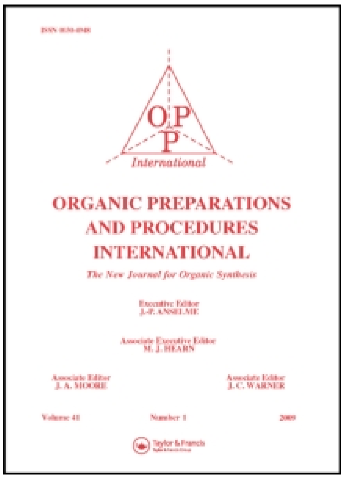

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

IMPROVED PREPARATION OF SUCCINYLCHOLINE CHLORIDE

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To cite this Article Wang, Cheng-Hsia , Tso, Hsi-Hua and Chen, Chao-Tung(1979) 'IMPROVED PREPARATION OF SUCCINYLCHOLINE CHLORIDE', Organic Preparations and Procedures International, 11: 2, 93 — 95

To link to this Article: DOI: 10.1080/00304947909354847

URL: http://dx.doi.org/10.1080/00304947909354847

ORGANIC PREPARATIONS AND PROCEDURES INT. 11(2), 93-101(1979)

OPPI BRIEFS

IMPROVED PREPARATION OF SUCCINYLCHOLINE CHLORIDE

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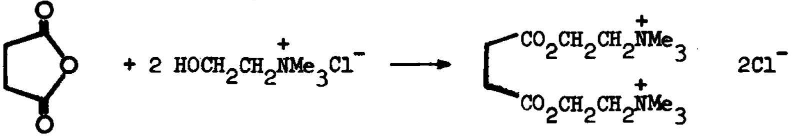
Succinylcholine chloride(I), a useful muscle relaxant has previously been prepared by the methylation of bis(2-dimethylaminoethyl)succinate (method 1),[1,2] and the alkylation of trimethylamine with bis(2-chloroethyl) succinate (method 2).[3,4] It has also been obtained by the reaction of choline chloride with succinoyl chloride (method 3)[5] or with succinic anhydride (method 4).[6] Methods 1 and 2 involve use of an autoclave which is less easily accessible and handled. Moreover, the product may become contaminated by heavy metal ions from the autoclave and would be hard to purify. Method 3 requires one more step of making succinyl chloride from succinic anhydride. The reported 56% yield of method 4 could not be duplicated, the half ester invariably resulting when the patented procedure was followed.



I

A modification of method 4 in which dry hydrogen chloride gas is used as the catalyst and the water formed is removed by azeotropic distillation with benzene, affords succinylcholine chloride(I) in 79-81% yields.

EXPERIMENTAL

Dry hydrogen chloride gas was passed into a mixture of succinic anhydride (3.20 g, 0.032 mole) and choline chloride (9.37 g, 0.067 mole) in 80 ml of benzene (dried over sodium wire and distilled) for 1 hr. The mixture was allowed to stand overnight, then refluxed for 10 hrs. The water produced in the reaction was azeotropically removed with benzene using a Dean-Stark trap. The reaction mixture was cooled and the benzene was decanted.

The solid remaining in the flask was washed twice with dry benzene (10 ml) and dried _in vacuo_. The dried solid was dissolved in methanol (Japan, Wako, reagent grade, 30 ml) to afford a white powdery product (10.32 g, 81% yield) (_Caution_: hygroscopic!), which was recrystallized from 95% ethanol in 82% yield, mp. 159-162°, lit.[3] 160-164°. Tlc on polyamide (E. Merck) layer developed with isopropanol (reagent grade) and visualized with iodine: R_f 0.71. IR(KBr): 1735(C=O), 1425($\overset{+}{N}$-CH_2), 1310, 1150 cm^{-1} (C-O-C). NMR (Room temperature, in D_2O, DSS internal standard): δ 2.71 (s, 4H, CH_2CO), 3.22 (s, 18H, CH_3), 3.65 (t, 4H, $CH_2\overset{+}{N}$), 4.52 (t, 4H, OCH_2), 4.61 (s, 1H, HDO).

Anal. Calcd. for $C_{14}H_{34}Cl_2N_2O_6$ (as dihydrate):

C, 42.32; H, 8.63; Cl, 17.85; N, 7.05
Found: C, 42.43; H, 8.55; Cl, 17.72; N, 6.81.

Acknowledgment.- We wish to thank National Science Council, Republic of China, for a financial support.

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AN IMPROVED SYNTHESIS OF FLUORENONE METHYLNITRONE

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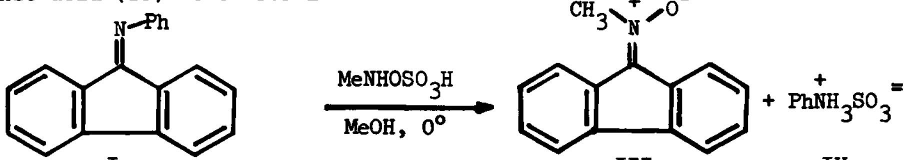
Fluorenone methylnitrone (III) was originally prepared from fluorenone in an overall yield of 47%, using drastic conditions for two days.[1] We now report a convenient synthesis of the title compound (III) in 90% yield by treating N-fluorenylideneaniline (I) with N-methylhydroxylamine-O-sulfonic acid (II) at 0° for 1 hr.



I III IV

The reaction is general for aldimines and ketimines and was found to be independent of the substituents on the imines.[2] When aldehyde imines are used, the methylnitrones obtained are in the more stable *trans* configuration.

EXPERIMENTAL

N-Fluorenylideneaniline (I).- This compound was prepared in 82% yield from commercially available 9-fluorenone (Aldrich Chemical Co.) *via* its conden-