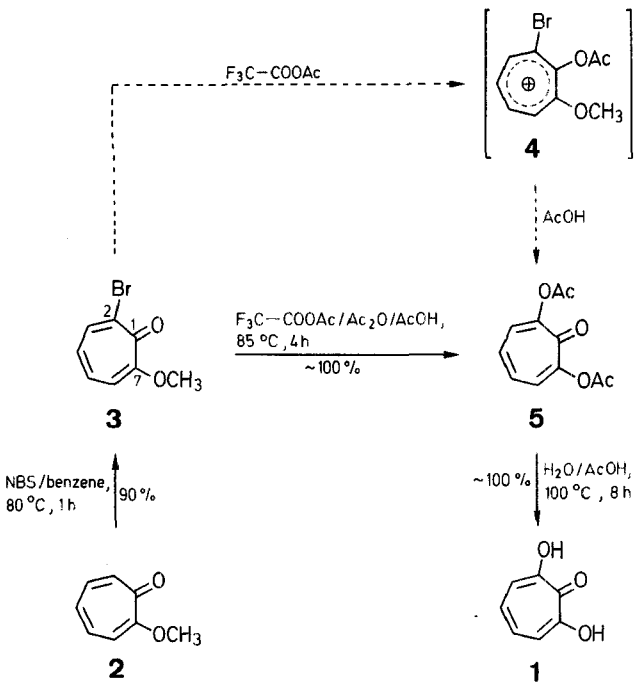
2,7-Dihydroxytropone is efficiently prepared from 2-methoxytropone by bromination with *N*-bromosuccinimide, reaction of the resultant 2-bromo-7-methoxytropone with acetyl trifluoroacetate *in situ*, and hydrolysis of the 2,7-diacetoxytropone thus obtained with aqueous acetic acid. The intermediacy of a 2-acetoxy-1-bromo-3-methoxytropylium salt in the acetoxylation step is suggested.

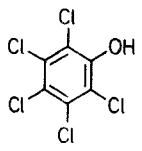
The known preparations of 2,7-dihydroxytropone (3-hydroxytropolone; **1**), an important tropolone derivative, have some drawbacks. Thus, the direct hydroxylation of tropolone with potassium peroxodisulfate[1] gives compound **1** in only 17% yield along with 30% of 2,5-dihydroxytropone; the reaction of 7-bromo-2-hydroxytropone with base under forced conditions causes a benzyne-type elimination-addition reaction to form both 2,7- and 2,6-dihydroxytropones or 7- and 6-alkoxy-2-hydroxytropones[2,3]; acid hydrolysis of 7-bromo-2-hydroxytropone under severe conditions has been shown to give compound **1** in 66% yield[4] but the preparation of the starting material 7-bromo-2-hydroxytropone is difficult.

We now report an improved synthesis of 2,7-dihydroxytropone (**1**) from 2-methoxytropone (**2**). This latter compound is brominated with *N*-bromosuccinimide using a modification of the procedure of Ref.[5]. Solvolysis of the resultant 2-bromo-7-methoxytropone (**3**) with acetic anhydride containing trifluoroacetic and acetic acids (acetyl trifluoroacetate *in situ*) at 85 °C affords 2,7-diacetoxytropone (**5**) in quantitative yield, probably via a 2-acetoxy-1-bromo-3-methoxytropylium salt (**4**) as intermediate. Hydrolysis of compound **5** with aqueous acetic acid affords the desired compound **1** in nearly quantitative yield, the overall yield of **1** from **2** being 89%.

Hydrolysis of polyhalotropones has hitherto only been effectively achieved for the first step, further hydrolysis of halotropones being very slow.



It is worthy of note that halophenols such as pentachlorophenol **(6)** were unreactive under the acetoxylation conditions used by us.



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2-Bromo-7-methoxytropone (3):
A solution of 2-methoxytropone (**2**; 1.14 g, 8.37 mmol) and *N*-bromosuccinimide (1.8 g, 10 mmol) is heated to reflux for 1 h. The mixture is then cooled and the succinimide formed is filtered off. Column chromatography of the filtrate on silica gel using ethyl acetate/hexane (1/1) as eluent affords product **3** as pale yellow crystals; yield: 1.61 g (90%); m.p. 92–93 °C (Ref.[6], m.p. 91–91.5 °C).

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 3.96 (s, 3 H); 6.59 (ddd, 1 H, J = 10, 9.5, 1 Hz); 6.84 (dd, 1 H, J = 9.5, 1 Hz); 7.19 (ddd, 1 H, J = 10, 9.5, 1 Hz); 8.16 ppm (dd, 1 H, J = 9.5, 1 Hz).

^{13}C-N.M.R. ($CDCl_3$/TMS_{int}): δ = 56.8 (CH_3); 112.6 (C-6); 125.3 (C-4); 133.3 (C-5); 137.5 (C-2); 139.9 (C-3); 162.6 (C-7); 173.6 ppm (C-1).

As a by-product (first fraction of chromatography), *2,4-dibromo-7-methoxytropone* is obtained; yield: 0.24 g (~10%); m.p. 206–207 °C (Ref.[5], m.p. 206–207 °C).

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 3.91 (s, 3 H); 6.54 (d, 1 H, J = 11 Hz); 7.44 (dd, 1 H, J = 11, 2 Hz); 8.41 ppm (d, 1 H, J = 2 Hz).

2,7-Diacetoxytropone (5):
A mixture of 2-bromo-7-methoxytropone (**3**; 480 mg, 2.23 mmol), acetic anhydride (4 ml), acetic acid (0.2 ml), and trifluoroacetic acid (0.4 ml) is heated at 85 °C for 4 h. The solvents are then removed in vacuo, and the residue is column-chromatographed on silica gel using ethyl acetate/hexane (1/1) as eluent; yield of **5**: 490 mg (99%); m.p. 90–91 °C (Ref.[7], m.p. 86–87 °C).

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 2.32 (s, 6 H); 7.0–7.35 ppm (m, 4 H).

^{13}C-N.M.R. ($CDCl_3$/TMS_{int}): δ = 20.6 (2C, CH_3); 129.3 (C-3, C-6); 131.2 (C-4, C-5); 157.8 (C-2, C-7); 167.9 ppm (3C, CO).

2,7-Dihydroxytropone (1):
A solution of 2,7-diacetoxytropone (**5**; 400 mg, 1.8 mmol) in aqueous 67% acetic acid (15 ml) is heated at 100 °C for 8 h. The volatile material is then removed in vacuo to give product **1**; yield: 245 mg (~100%); m.p. 143–144 °C (Ref.[7], m.p. 138–140 °C).

^{1}H-N.M.R. (CD_3OD/TMS_{int}): δ = 7.0–7.55 ppm (m, 4 H).

^{13}C-N.M.R. (CD_3OD/TMS_{int}): δ = 122.1 (C-3, C-6); 130.3 (C-4, C-5); 161.8 (C-2, C-7); 169.8 ppm (C-1).

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[1] Nozoe, T., Seto, S., Itô, S., Sato, M., Katono, T. *Sci. Rep. Tohoku Univ. Ser. I* **1953**, *37*, 191.
[2] Kitahara, Y. *Sci. Rep. Tohoku Univ. Ser. I* **1956**, *39*, 258.
[3] Yamatani, T., Yasunami, M., Takase, K. *Tetrahedron Lett.* **1970**, 1725.
[4] Johns, R.B., Johnson, A.W., Tišler, M. *J. Chem. Soc.* **1954**, 4605.
[5] Yasunami, M., Sagasawa, Y., Takase, K. *Chem. Lett.* **1980**, 205.
[6] Nozoe, T., Seto, S., Takeda, H., Morosawa, S., Matsumoto, K. *Proc. Jpn. Acad.* **1951**, *27*, 556.
[7] Hirama, M., Itô, S. *Tetrahedron Lett.* **1975**, 1071.