

NOVEL DEBENZYLATION OF QUATERNARY AMMONIUM SALTS WITH THIOPHENOL

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(Received in Japan 25 December 1968; received in UK for publication 15 January 1969)

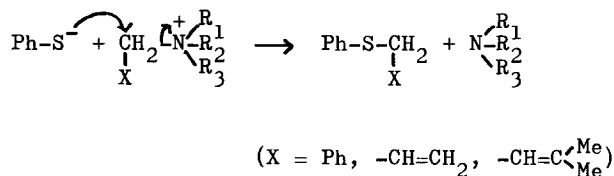
In general, the N-benzyl group of quaternary ammonium salts could be removed by reduction with sodium amalgam or pyrolysis, but undesirable results have often been obtained in case of the N-benzyl derivatives having the other readily reducible functions such as halogeno, cyano, nitro groups and double bond in their moiety. Therefore, we have investigated the selective N-debenzylation reaction without hydrogenolysis and wish to report a novel N-debenzylation of the quaternary ammonium salts with thiophenol in the presence of aqueous alkaline solution.

Shamma and his co-workers¹ have previously reported the demethylation of triethylamine methochloride with sodium thiophenoxide in 2-butanone, acetonitrile and dimethylformamide, but the application of this method to debenylation has not yet been investigated.

Heating of various N-benzyl ammonium salts with thiophenol in 5 - 20 % aqueous sodium hydroxide solution gave the corresponding debenzylated tertiary amines in good yields as shown in Table I. The cleavage of -C-N- single bond by pyrolysis or by treatment with inorganic salt containing sulphur has been known in case of both allylic and benzylic ammonium salts². Therefore, we investigated whether either of selective debenylation and deallylation would be occurred in the N-benzyl-N-allylammonium salts or not. Thus, in case of N-benzyl-N-(3,3-dimethylallyl)piperidinium bromide (XI), the competitive debenylation and deallylation were occurred to give a mixture of the tertiary amine (XV)

and (XVI), but in case of (XII), N-benzyl-(XVII) and N-(3,3-dimethylallyl)-1,2,3,4-tetrahydroisoquinoline (XVIII) were obtained as shown in Table II, and both N-benzyl-(XIX and XXI) and N-allyl derivatives (XX and XXII) were also obtained in case of N-allyl-N-benzylammonium salts (XIII and XIV).

All the tertiary amines obtained here were found to be identical with the authentic samples as free bases and/or their salts by mixed melting point test, i.r. spectral and thin layer chromatographic comparisons. Benzyl phenyl thioether³ was obtained as by-product in all the reaction listed in Table I and II. This fact indicates that the reaction would proceed in one stage as follow.⁴



This reaction seems to provide a new and useful method for debenylation and deallylation. Further application of this reaction is in progress, especially aimed at the debenylation of the compounds having the other reducible functions together with N-benzyl group.

Acknowledgement We thank President A. Yanagisawa and Director O. Takagi of The Grelan Pharmaceutical Co. Ltd. and Dr. H. Yagi of Pharmaceutical Institute, Tohoku University for their assistance. We also thank Miss R. Hasebe, Miss A. Kawakami, Miss Y. Tadano, Miss T. Yoshida, Miss K. Shima, and Miss R. Kato for u.v., i.r., and n.m.r. spectral determinations and for microanalyses.

Table I Debenzylation of Various Quaternary Ammonium Salts

Quaternary ammonium salt (g.)	Thiophenol (g.)	aq-NaOH solution (ml.) (%)	Temp. (°C)	Time (hr.)	Yield of tertiary amine (g.) (%)
N,N-Dibenzyl-N,N-dimethyl-ammonium chloride ⁵ (I) (2.61)	5.5	10(20)	90	5	N,N-Dimethylbenzylamine ⁶ (VI) (1.14) (85.1)
N-Benzyl-N,N-dimethyl-N-(β-phenethyl) ammonium chloride ⁷ (II) (1.38)	2.75	10(20)	90	7	N,N-Dimethyl-β-phenethylamine ⁸ (VII) (0.52) (69.7)
N,N,N-Triethyl-N-benzylammonium chloride ⁷ (III) (1.9)	3.0	10(20)	90	10	Triethylamine (VIII) (0.51) (18.5)
N-Benzyl-N-methylpiperidinium chloride ⁷ (IV) (1.12)	1.1	2(20)	90	5	N-Methylpiperidine ⁹ (IX) (1.0) (60.9)
N-Benzyl-N-methyl-1,2,3,4-tetrahydroisoquinolinium chloride ⁷ (V) (1.37)	5.5	4(5)	70	7	1,2,3,4-Tetrahydro-2-methyl-isoquinoline ¹⁰ (X) (0.38) (51.4)

Table II Debenzylation and Deallylation of Quaternary Ammonium Salts

Quaternary ammonium salt (g.)	Thiophenol (g.)	aq-NaOH solution (ml.) (%)	Temp. (°C)	Time (hr.)	Yield of tertiary amine (g.) (%)
N-Benzyl-N-(3,3-dimethylallyl)-piperidinium bromide ⁷ (XI) (5.0)	5.0	18(10)	70	4	N-Benzylpiperidine ¹¹ (XV) (1.7) (69.5) N-(3,3-Dimethylallyl)piperidine ¹² (XVI) (0.5) (23.5)
N-Benzyl-N-(3,3-dimethylallyl)-1,2,3,4-tetrahydroisoquinolinium iodide ⁷ (XII) (10.8)	8.5	32(10)	70	4	N-Benzyl-1,2,3,4-tetrahydroisoquinoline ¹³ (XVII) (2.9) (49.5) 1,2,3,4-Tetrahydro-N-(3,3-dimethylallyl)isoquinoline ⁷ (XVIII) 1.55 (30.1)
N-Allyl-N-benzyl-N,N-dimethyl-ammonium bromide ¹⁴ (XIII) (6.0)	8.0	30(10)	75	5	N,N-Dimethylbenzylamine ⁶ (XIX) (1.53) (55.6) N-Allyl-N,N-dimethylamine ¹⁵ (XX) (0.49) (28.3)
N-Allyl-N-benzylpiperidinium bromide ⁷ (XIV) (4.5)	5.2	20(10)	75	4	N-Benzylpiperidine ¹¹ (XXI) (1.33) (43.5) N-Allylpiperidine ¹⁶ (XXII) (0.74) (34.0)

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