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THE BROMINATION OF ENAMINONITRILES

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Abstract—3-Monoalkylamino and 3-dialkylamino-2-phenylpropenenitriles have been brominated at the *p*-position. Instead, the bromination of 3-phenylamino-2-phenylpropenenitrile produces substitution at the *p*-position of the N-phenyl moiety.

THE halogenation of enamines can follow several pathways, depending on the nature of the enamine, but in every instance the double bond participates in the reaction.

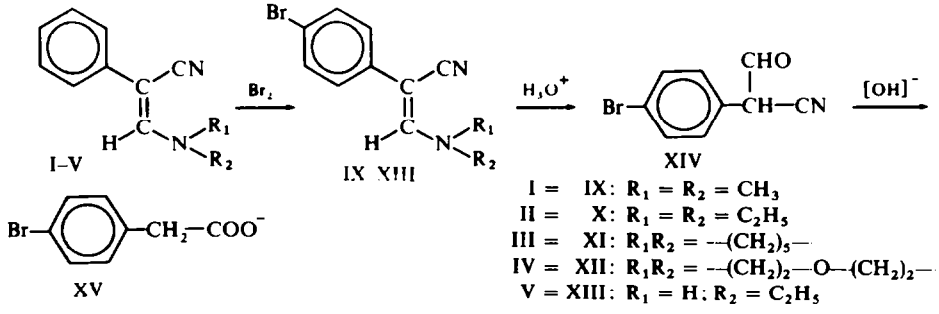
The bromination of these compounds takes place by addition and substitution,[1] or addition.[2] When N-haloimides are used substitution without addition is produced.[3] In a previous report[4] it was mentioned that enaminonitriles derivated from 2-cyano-2-phenylacrylamine, behave in a special manner upon bromination.

When a chloroform or carbon tetrachloride solution of 3-dimethylamino-2-phenylpropenenitrile (I), was treated at 0° with an equimolecular amount of bromine in the same solvent, the reaction proceeded as if a simple halogen addition to a double bond had occurred. The colour of the bromine solution was instantaneously discharged and no hydrogen bromide evolution was observed. When the solvent was removed at reduced pressure and room temperature, hydrogen bromide was evolved, leaving a crystalline residue (IX) whose analytical data corresponded to $C_{11}H_{11}N_2Br$. The IR spectrum of IX showed strong absorption bands at 2188 (conj nitrile), 1626 and 937 (trisubst C=C), 1079, 1001 and 821 cm^{-1} (*p*-disubst benzene).

The NMR spectrum presented peaks at δ: 7·20 (4H, aromatic) 6·85 (1H, vinyl) and 3·13 ppm (6H, N-dimethyl), and the UV spectrum gave bands at 253 (log ε: 3·76), 295 (shoulder, log ε: 4·13) and 313 nm (log ε: 4·18).

This data suggested, for compound IX, an enamine structure, which was supported by the chemical evidence obtained from acid and alkaline hydrolysis.

Acid hydrolysis of IX gave a compound XIV whose analytical and spectral data



I = IX: $R_1 = R_2 = CH_3$
II = X: $R_1 = R_2 = C_2H_5$
III = XI: $R_1R_2 = -(CH_2)_5-$
IV = XII: $R_1R_2 = -(CH_2)_2-O-(CH_2)_2-$
V = XIII: $R_1 = H$; $R_2 = C_2H_5$

is very similar to that of the phenylformylacetonitrile. By alkaline hydrolysis of XIV a compound identified (IR and m.p.) as *p*-bromophenylacetic acid (XV) was obtained.

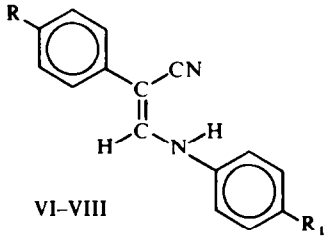
All this is in accordance with the properties of this class of enamines.[5] so the reaction must have occurred by substitution at the *p*-position.

The identity of XIV was checked by its reaction with morpholine and *p*-toluenesulphonic acid.[6] The bromoenamine thus obtained was identical with that prepared by bromination of IV. Due to the more basic character of this enamine, the bromination of IV gave the bromoenamine XII together with its hydrobromide.

The reaction was extended to other N-monosubstituted and N,N-disubstituted enamines. When R_1 and R_2 were aliphatic or heterocyclic groups, the reaction proceeded in an analogous way, and the *p*-bromophenylenamines were obtained.

Incidentally, we must point out that this is a practical method for the synthesis of *p*-bromophenylacetic acid without isomer formation or lachrymatory intermediates, and with overall yields of 60–70%.

The reaction took a different direction when N-aryl substituted enamines were brominated; thus, with 3-phenylamino-2-phenylpropenenitrile[7] (VI), the bromine attacked the *p*-position of the N-phenyl moiety, yielding 3-(*p*-bromophenylamino)-2-phenylpropenenitrile (VIII). Lamant and Le Moine[7] brominated VI, but they failed to identify the reaction product.



VI–VIII

VI: $R = R_1 = H$
VII: $R = Br; R_1 = H$
VIII: $R = H; R_1 = Br$

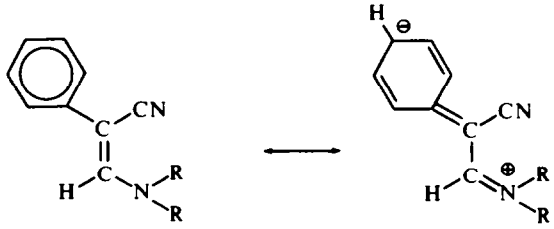
The structure of this enamine was confirmed by alkaline hydrolysis, since in acid medium it is extremely slow,* yielding phenylacetic acid and *p*-bromoaniline. Another proof was obtained by comparison of the m.p. and IR spectrum of IV with those of 3-phenylamino-2-(*p*-bromophenyl)propenenitrile (VII) and 3-(*p*-bromophenylamino)-2-phenylpropenenitrile (VIII), both prepared by the general method of synthesis.[5]

In our previous report, we mentioned the possibility that the reaction was an addition to the double bond, followed by a rearrangement and final elimination of hydrogen bromide.

To check this possibility, I was brominated in methanolic solution, but only the bromoenamine IX was obtained. The UV absorption spectrum of the reaction product of I prior to the work-up, didn't show any appreciable change, but a hypsochromic shift for all bands of 2–4 nm.

These enamines have a very low double bond contribution to the resonance hybrid, as demonstrated when we tried to make them react with iodine, cyanogen bromide, diazomethane, acrylonitrile or methyl acrylate. In every instance the unchanged enamine was recovered.

* After boiling it for 24 hours with 1:1 HCl–H_2O, the bromoenamine was recovered unchanged.



The failure of all these typical addition reactions to double bonds, in addition to the lack of evidence for it, from the UV data, made us discard the idea of an addition-elimination mechanism. The probable mechanism for this reaction is to be the subject of a separate paper.[8]

EXPERIMENTAL

All m.ps are uncorrected and were taken on a Fisher–Johns hot stage. IR spectra were run as Nujol mulls between NaCl plates with a Perkin–Elmer 137-E; the NMR spectra with a T-60 spectrometer using CCl_4 or $DCCl_3$ as solvent and TMS as an internal standard. UV spectra were obtained with a Beckman DB-G spectrophotometer using EtOH as solvent. Enamines I–IV were prepared as described.[5] The synthesis of the enaminonitriles V–VI will be published in a separate paper.

(1) *Bromination of enaminonitriles*

A soln of Br_2 (0·03 mole) in $CHCl_3$ (20–25 ml) was added slowly and with stirring, to a soln of the enamine (0·03 mole) in the same solvent at 0–5°. The mixture was stirred for a further 10 min, filtered, and the solvent was removed at reduced pressure (room temp). The oily or crystalline residue was dissolved in boiling EtOH or light petroleum (60–80°). Upon cooling the crystals were collected and dried at 40°. Recrystallization from EtOH or ligroine afforded the pure products.

(2) *Synthesis of* XII

Method A: IV (5 g, 0·023 mole) was brominated as above. After approximately half of the Br_2 was added, a yellow ppt formed. After all the Br_2 was added, the ppt was filtered off, washed with cold $CHCl_3$ and dried in a vacuum desiccator, giving 1·9 g, m.p. 102–118° (d). Recrystallization from abs EtOH–anhyd ether gave white crystals, m.p. 212·5–213° of the bromoenaminium bromide. (Found: C, 41·80; H, 3·70; N, 7·52; Br: 42·65. $C_{13}H_{14}Br_2N_2O$ requires: C, 41·74; H, 3·77; N, 7·48; Br, 42·72%); IR: 2463 ($NH(R)_3$), 2174 (conj. —CN), 870 (trisubst. C=C), 821 cm^{-1} (*p*-disubst. benzene).

After removing the $CHCl_3$ from the filtrate 5·5 g (80·6%) of XII, light yellow crystals m.p.: 111–115°, were obtained. Two recrystallizations from EtOH gave the analytical sample as white crystals m.p.: 140–140·5°.

Method B. To a suspension of XVII (7·2 g; 0·032 mole) in xylol (100 ml), morpholine (4 ml; 0·057 mole) and a catalytic amount of *p*-TsOH were added. The mixture was refluxed (Dean–Stark trap) for 14 hr and the solvent was removed at reduced pressure. The residual oil crystallized upon cooling giving XII (7·2 g; 94·1%) as light yellow crystals m.p.: 134–138°. Recrystallization from benzene–light petroleum gave white crystals m.p.: 138–139°.

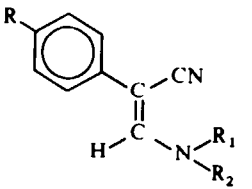
(3) *Bromination and hydrolysis of* I

Compound I (5 g, 0·03 mole) was brominated as above, and after elimination of the solvent the residue was dissolved in hot EtOH (20 ml). The warm soln was diluted with 100 ml 10% HCl aq and boiled under reflux until a clear soln was obtained. Upon cooling, 5·65 g (86·7%) of XVII, white crystals m.p. 166–168° were obtained. Recrystallization from dil AcOH gave m.p. 174–175·5°.

(4) *Alkaline hydrolysis of* XVII

A suspension of XVII (2 g; 0·009 mole) in 75 ml 10% NaOH aq was refluxed until the evolution of NH_3 ceased. The cold soln was filtered to remove some impurities, acidified with 10% HCl aq, boiled a few min

TABLE. BROMINATION OF ENAMINONITRILES



	R	R_1	R_2	m.p.	Yield %	Requires				Found			
						C	H	N	Br	C	H	N	Br
IX		CH_3	CH_3	90–90·5	52·0	52·61	4·42	11·15	31·82	52·65	4·45	11·19	31·69
X	Br	C_2H_5	C_2H_5	84·5–85	82·0	55·92	5·41	10·03	28·64	55·98	5·43	10·09	28·48
XI	Br	—$(CH_2)_5$—		136–136·5	32·0	57·74	5·19	9·62	27·45	57·69	5·12	9·71	27·46
XII	Br	—$(CH_2)_5$—O—$(CH_2)_2$—		140–140·5	80·0	53·26	4·46	9·55	27·25	53·01	4·41	9·62	27·45
XIII	Br	H	C_2H_5	60·5–61	39·4	52·61	4·42	11·15	31·82	52·58	4·40	11·18	31·83
XIV	H	H	p-BrC_6H_4	178·5–179	86·7	60·22	3·70	9·36	26·70	60·5	3·99	9·23	26·52

and cooled. The solid was collected and dried, giving 1·72 g (90%) of XVIII, white crystals m.p.: 116–117° (lit.: 114–115°).[9]

(5) *Synthesis of 3-arylamino-2-arylpropenenitriles* (VII, VIII)

A suspension of the arylformylacetonitrile (0·03 mole) and the aromatic amine (0·03 mole) in xylol (50–75 ml) was boiled under reflux (Dean Stark trap) for 2–3 hr. The solvent was removed under reduced pressure and the residue recrystallized from boiling benzene. The following enaminonitriles were obtained: 3-phenylamino-2-(*p*-bromophenyl)-propenenitrile (VII) 65·2%, m.p. 192·5–193·5°C. (Found: C, 60·15; H, 3·67; N, 9·40; Br, 26·81; $C_{15}H_{11}N_2Br$ requires: C, 60·22; H, 3·70; N, 9·36; Br, 26·72%). IR: 3268 (NH), 2212 (conj —CN), 928 (trisubst C=C), 753 and 689 (monosubst benzene) and 817 cm^{-1} (*p*-disubst benzene)). 3-(*p*-bromophenylamino)-2-phenyl-propenenitrile (VIII) 97·7%, m.p.: 178·5–179·5°. (Found: C, 60·17; H, 3·70; N, 9·32; Br, 26·65; $C_{15}H_{11}N_2Br$ requires: C, 60·22; H, 3·70; N, 9·36; Br 26·72%). IR: 3268 (NH), 2212 (conj —CN), 921 (trisubst C=C), 752 and 687 (monosubst benzene) and 825 cm^{-1} (*p*-disubst benzene)).

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