HETEROCYCLES, Vol. 5, 1976

N-MONOMETHYLATION OF AROMATIC PRIMARY AMINES

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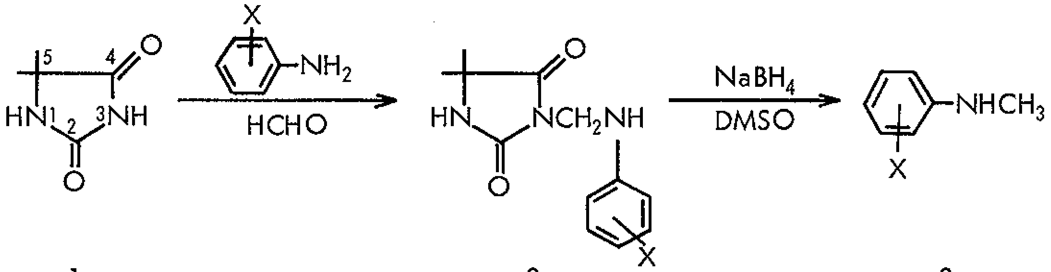
N-Monomethyl aromatic amines were conveniently prepared by reduction of 3-(N-arylaminomethyl)-5,5-dimethylhydantoin (2) with sodium borohydride in dimethyl sulfoxide.

Although a number of methods have been reported, there is still lacking a simple and efficient procedure to obtain N-monomethylated products from aromatic primary amines.[1] During the course of preparations of 3-(N-arylaminomethyl)-5,5-dimethylhydantoin derivatives (2) we anticipated that these derivatives might also provide N-monomethylated aromatic amines, because Kadin[2] reported to yield the amines by reduction of N-arylaminomethylsuccinimides with sodium borohydride in dimethyl sulfoxide (DMSO).

Treatment of aromatic primary amines with aqueous formaldehyde and 5,5-dimethylhydantoin (1) in refluxing ethanol led to 3-(N-arylaminomethyl)-5,5-dimethylhydantoins (2), the structures of which were characterized by the absence of N^3-H in nmr.[3] Then, these aminal-type derivatives (2) were treated with sodium borohydride



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in DMSO on a steam bath to result in an exothermic reaction forming the N-monomethylated aromatic amines (3) which were isolated from the reaction mixture by extraction with ether and purified by distillation. Practically the intermediate aminals (2) can be used for the next reduction without purification; the reaction mixture was concentrated by evaporation of ethanol followed by azeotropic removal of water with benzene. Yields were satisfactory as listed in Table.

TABLE

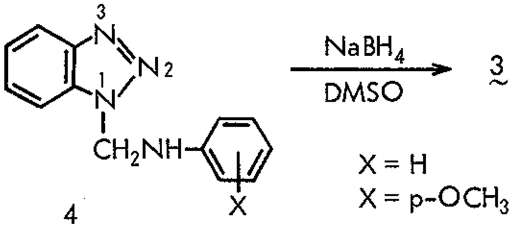
Substituent, X	mp of (2),[a] °C	bp of (3),[a] °C (mm)	Yield of (3) from (1), %
H	149-151	80-82 (15)	58.4 (66)[b]
p-OCH_3	119-121	120-121 (11)	63.9
o-Br	132-135	106-108 (10)	64.5
p-CH_3	163-165	92-93 (10)	68.6 (74.4)[b]
2,4-$(CH_3)_2$	148-150	105-107 (15)	80.6
p-CN	202-203.5	86-87[c]	36

[a] Satisfactory spectra (nmr, ir) were obtained for all compounds.

[b] The values in parentheses are the yields from (2).

[c] Melting point.

In addition, the fact that benzotriazole has a similar pKa to that of (1)[4] prompted us to investigate on N^1-arylaminomethylbenzotriazoles (4) which are also expected to give the similar results to the above. Treatment of N^1-anilinomethyl- and N^1-p-methoxyanilinomethylbenzotriazole(4)[5] with sodium borohydride in DMSO as described above gave the corresponding N-monomethylaniline derivatives (3) in 79 and 76.6% yield, respectively. The yields were thus satisfactory, but they were contaminated with a small amount of impurities which were unable to eliminate by distillation. Therefore, 3-(N-arylaminomethyl)-5,5-dimethylhydantoin derivative (2) was of better use for the preparation of N-monomethyl aromatic amines.



4

The mechanism of these reactions is considered to be the same to that proposed by Kadin.[2] Further works on other heteroaromatic amines are now in progress.

Acknowledgement

The author wishes to thank Dr. H. Tanida for encouragement throughout this work.

References and Notes

1 R. A. Crochet, Jr. and C. D. Blanton, Jr., Synthesis, 1974, 55.

2 S. B. Kadin, J. Org. Chem., 1973, **38**, 1348.

3 N^3-H generally appears around 9 δ in $CDCl_3$. R. A. Corral and O. O. Orazi, Spectrochim. Acta, 1965, **21**, 2119.

4 pKa of benzotriazole is 8.65 and that of (**1**) is 9.12. M. Ravaux, M. Laloi-Diard and M. Vilkas, Tetrahedron Lett., 1971, 4015. O. O. Orazi and R. A. Corral, Tetrahedron, 1961, **15**, 93.

5 Satisfactory elemental analyses were obtained for these compounds. N^1-Anilinomethylbenzotriazole, mp 134-135°C; N^1-p-methoxyanilinomethylbenzotriazole, mp 137-139°C.

Received, 26th July, 1976