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ORIENTATION OF AMIDE ION ADDITION TO THE TRIPLE BOND IN MONOSUBSTITUTED BENZYNES

G.B.R.de Graaff, H.J.den Hertog and W.Ch.Melger
Laboratory of Organic Chemistry of the
Agricultural University,Wageningen,the Netherlands

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In spite of the many investigations in the field of aryne chemistry, relatively few data have been collected on the mode of addition of reagents to the triple bond in monosubstituted benzynes. Huisgen and Herbig[1] have published results of an investigation on aminations of substituted halogenobenzenes with lithium piperidide and piperidine in ether, determining ratios of amounts of isomeric piperidino compounds formed. Roberts and collaborators[2] gave addition ratios observed when reacting monosubstituted halogenobenzenes with potassium amide in liquid ammonia. In connection with studies on the reactivities of heterocyclic arynes being carried out in our laboratory, it was desirable to extend the available information on the course of aminations with potassium amide. Roberts c.s. converted o-, m- and p-methoxy-, methyl-, trifluoromethylbromo- or chlorobenzenes and p-fluorobromobenzene with an excess of sodium or potassium amide in liquid ammonia and determined compositions of mixtures of products by infrared analysis. Results of additions to the triple bond in 3-

substituted benzynes were explained by assuming the amide ion to add so as to provide the most favourable location of the negative charge with respect to the inductive effect of the substituent present. Orientation of additions to 4-substituted benzynes was considered not only to depend on inductive effects, but also to be influenced by conjugative electrical effects.

We have repeated the above-mentioned experiments,reacting the derivatives of bromobenzene with at least the fourfold molecular amount of potassium amide and analyzing the reaction mixtures by G.L.C. and we were able to confirm the results of the aminations of the isomeric methoxy-(III^{a-c}) and methyl-(IV^{a-c}) derivatives of bromobenzene and of p-fluorobromobenzene (II^{a}). Awaiting the publication of an extensive series of experiments on aminations of these and several other derivatives of bromobenzene under divergent conditions, in this letter a preliminary account is given of the reinvestigation mentioned above and a study on aminations of isomeric bromoanilines(VII^{a-c}), bromodimethylanilines(V^{a-b}), bromobenzonitriles(I^{a-c}) and bromophenols(VI^{a-c}), compounds which contain substituents with high negative I- and M-effects(I), high positive I- and M-effects(in the anions present in the reaction mixtures of VI and VII) and a small I-effect combined with a high +M-effect(V) respectively.

Results obtained are summarized in the table.

Aminations of monosubstituted bromobenzenes
with potassium amide in liquid ammonia

Substituent		a. Ratio of products from para-isomers p : m	b. Ratio of products from ortho-isomers m : o
I	-CN(--I,-M)	95-100 : 0-5	85-90 : 10-15
II	-F(--I,++M)	75-80 : 20-25	99-100 : 0-1
III	-OCH$_3$(--I,++M)	50-55 : 45-50	95-100 : 0-5
IV	-CH$_3$(+I,+M)	40 : 60	45 : 55
V	-N(CH$_3$)$_2$(-I,++M)	30-35 : 65-70	95-100 : 0-5
VI	-O$^-$(++I,++M)	0 : 100	10-15 : 85-90
VII	-NH$^-$(++I,++M)	0 : 100	5-10 : 90-95

Molar ratio of bromobenzene derivatives to potassium amide 1 : 4, reaction temperature -33°; reaction time 15 min, yields higher than 50% in the experiments mentioned under I - V.

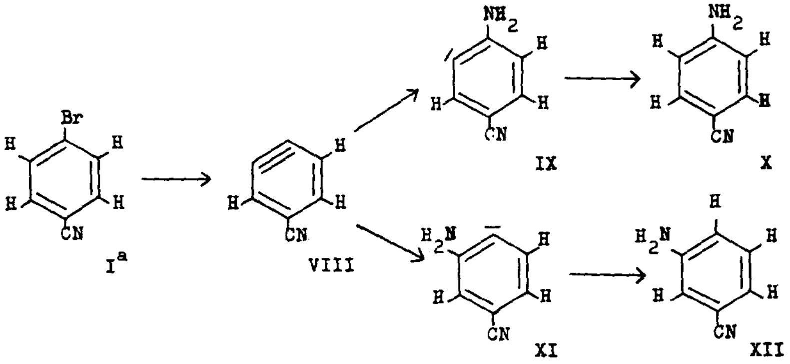
In the aminations of bromoanilines (VII) and bromophenols (VI) the molar ratio of reaction components was 1 : 8 and the reaction time 1 h; yields amounted to 20%, a large quantity of the substrate remaining unchanged.

Some preliminary experiments were carried out on the amination of m-substituted derivatives of bromobenzene. It was found that m-bromobenzonitrile (I^c), m-bromophenol (VI^c) and m-bromoaniline (VII^c) yielded mixtures of m- and o-amino derivatives of about the same composition as those formed from the corresponding o-substituted bromobenzenes (I^b,VI^b and VII^b).

From the results obtained by Roberts c.s. and by us, it can be concluded that all aminations described occur via benzyne derivatives as intermediates. Furthermore, it appears that the orientation of the addition of the amide ion to the triple bond in 3- as well as in 4-substituted benzynes is determined by both I- and M-effects of the substituents present. In agreement with Roberts c.s. we think that conjugative effects, though having but a secondary influence on the mode of addition, certainly are involved in affecting the position of attack on benzyne derivatives.

Evidence for the view that the addition of the amide ion depends on both I- and M-effects acting in 4-substituted benzynes, results from the aminations of p-bromobenzonitrile (I^a) and p-bromodimethylaniline (V^a).

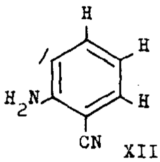
The ratio of the amounts of p- and m-aminobenzonitrile (X and XII) formed from I^a surpasses considerably that of the p- and m-aminofluorobenzenes formed from fluorobromobenzene (II^a). As the cyano group and the fluorine atom have about equal -I-effects, the distinct preference for the formation of the transition state IX from the benzyne intermediate VIII can not be explained from the electron-attraction of the cyano group by its inductive effect only, but must also be due to the conjugation between amino and cyano group.

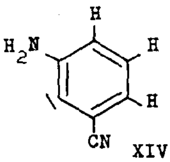


From the inductive effects of dimethylamino and methyl groups in p-bromodimethylaniline (V^a) and p-bromotoluene (IV^a) it might be expected that the ratio of p- and m-dimethylaminoanilines formed from V^a would be higher than that of p- and m-toluidines formed from IV^a. The divergence in the M-effects of the substituents brings about that it is just the other way round.

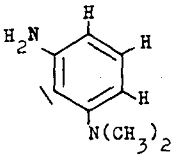
As for the additions to the triple bond in 3-substituted benzynes, the subsequent results seem to indicate that also in these reactions M-effects influence the mode of addition.

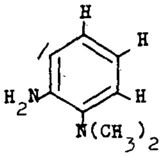
From o-bromobenzonitrile (I^b) and not from o-bromofluorobenzene (II^b), an amount of o-amino product is formed in spite of the slightly higher -I-effect of the cyano group. The formation of o-aminobenzonitrile must be attributed to the transition state XIII being more stable than XIV as a result of conjugation of amino and cyano groups.


XIII


XIV

Furthermore, it seems doubtful to us that the amination of o-bromodimethylaniline(V^b), proceeding practically exclusively via XV and not via XVI, can be explained from the slightly negative I-effect of the dimethylamino group and some steric hindrance without considering that XV is more stable than XVI from the M-effects of the amino and dimethylamino groups.


XV


XVI

Finally, we draw attention to the fact that complete rearrangements occur during the aminations of p-bromophenol(VI^a) and p-bromoaniline(VII^a) resulting from the co-operating +I- and +M-effects of the O^- and NH^- groups and partial rearrangements during the aminations of the m-isomers of the substances just-mentioned(VI^c and VII^c) promoted by the high +I-effects of the substituents and somewhat counteracted by their +M-effects.

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