BROMINATION OF ACETOACETANILIDE: A REVISION OF STRUCTURE

BY

R. J. CHUDGAR AND K. N. TRIVEDI

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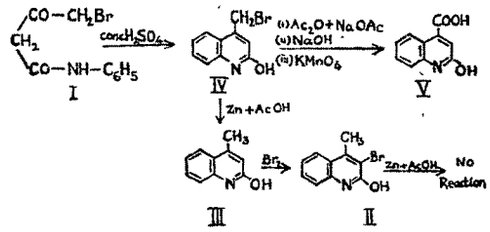
BROMINATION OF ACETOACETANILIDE : A REVISION OF STRUCTURE

KNORR[1] brominated acetoacetanilide in chloroform solution and claimed to have obtained α-bromoacetoacetanilide. Hasegawa[2] and Cook *et al.*[3] repeated the above experiment in chloroform and gave ω-bromoacetoacetanilide (I) structure to this product. Mehta and coworkers[4,5] brominated acetoacetanilide in acetic acid solution and claimed to have obtained α-bromoacetoacetanilide. They further reported that this product on cyclisation gave 3-bromo-4-methyl-2-hydroxyquinoline (II) which was identical with the product obtained on bromination of 4-methyl-2-hydroxyquinoline (III). In



I IV V III II

view of these contradictory reports, it was thought of interest to repeat the work by both the procedures. In both the cases, the same product (Found : N = 5·84%, Br = 31·69% ; $C_{10}H_{10}O_2BrN$ requires: N = 5·46%, Br = 31·25%) with m.p. and mixed m.p. 135–36° was obtained. The product is assigned ω-bromoacetoacetanilide structure on the basis of the following series of reactions. It gave on cyclisation with concentrated sulphuric acid 4-bromomethyl-2-hydroxyquinoline (IV), m.p. 254–56° which is different from the 3-bromo-4-methyl-2-hydroxyquinoline (II) (Found : N = 5·84%, Br = 33·97%; $C_{10}H_8ONBr$ requires: N = 5·88%, Br = 33·61%), m.p. 274° obtained by the bromination of 4-methyl-2-hydroxyquinoline. 4-Bromomethyl-2-hydroxyquinoline (IV) is converted to known 2-hydroxy cinchoninic acid[6] (V) (Found : N = 7·14% ; $C_{10}H_7O_3N$ requires : N = 7·4%) by treatment with acetic anhydride and fused sodium acetate followed by hydrolysis and oxidation with $KMnO_4$. 4-Bromomethyl-2-hydroxyquinoline (IV) on reduction with zinc and acetic acid gave 4-methyl-2-hydroxyquinoline (III) while 3-bromo-4-methyl-2-hydroxyquinoline (II) remained unaffected under similar conditions.

The authors record their thanks to Dr. S. S. Lele for carrying out the microanalysis.

Chemistry Department,
Faculty of Science,
M.S. University of Baroda,
Baroda-2, *March* 8, 1965.

R. J. CHUDGAR.
K. N. TRIVEDI.

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SYNTHESIS OF 4-AMINOMETHYL CARBOSTYRIL DERIVATIVES

CHUDGAR AND TRIVEDI[1] conclusively proved that bromination of acetoacetanilide gave *w*-bromo acetoacetanilide which on cyclisation gave 4-bromomethyl carbostyril. These 4-bromomethyl carbostyril derivatives are now used as intermediates for the synthesis of 4-aminomethyl carbostyril derivatives.

4-Aminomethyl carbostyrils are prepared by refluxing equimolecular quantities of dimethylamine, piperidine and morpholine respectively with 4-bromomethyl carbostyrils, dissolved in alcohol, for 2 to 3 hrs. The separated 4-aminomethyl carbostyril derivatives (Table I) are filtered, dried and recrystallised from alcohol or benzene.

The authors record their thanks to Dr. Lele for microanalysis. One of us (R. J. C.) thanks the U.G.C. for the award of a research scholarship.

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R. J. CHUDGAR.
K. N. TRIVEDI.

1. Chudgar, R. J. and Trivedi, K. N., *Curr. Sci.*, 1965, 34, 560.

TABLE I

Sl. No.	Substituents in carbostyril	m.p. °C.	Molecular formula	Found % N	Required % N
	4-Dimethylaminomethyl Carbostyril				
1	None	197	$C_{12}H_{14}N_2O$	14·45	13·88
2	8-Methyl	199	$C_{13}H_{16}N_2O$	12·63	12·96
3	6-Methoxy	183	$C_{13}H_{16}N_2O_2$	12·33	12·07
4	6-Chloro	230–32	$C_{12}H_{13}N_2ClO$	11·89	11·85
5	6-Bromo	230	$C_{12}H_{13}N_2BrO$	10·22	9·964
6	7-Chloro	183	$C_{12}H_{13}N_2ClO$	11·73	11·85
	4-Piperidinomethyl Carbostyril				
1	None	209	$C_{15}H_{18}N_2O$	11·99	11·57
2	8-Methyl	232–33	$C_{16}H_{20}N_2O$	11·05	10·94
3	6-Methoxy	221–23	$C_{16}H_{20}N_2O_2$	10·17	10·30
4	6 Chloro	245	$C_{15}H_{17}N_2ClO$	10·23	10·13
5	6-Bromo	242	$C_{15}H_{17}N_2BrO$	8·41	8·616
6	7-Chloro	239	$C_{15}H_{17}N_2ClO$	10·33	10·13
	4-Morpholinomethyl Carbostyril				
1	None	235	$C_{14}H_{16}N_2O_2$	11·43	11·48
2	8 Methyl	240–41	$C_{15}H_{18}N_2O_2$	11·13	10·85
3	6-Methoxy	208	$C_{15}H_{18}N_2O_3$	10·21	10·22
4	6-Chloro	240–42	$C_{14}H_{15}N_2ClO_2$	9·96	10·06
5	6 Bromo	230	$C_{14}H_{15}N_2BrO_2$	8·382	8·67
6	7 Chloro	234	$C_{14}H_{15}N_2ClO_2$	10·48	10·06

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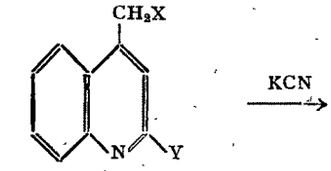
SYNTHESIS OF 4, 4'-CYANOETHYLENE *BIS*-(2, 2'-DICHLORO QUINOLINE) AND 4, 4'-CYANOETHYLENE *BIS*-(2, 2'-DIHYDROXY QUINOLINE) DERIVATIVES

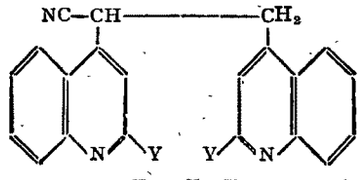
CHUDGAR and Trivedi[1] conclusively proved that bromination of aceto-acetanilide gave ω-bromo-acetoacetanilide which on cyclisation gave 4-bromomethyl carbostyril (I *a*). This on treatment with phosphorus oxychloride, gave 2-chloro-4-chloromethyl quinoline (I *b*), m.p. 97°. (I *b*) when refluxed with alcoholic potassium cyanide solution gave 4, 4'-cyanoethylene *bis*-(2, 2'-dichloro quinoline) (II *a*), m.p. 211°, and not 2-chloro-4-cyanomethyl quinoline (I *c*).



I *a*: X=Br, Y=OH

I *b*: X=Cl, Y=Cl

I *c*: X=CN, Y=Cl



II *a*: Y=Cl

II *b*: Y=OH

4-Bromomethyl-2-hydroxyquinoline (I *a*), on a similar condensation with potassium cyanide, gave 4, 4'-cyanoethylene *bis*-(2, 2'-dihydroxy quinoline), m.p. > 300° (II *b*). This when refluxed with phosphorus oxychloride gave (II *a*). M.p. and mixed m.p. was 211°. All compounds described above gave satisfactory analytical results.

The structure of 4, 4'-cyanoethylene *bis*-(2, 2'-dichloro quinoline) is confirmed by NMR spectra shown in Table I.

TABLE I

NMR spectra of (II a). (60 MC. $CDCl_3$)

Shift (δ)	Coupling constant J (c/sec.)	Signals	Assignment
7·5 to 8·5	..	Multiplet	10 H (aromatic)
5·1	8	Triplet	1 H
4·2	8	Doublet	2 H

Synthesis of 4, 4'-cyanoethylene *bis*-(2, 2'-dichloro quinoline) derivatives having different groups is in progress and will be published elsewhere.

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Chemistry Dept.,
Faculty of Science,
M.S. University of Baroda,
Baroda-2, *March* 19, 1968.

R. J. CHUDGAR.
K. N. TRIVEDI.*

* Present address : Chemistry Department, Wollongong University College, Wollongong, N.S.W., 2500, Australia.

1. Chudgar and Trivedi, *Curr. Sci.*, 1965, **34**, 560.