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REACTIONS OF ORGANIC ANIONS—L

REACTIONS OF PHENYLACETONITRILE DERIVATIVES WITH AROMATIC NITROCOMPOUNDS IN BASIC MEDIA

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Abstract—Reaction of phenylalkanenitriles and diphenylacetonitrile with aromatic nitro compounds were studied using various base-solvent systems. Four independent types of reaction: substitution of halogen, substitution of nitro group, substitution of hydride anion and electron transfer were observed. Relationship—reaction pathway—conditions have been discussed.

Reactions of aromatic nitro compounds with various nucleophiles have been studied extensively. The progress in this field, and many features of these reactions have been recently reviewed.[1,2] However despite numerous original papers in this field reactions between nitroaromatic compounds and carbanions have gained only limited attention. In his excellent monograph Miller[2] has pointed out that this situation is due to the difficulties in quantitative treatment of such systems. The main reasons for these difficulties are: (i) some uncertainty concerning the true concentration of carbanions due to the acid-base equilibrium between carbanions and their parent C–H acids or solvents; (ii) the uncertainty surrounding the state of the carbanion which may exist as solvent separated or contact ion pairs, free ions with various degrees and energies of solvatation or as high molecular weight agregates; (iii) the fact that carbanions are able to react with aromatic nitro compounds in a variety of ways, including electron transfer processes, which result in complicated reaction patterns. Lack of quantitative or even semiquantitative data for these systems, carbanions—aromatic nitro compounds, make deep analysis of these reactions impossible consequently only a phenomenological approach to these systems has been undertaken so far.

Nevertheless reaction of carbanions with aromatic nitro compounds offer extremely large and diverse synthetic possibilities and lead to some unusual transformations. Thus Davis[3] has described the formation of heterocyclic compounds and cyanomethylenequinoneoxime when phenylacetonitrile was treated with *p*- and *o*-chloronitrobenzene in alkaline medium. Pietra and Casiraghi[4] have observed substitution of hydride anion with simultaneous reduction of N-oxide function when nitrophenazine N-oxide was treated with various carbanions. Interesting addition products of some ketones to trinitrobenzene have been described by Strauss.[5]

These and many other examples of reactions of carbanions with aromatic nitro compounds illustrate the growing interest that has been aroused by these reactions over the last few years.

For some years we have been working on reactions of carbanions with various electrophiles, particularly on the new catalytic method of generating of carbanions in a two-phase system.[6] This method makes use of conc aqueous NaOH solution and quaternary ammonium catalyst as a basis system and is convenient for some reactions of arylacetonitriles e.g. alkylation.

We have reported preliminarily[7] that under these conditions arylalkanenitriles (1) react smoothly with halonitroaromatic compounds (2) giving nitroaryl derivatives of phenylalkanenitriles (3) with high yields. Some observations we have made then attracted our attention to these systems and, as a result of a more detailed study, we have found some interesting transformations[7c,8] that are of practical interest. During this study we observed dramatic changes in the reaction pathway in many cases when the solvent and/or the counter ion associated with the carbanion were varied.

A study of the reaction between phenylalkanenitriles carbanions and aromatic nitro compounds has shown that at least 4 independent main processes occur in these systems. Any of which can predominate in a particular case (i.e. choice of starting material or conditions). These processes are:

1. Nucleophilic substitution of halogen atom in *ortho*- or *para*-position to nitro group by carbanion moiety.[7a,b]
2. Nucleophilic substitution of nitro group when it is located in *p*-position to carbonyl group.[7c]
3. Substitution of hydride anion by carbanion moiety followed by various further transformations.[8]
4. Electron-transfer (E–T) processes leading to products of redox reactions via species with an unpaired electron.[7b,c,8]

RESULTS

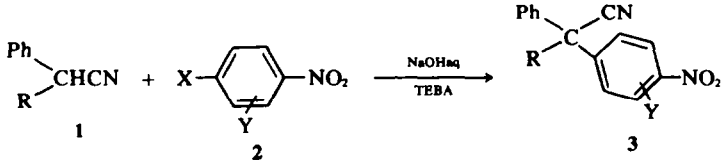
1. *Nucleophilic substitution of halogen in halonitrobenzene derivatives*

Phenylalkanenitriles of general formula PhRCHCN (1) react with *p*- and *o*-chloronitrobenzenes in the presence of 50% aqueous sodium hydroxide and catalytic amounts of triethylbenzylammonium chloride (TEBA) yielding corresponding products of replacement of Cl atom. The same results were obtained in general with corresponding bromonitrobenzenes

The results (yields, physical constants and structure of nitroarylated nitriles 3) are given in Table 1. All the nitronitriles are new compounds, their identification was based on correct elemental analyses, PMR and IR spectra (characteristic patterns of all substituents, typical NO_2, CN and other functional groups absorption) as well as on chemical transformation. The results demonstrated a certainty that arylacetonitrile moiety directly replaces the halogen atom in nitroaromatic ring.

It is important to note that if non-catalytic conditions are used for the generation of arylacetonitrile anions (e.g. $NaNH_2/NH_3$, $NaNH_2$ in benzene, ether or THF; NaH/THF[10]), then nitroarylation of these nitriles does not as a rule proceed satisfactorily. Under these conditions the nitronitriles 3 were obtained (if at all) in low yields along with considerable amounts of tars and by-products. Only non-catalytic conditions, that we were able to apply successfully to these reactions, consisted in using DMSO solvent and employing NaH or alkali metal hydroxides as basic agents. These conditions give similar results to those obtained using quaternary ammonium salts as catalysts. Some halonitrobenzenes also react with 2-phenyl alkane nitriles in the presence of sodium methoxide in methanol although yields of 3 are low.

A secondary problem arises with compounds such as 2,4-dichloronitrobenzene where the two Cl atoms have different degrees of reactivity.



X = Cl, Br, also X in orto-position to NO_2 group

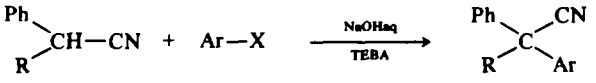
SCHEME 1

Yields of corresponding nitroarylated nitriles 3 are almost always high (about 80–90%) and their isolation and purification is very simple. Generally the reactions proceed without formation of any by-products and tars; in some cases it is possible to obtain almost pure nitroarylderivative (3) by dilution of the reaction mixture with water followed by filtering off and washing the product with dilute hydrochloric acid. We have also applied this reaction to diphenylacetonitrile (R = Ph) and Reissert compound from isoquinoline,[9] whose structure is close related to the arylalkanenitriles. As nitroarylating agents (2) it is possible to use many substituted mono and even dinitrohalobenzenes possessing at least one Cl (or Br) atom in *para* or *ortho* position to nitro group. Other substituents which are stable under the reaction conditions and do not contain "active" H atoms do not interfere.

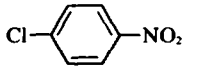
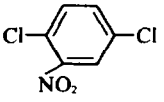
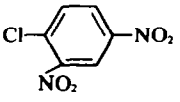
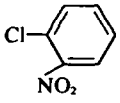
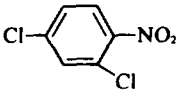
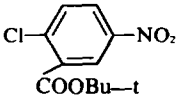
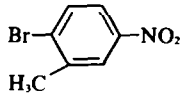
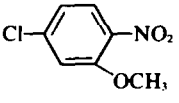
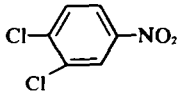
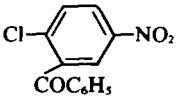
An exothermic reaction took place between phenylbutyronitrile and 2,4-dichloronitrobenzene in the presence of aqueous NaOH and TEBA; the product of substitution of one chlorine atom was isolated in high yield by distillation. This product was resolved using column chromatography on alumina into two individual components. The major component (about 97% of the starting mixture, mp. 74°C) was identified as 2 - phenyl - 2 - (4 - nitro - 3 - chlorophenyl)butyronitrile **3a**, whereas the minor one (mp. 112°) was identified as 2 - phenyl - 2 - (2 - nitro - 5 - chlorophenyl)butyronitrile **3b**.

The structural assignments were based on the following consideration: elemental analyses and spectral data (PMR and IR) of the both compounds supported the view that they arose from the substitution of one Cl atom in 2,4-dichloronitrobenzene by the 2-phenylbutyronitrile moiety therefore sug-

Table 1. Products of nucleophilic substitution of halogenes in nitrobenzene derivatives by 2-phenylalkanenitrile and diphenylacetonitrile carbanions[1]



1 2 3

No	R	Ar-X	Yield %	M.p. B.p.	No	R	Ar-X	Yield %	M.p. B.p.
1	Me		92	76 170/0·3	18	Me		85	92
2	Et		95	95	19	Et		75	144
3	Pr		63	76 185/0·8	20	$PhCH_2$		98	173
4	i-Pr		62	72	21	Ph		93	160
5	$PhCH_2$		87	95	22	Me		75	117
6	Ph		71	96					
7	Me		80	74 180/0·8	23	Et		61	97
					24	i-Pr		20	158
8	Et		95	104	25	$PhCH_2$		86	194
9	$PhCH_2$		84	189	26	Ph		91	159
10	Ph[2]		88	196	27	Me[3]		82	51 184/0·2
11	Me		83	166	28	Et[4]		78	74 186/0·6
					29	Et[4]		3	112
12	Me		88	155/0·15	30	Me		81	109
13	Me		92	92	31	Me		67	139
14	Et		61	75	32	Et		90	130
15	i-Pr		30	110	33	Pr		60	151
16	$PhCH_2$		82	169	34	i-Pr		60	150
17	Ph		90	164	35	$PhCH_2$		62	224

[1]All compounds give satisfactory elemental analysis: C, H and N.
[2]The reaction was carried out in DMSO.
[3]Only one isomer has been obtained/substitution of 4-Cl.
[4]Two isomers have been formed No 28 product of substitution of 4-Cl IIIa, No 29 product of substitution of 2-Cl IIIb. The yield of the mixture 81%.

gesting the compounds are isomers formed by substitution of one Cl atom. The major component on reduction with Fe/HCl gave corresponding substituted aniline derivative in high yield whereas the minor one under these conditions did not. As we have shown in a previous paper[11] reduction of *o*-nitroaryl derivatives of arylalkanenitriles is accompanied by cyclization leading to the consecutive formation of aminoindolenines N-oxides and aminoindolenines.

Further evidence for the assignments **3a** and **3b** was obtained by independent synthesis of **3b** by nucleophilic substitution of NO_2 group in 3,4-dinitrochlorobenzene, which is known to substitute 3-NO_2 group in reaction with nucleophiles.[12a] The product of the reaction of 2-phenylbutyronitrile

with 3,4-dinitrochlorobenzene carried out under catalytic conditions was identical with the minor component of the mixture thus establishing its structure as **3b** and the major component as **3a**. Reaction of sodium methoxide with 2,4-dichloronitrobenzene is known to give 4 - chloro - 2 - methoxynitrobenzene.[12b] The latter reacts with 2-phenylpropionitrile under catalytic conditions yielding 2 - phenyl - 2 - (4 - nitro - 3 - methoxyphenyl) - propionitrile (mp. 108°) identical with product obtained by action of sodium methoxide on **3c**. Thus the main product of reaction of 2-phenylpropionitrile with 2,4-dichloronitrobenzene (**3c**) is 2 - phenyl - 2 - (4 - nitro - 3 - chloro)propionitrile which again suggests that *para* Cl atoms are more susceptible to nucleophilic displacement by phenylalkanenitrile carbanions then are *ortho* Cl atoms.

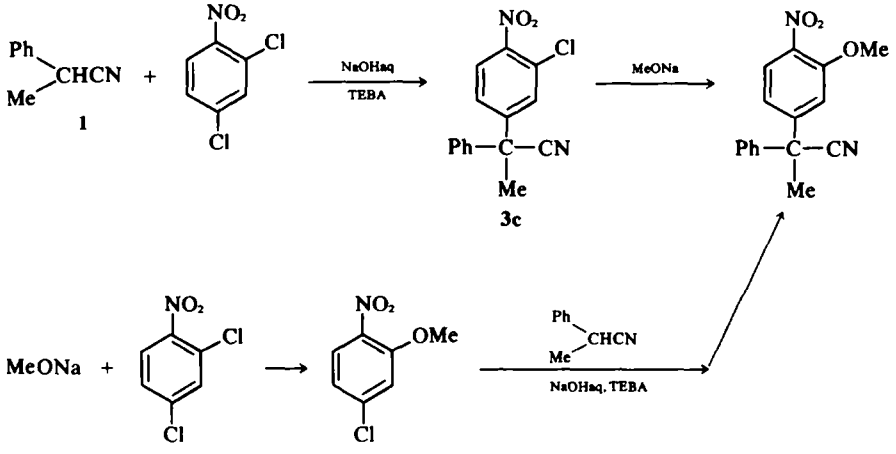
2. *Nucleophilic substitution of nitro group by arylacetonitriles carbanions*

Nitro groups in aromatic compounds are known to be readily replaced by nucleophilic agents. Direct comparison of relative activity of NO_2 group and halogens as leaving groups in reactions with carbanions has not previously been reported. In order to investigate this point it is necessary to select a class of compounds where the halogens and nitro groups are almost equally activated and accordingly we have studied the reactions of 4-halo 4'-nitrobenzophenones with carbanions.

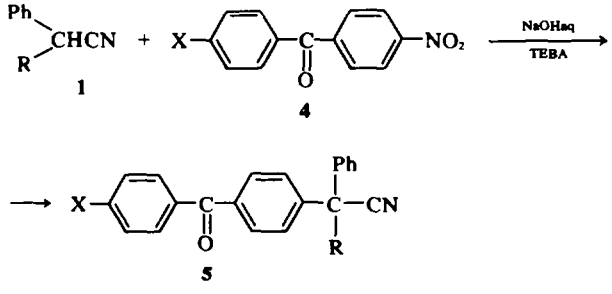
Reactions of 2-phenylalkanenitriles with 4-chloro 4'-nitrobenzophenone (**4a**) carried out in the presence of aqueous NaOH and quaternary ammonium catalyst result exclusively in substitution of nitro group by nitrile moiety with the formation of 2 - phenyl - 2 - [4 - (4 - chlorobenzoyl) - phenyl]alkanenitriles (**5**). Reactions proceed with moderate exothermic effects to give the corresponding ketonitriles (**5**) in high yields.

Titrimetric analysis of the aqueous phase showed a slight increase in chlorine ion over that introduced as catalyst; the presence of nitrite ions was established qualitatively.

Substitution of nitro group in *p*-nitrobenzophenone derivatives by phenylalkanenitriles moiety is a rather general reaction that proceeds with benzophenones **4** (X = Br, H, Me and even OMe) and nitriles **1** when R is primary alkyl group (Me, Et, Pr, $PhCH_2$). Yields and physical constants of the ketonitriles (**5**) as obtained are given in Table 2. However slight change in structure of nitriles (R-

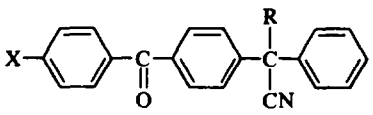


SCHEME 2



SCHEME 3

Table 2. Products of nucleophilic substitution of nitro group in 4-X-4-nitrobenzophenones by 2-phenylalkanenitrile carbanions[1]



No	R	X	Yield	B.p./mm	M.p. °C
1	CH_3	Cl	75	220/0·3	99
2	C_2H_5	Cl	70	235/0·4	
3	n-C_3H_7	Cl	78	210/0·3	79
4	$C_6H_5CH_2$	Cl	67		137
5	CH_3	Br	69	270/0·5	88
6	C_2H_5	Br	61	242/0·5	
7	$C_6H_5CH_2$	Br	90		140
8	CH_3	CH_3O	64	235/0·4	84
9	$C_6H_5CH_2$	CH_3O	90		138
10	CH_3	CH_3	93		130
11	$C_6H_5CH_2$	CH_3	98		126
12	CH_3	H	82	220/0·5	63
13	C_2H_5	H	89	240/0·5	
14	$C_6H_5CH_2$	H	92		109

[1]All compounds give satisfactory elemental analysis.

sec-alkyl group) results in profound change of the reaction pathway. Reactions of 2 - phenyl - 3 - methylbutyronitrile (**1**, R = i-Pr) with benzophenones **4** proceed exclusively as electron-transfer processes giving iso-butyrophenone and azoxy compounds.

As with the substitution of halogens in halonitrobenzene derivatives, substitution of nitro groups in nitrobenzophenones by phenylalkanenitriles moiety proceeds satisfactorily only under the catalytic conditions. Sodium methylphenylcyanomethylide (prepared from 2-phenylpropionitrile and sodium amide in liquid ammonia and then suspended in organic solvent) does not react with **4**, X = Cl, in boiling ether whereas in boiling benzene electron transfer occurs leading to the corresponding azoxybenzene derivatives.

3. *Nucleophilic substitution of hydride anion*

We have shown that reaction of some 2-phenylalkanenitrile with *p*-chloronitrobenzene in the presence of NaOH or NaOMe in methanol proceeds as substitution of halogen. However under almost the same conditions reaction of diphenylacetonitrile with *ortho*-chloronitrobenzenes gave 2,2-diphenyl N-2-chloro 4-(diphenylcyanomethyl)phenyl nitrone (**6a**) in 92% yield.

The stoichiometry of the reaction was established by the titrimetric estimation of the cyanide ion liberated.

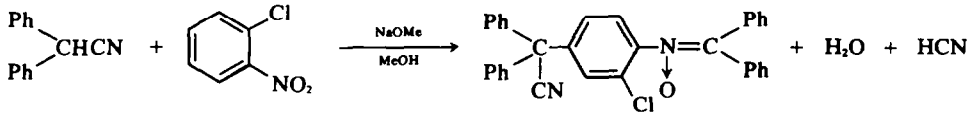
The structure of the nitrone **6a** was established on the basis of elemental analysis, spectral data (IR: N→O 1247 cm^{-1}; UV: λ_{max}^{EtOH} 304 mμ, $\epsilon = 1{\cdot}7 \times 10^4$) characteristic for nitrones,[13] as well as chemical transformations. Thus hydrolysis of **6a** results in formation of benzophenone and *p*-diphenylcyanomethylphenylhydroxylamine which undergoes oxidative condensation yielding corresponding azoxycompounds **7**.

Like other nitrones[14] **6a** undergoes 1,3-dipolar cycloaddition with phenylisocyanate with the formation of 1,2,4-oxadiazoline-5-one derivative (**8a**).

Similarly nitrobenzene and many other nitroaromatic compounds with free *para* position react under these conditions with diphenylacetonitrile with the formation of corresponding nitrones **6** whose spectra and chemical properties are similar to **6a** (see Tables 3, 4, 5).

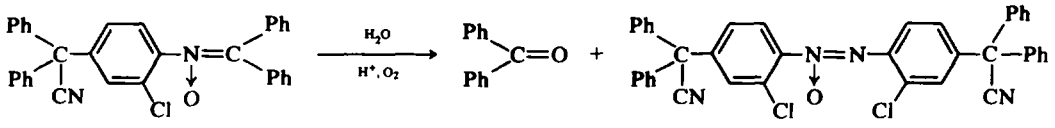
Reduction with Fe in acetic acid of nitrones **6** or azoxycompounds **7** obtained from **6** leads to corresponding amines (Table 6).

Phenylalkylacetonitriles (**1**, R = alkyl) also react with aromatic nitro compounds having free *para* positions in the presence of NaOH or NaOMe in methanol. The reaction involves initial attack at the *para* positions and displacement of a hydride ion.



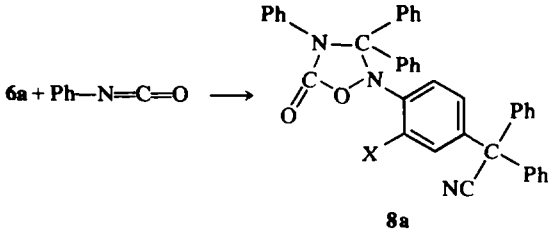
6a

SCHEME 4



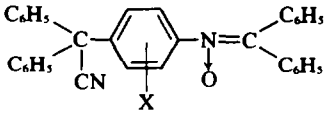
7a

SCHEME 5



SCHEME 6

Table 3. Nitrones 6 obtained from diphenylacetonitrile and aromatic nitrocompounds[1]



No	X[2]	Yield %	M.p.	UV spectr.	IR spectr. cm^{-1} —N→O	IR spectr. cm^{-1} CN
1	H	96	212	310,12200	1243	2240
2	Cl-2	88	201	304,17000	1247	2240
3	Br-2	87	204	308,17000	1250	2240
4	OCH_3-2	66	199	300,17400	1244	2240
5	OCH_3-3	91	217	312,18300	1210	2220

[1]All compounds give satisfactory elemental analysis.
[2]Position were numbered in relation to N = group (1).

Table 4. Products of 1,3-dipolar cycloaddition of nitrones 6 to phenylisocyanate 8[1]

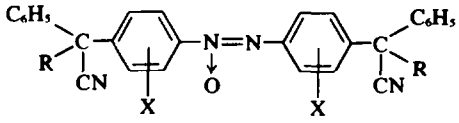
No	X	M.p.	Yield
1	H	214	80
2	3-Cl	207	89
3	3-Br	216	92
4	3-CH_3O	234	85
5	2-CH_3O	237	75

[1]All compounds give satisfactory elemental analysis.

However the final products are mixture of *p*-nitro- and *p*-aminoarylated nitriles 3, azoxycompounds 7 and corresponding ketones. The following stoichiometry has been found.

In the case of nitrobenzene (Z = H) the obtained compounds were identical with corresponding *p*-nitrophenyl and *p*-aminophenyl derivatives of phenylalkanenitriles obtained by direct nitroarylation and then reduction. Also azoxy compounds were identical with products obtained by partial reduction of 3, they were also identified on the basis of elemental analysis and spectral data. Similar results were obtained also under other conditions ($NaNH_2/NH_3$ liq, $NaNH_2$/THF).

Table 5. Azoxycompounds 7 obtained by oxidative hydrolysis of nitrones 6 (path A) or direct reaction between 1 and 2 (path B)[1]



No	R	X[2]	Path	Yield %	M.p.
1	C_6H_5	H	A	91	270
2	C_6H_5	Cl-2	A	91	233
3	C_6H_5	Br-2	A	85	261
4	C_6H_5	OCH_3-2	A	80	203
5	C_6H_5	OCH_3-3	A	84	175
6	C_6H_5	Cl-3	B	22	297
7	CH_3	H	B	46	146
8	C_2H_5	H	B	53	181
9	CH_3	3	B	41	311
10	C_2H_5	3	B	49	281

[1]All compounds give satisfactory elemental analysis.
[2]Positions are numbered in relation to N=N group (1).

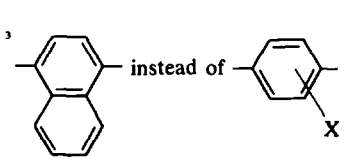
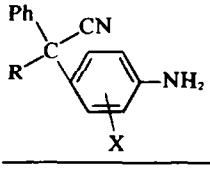


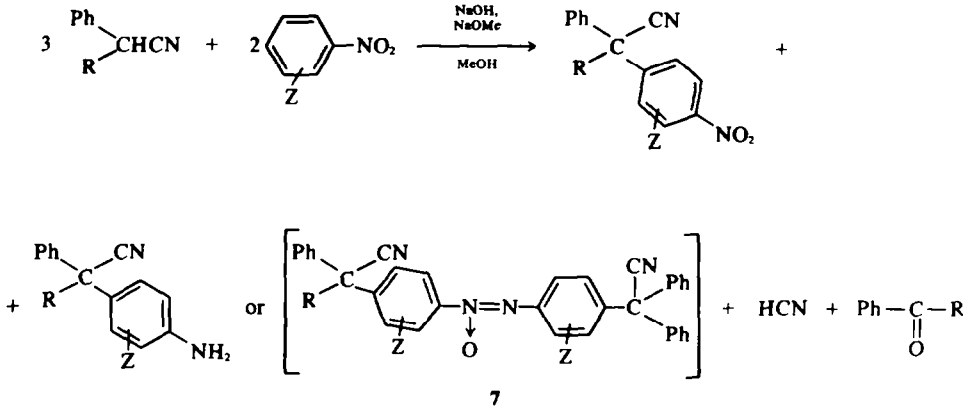
Table 6. Amines obtained by reduction of nitrones 6 or azoxycompounds 7[1,2]



A—acetyl derivative
B—benzoyl derivative

No	R	X[3]	M.p.	Derivative	M.p.
1	CH_3	H	64	B	145
2	C_2H_5	H	78	B	158
3	BH_3	Cl-3	118	B	164
4	C_2H_5	Cl-3	144	B	186
5	i-C_3H_7	H	101	B	177
6	C_6H_5	H	175	B	165
7	C_6H_5	Cl-3		A	208
8	C_6H_5	OCH_3-3		A	210
9	C_6H_5	OCH_3-2	158	A	187
10	C_6H_5	Cl-2	142	B	165
11	C_6H_5	Br-2	142	B	172

[1]All compounds give satisfactory elemental analysis.
[2]No yields are given since they depend upon whether 6 or 7 are reduced and conditioned.
[3]Positions are numbered in relation to NH_2 group.



7

SCHEME 7

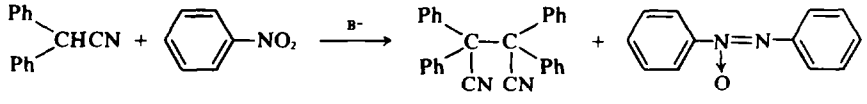
The yields of the mixtures obtained are quite good, about 55–60% on the nitrile used. For synthetic purpose the best way of working up the complexe mixture is via its total reduction and then isolation of aminoarylated nitriles thus obtained. This reduction can be accomplished with Fe/HCl, Sn/HCl or H_2/Pd and affords a simple method for the introduction of *p*-aminoarylsubstituents into arylalkanenitriles.

4. *Electron transfer processes between phenylalkanenitrile anions and aromatic nitrocompounds*

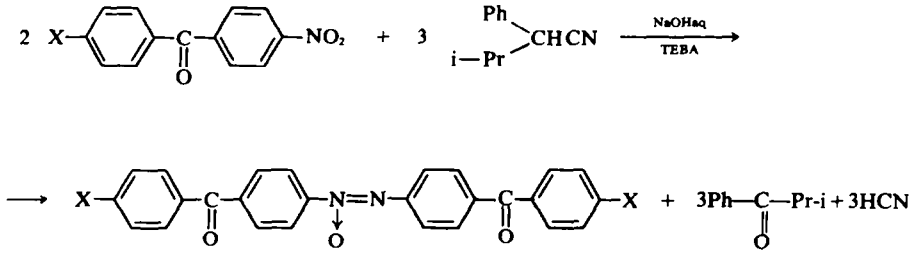
In addition to previously described reactions which result in coupling of nitrile moiety with nitroaromatic ring we have often observed transformation of both reactants without coupling. Thus reactions of diphenylacetonitrile with many aromatic nitrocompounds under various basic conditions lead to the formation of tetraphenylsuccinonitrile[15] and products of reduction of nitroaromatics (often azoxybenzene derivatives).

We have observed such reactions with nitrobenzene, *o*-chloro-, *o*-bromo-, 3,4- and 2,5-dichlorobenzene, 2 - chloro - 5 - nitro - and 4 - chloro - 4' - nitrobenzophenone under catalytic conditions (in the presence of aqueous NaOH and TEBA) and also when the reactions were carried out with $NaNH_2$ in benzene or THF. The same reactions occured with *m*-chloro-, *m*-bromo-, and *m*-amino-nitrobenzene in the presence of MeONa in methanol.

Electron transfer processes occurs also in reaction of *p*-nitrobenzophenone derivatives with 2 - phenyl - 3 - methylbutyronitrile (1, R = iso-Pr) under catalytic conditions as well as with 2-phenylpropionitrile carbanion (obtained using $NaNH_2$) in benzene. In both these cases electron transfer results in formation of corresponding azoxybenzophenone derivatives together with isobutyrophenone or acetophenone. These ketones were identified by GLC as well as by formation of 2,4-dinitrophenylhydrazones.



SCHEME 8



SCHEME 9

DISCUSSION

The results presented illustrate the various processes which can occur in the system arylalkanenitrile anion—aromatic nitro compounds. Some changes in reaction pathways can be rationalized on the basis of changes in structure of the reactants which affect their reactivity. However there are many dramatic changes of reaction pathway caused by rather minor changes of conditions (base - solvent - counter-ion).

The first problem that has to be discussed is: why reactions of arylalkanenitriles (1) with *p*- (or *o*-) halonitrobenzene derivatives give, as a rule, high yields of corresponding products of halogen replacement when carried out under catalytic conditions or in DMSO solvent, whereas under typical conditions used for alkylation of these nitriles such as NaH, $NaNH_2$ in ether, THF, benzene or liquid ammonia[10] the yields of these products are rather low and considerable amounts of by-products and tars are formed. There are at least two main factors that could be responsible. The first one arises from differences of concentrations of carbanions under the catalytic and "classical" conditions. In the former case the maximum concentration of carbanions is limited by the amount of catalyst added (1–2% of nitrile). Thus under these conditions the ratio of carbanion to electrophile is low and so the reaction occurs preferentially with the more electrophilic halonitrobenzenes rather than with the nitroarylated products. However this explanation is not consistent with the fact that separately prepared ammonium derivative of nitrile **1** ($R = C_6H_5$) reacts with *p*-chloronitrobenzene giving corresponding product **3** in high yield. Thus the decisive factor must be the form in which carbanions exist under various conditions. Under the catalytic conditions carbanions form ion pairs with quaternary ammonium cations. Anion-cation interaction in these ion pairs is essentially electrostatic in nature with very little co-ordination or covalent character as compared with the cases of alkali metal counter ions.

It is well known that due to these interactions sodium or lithium derivatives of various enolates form in organic solvents agregates often of high molecular weight*.

We have not, to date, obtained information about the degree of association of sodium and ammonium derivatives of arylacetonitriles in various solvents, nevertheless association of sodium derivatives seems to be higher. For example lithium phenylcyanomethylide even in DMSO has molecular weight about 240, which means that it exists predominantly as the dimer.[17]

The nature of the reacting species also seems to play a decisive role in experiments with KOH, NaOH or NaH in DMSO, systems which are also convenient for nitroarylation of arylalkanenitriles. Due to the high degree of cation solvatation in this solvent cation—carbanion interaction is rather weak and the degree of association is small and the carbanions exist as loose ion pairs or free ions. Thus the results obtained in DMSO are similar to those obtained under catalytic conditions.

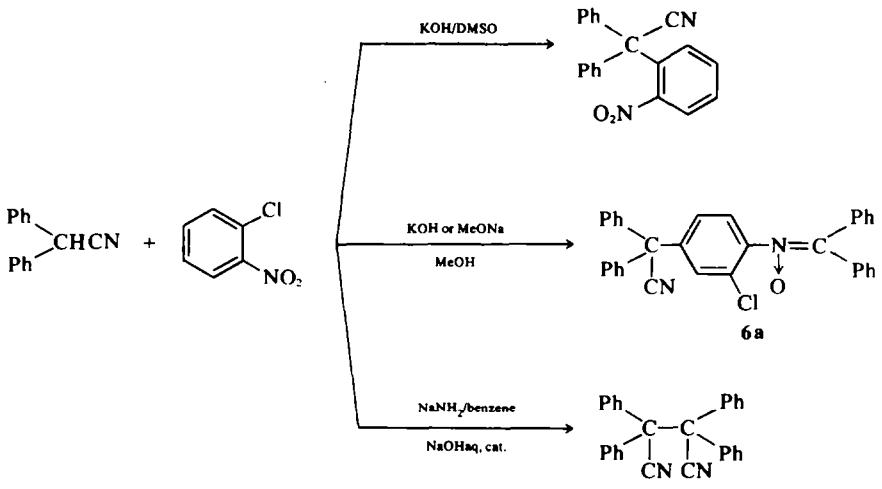
Similarly this explanation could also account for results of the reactions between the carbanions studied and *p*-nitrobenzophenone derivatives. The reactions carried out under catalytic conditions yield products of substitution of NO_2 group whereas the only reaction observed with corresponding sodium phenylalkylcyanomethylide in benzene is electron-transfer which results in formation of azoxybenzophenones and arylalkane ketone. The results show definitely higher leaving ability of nitro group as compared to halogenes in nucleophilic aromatic substitution with carbanions, although the halogen atoms are more strongly activated then nitro group (by *p*-nitro- and *p*-halobenzoyl substituent correspondingly). It is known that relative rate of substitution of various leaving groups in S_NAr depends strongly on the nature of nucleophilic agent and the conditions employed. For example we have found that piperidine selectively replaces the chlorine atom in 4-chloro 4-nitrobenzophenone without affecting the nitro group. This result contradicts that of Miller[18] whose values for the SRF's (substituent rate factors) for NO_2 to chlorine are 183 and 207, for methoxide ion and piperidine respectively.

The more complicated problems arise when considering the reactions of arylacetonitriles with aromatic nitro compounds with free *para* position under various basic conditions. Thus, there are three different pathways for the reactions between diphenylacetonitrile and *o*-chloronitrobenzene depending on the nature of the base and solvent employed: KOH in DMSO cause nucleophilic substitution of chlorine atom, KOH or MeONa in methanol—formation of nitrone **6a** whereas under the catalytic conditions or with $NaNH_2$ in THF electron transfer occurs giving tetraphenylsuccinonitrile (TPSN) and partial reduction products of *o*-chloronitrobenzene.

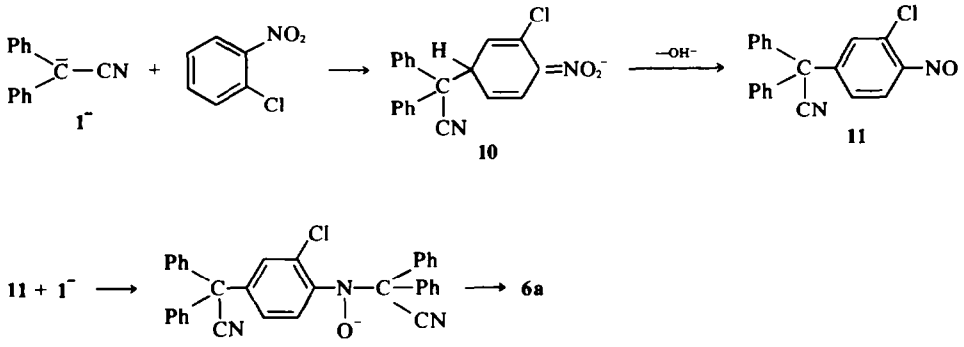
The first process is obvious and was discussed earlier. To explain the formation of **6a** we have to consider multistep transformation in which the initial step is an attack of the carbanion of **1** on *para* position of *o*-nitrochlorobenzene.

The resulting Meisenheimer complex **10** loses an hydroxyl ion which leads to the formation of nitrosocompound **11**. According to Davis formation of phenylcyanomethylene quinonoxime from phenyl-

*Zaugg[16] has found that apparent molecular weight of sodium diethyl buthylmalonate in benzene exceeds 10000, the addition of solvent such as DMSO which is able to solvate sodium cations brings about a decrease in the molecular weight.



SCHEME 10



SCHEME 11

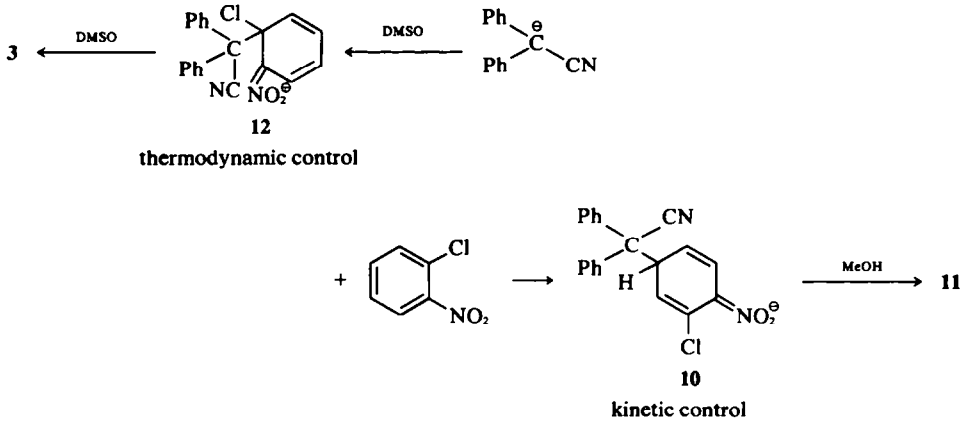
acetonitrile and nitrobenzene proceeds via formation of nitrosocompounds in similar way.[3] The nitroso compound (**11**) being very active electrophile adds immediately second diphenylacetonitrile anion and the addition product loses CN^- to give nitrone **6a**.

The formation of nitrones in reaction between diphenylacetonitrile and aromatic nitroso compounds (established by Aurich[19]) was independently proved by synthesis of known triphenylnitrone from the reaction of diphenylacetonitrile with nitrosobenzene in the presence of NaOH in methanol. The question why changing a solvent from DMSO to methanol results in such a dramatic change of the reaction pathway may be rationalized on the basis of kinetic versus thermodynamic control of the formation of the Meisenheimer complex.

These complexes can be formed by attack of nucleophile on position bearing hydrogen (H) or substituents (Y) (Y—good leaving groups e.g. halogens). Servis[20] has shown that the formation of the first type complexes occurs faster, they are however unstable and undergo reverse cleavage, that finally leads to the formation of more stable complexes of the second type; elimination of substituent Y gives then overall substitution process. In the case under consideration hydroxylic solvent probably assists rapid irreversible transformation of kinetically controled complex **10** whereas DMSO does not; this leads to the equilibration of the complexes **10** and **12** in the system and thermodynamic control of the reaction pathway.

It is not clear how the conversion **10–11** proceeds. There are two main possibilities: intramolecular transport of proton from position 4 to the negatively charged nitro group accompanied by reorganization of the electron clouds, or intermolecular addition—elimination process with participation of OH groups protons. We have not obtained any evidence to enable a choice to be made between either of these possibilities.

Formation of azoxycompounds or (and) mixture of nitro and amino derivatives of phenylalkanenitriles in reaction between **1** (R = alkyl) and **2** when the latter have free *para* position, under various conditions can be rationalized in a similar

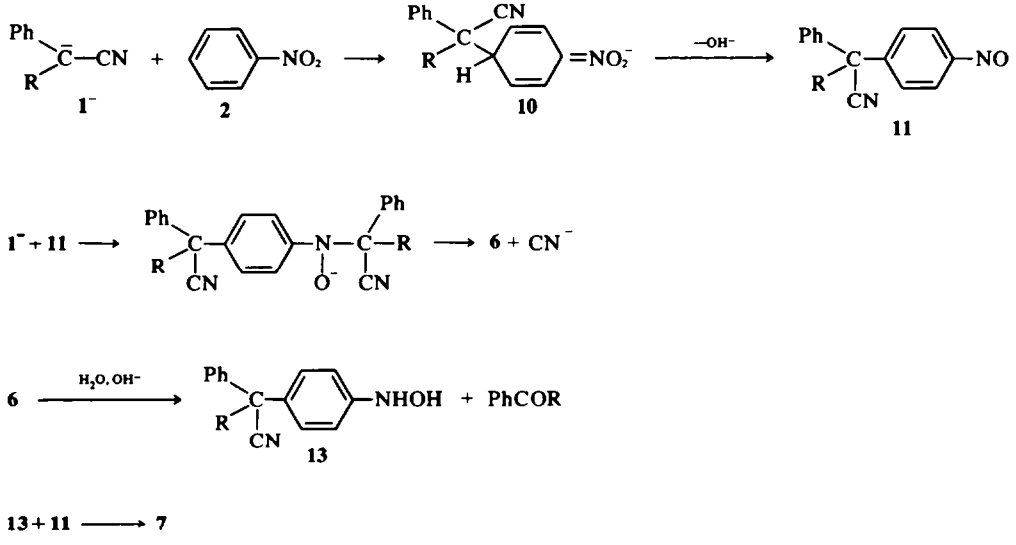


SCHEME 12

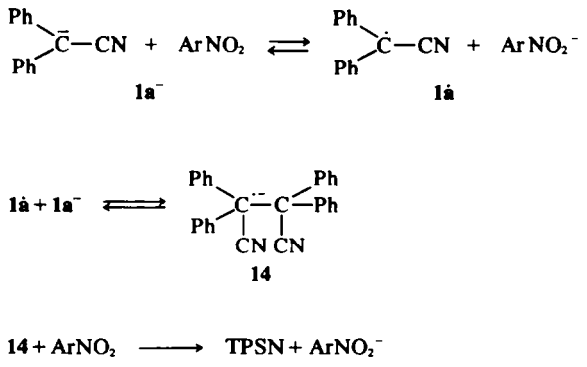
way. Initial attack of 1^- on *para* position of nitro compounds leads to the formation of Meisenheimer type complexes **10**, which loses OH^- giving nitroso compounds **11**. The latter react immediately with second molecule of 1^- with the formation of nitrone **6**. Nitrones with aliphatic substituents are known to be of limited stability so under the reaction conditions they decompose giving corresponding arylhydroxylamine derivatives **13** and arylketones. The former undergo further transformation giving azoxycompounds **7** or mixture of **3** and corresponding amine.

In almost all reactions between carbanions and aromatic nitro compounds it was possible to observe ESR signal that could be attributed to nitroaromatic radical-anions. In similar systems Russell has reported electron-transfer processes.[21] On the basis of ESR spectra of nitroaromatic radical-anions he has been able to estimate quantitatively degree of electron transfer. Because of the high sensitivity of ESR method, it is difficult, without quantitative data to decide whether electron transfer processes are main or side reactions in the systems. However, examination of the products of the reaction of diphenyl acetonitrile with various halonitrobenzenes (**2**) shows that essentially tetraphenyl succinonitrile is formed and this in addition to the absence of cross-coupled products implicates free radical processes occurring via initial electron transfer. In this case electron transfer is favoured because of the stabilities of the intermediate diphenylcyanomethyl radical and the nitroaryl radical anion.

We can conclude that relatively "free" carban-



SCHEME 13



SCHEME 14

ions, which exist in solvents such as DMSO exhibit predominantly nucleophilic character whereas in non-polar solvents they tend to form agglomerates and electron transfer processes are favoured. The formation of the succinonitriles probably arises from coupling between a radical and a radical anion rather than direct radical combination.[22,23]

This premise is reinforced by the probability that the newly formed radical is surrounded by a number of carbanions within an agregate. Electron transfer is a main reaction path in some reactions of phenylalkanenitriles with aromatic nitro compounds. Thus 1 (R = i-Pr) under catalytic conditions reacts with *p*-nitrobenzophenone derivatives giving azoxybenzophenones and arylketones. The mechanism of transformation of initially formed nitrobenzophenone radical-anions to azoxybenzophenones is obvious. However it is rather difficult to explain how phenylcyanoalkyl radicals are transformed into the ketones. Probably the radical combines with OH ions; the radical anion so formed is then oxidized by nitroaromatic molecule giving cyanohydrin which is unstable under these conditions and decomposes to ketone and HCN.

On the basis of our study we cannot come to a conclusion about the role of electron transfer in nucleophilics substitution of halogen atoms, nitro group or hydride anions. Recently Shein[24] has proposed reversible electron-transfer process as a step in Meisenheimer complex formation and nucleophilic substitution, however this conclusion seems to overestimate the role of these processes. The most probable pathway is presented on Scheme 15.

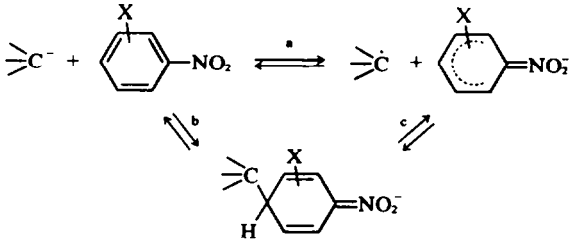
Formation of Meisenheimer complex occurs on path b. E–T process (a) proceeds reversibly and when the equilibrium is unfavorable, or further transformation of the resulting paramagnetic species is slow compared with (b) no products of E–T processes are observed. Participation of path (c) in overall reaction scheme is rather doubtful and Meisenheimer complex formation and E–T processes are parallel but not consecutive reactions.

EXPERIMENTAL

Starting materials were commercial or obtained by known methods: phenylalkylacetonitriles by catalytic alkylation of phenylacetonitrile, t-butyl 2-chloro-5-nitrobenzoate by reaction of the acid chloride with t-butanol, 2-chloro-5-nitrobenzophenone and 4-X-4-nitrobenzophenones by Friedel-Crafts reaction.

NMR spectra were performed using Jeol JNM-60 H spectrometer operating at 60 mhz with TMS as an internal standard. IR spectra were performed using Perkin-Elmer 237 and Unicam SP-100 spectrometers, UV spectra are obtained using Unicam SP-500 spectrometer.

All mp. are taken in capilary tubes and were uncorrected.



SCHEME 15

1. *Nitroarylation of phenylalkanenitriles and diphenylacetonitrile*

1 (*General procedure*) see Table 1. The nitrile 1 (0·05 mole), the aromatic chloro (or bromo) nitro compound 2 (0·05 mole) and triethylbenzylammonium chloride (TEBA) (0·2–0·3 g, about 0·001 mole) were placed in a 3-necked flask equiped with efficient stirrer and thermometer. In the case of solid compounds benzene or acetonitrile (5–10 ml) was added in order to dissolve the reactants. After short stirring period 50% NaOH aq (10–15 ml) was added portionwise and the reaction cooled if necessary. The mixture was then maintained at 40–50° for 3–4 h with vigorous stirring, cooled, diluted with water, the solid products were filtered off and recrystallized, the liquid products were extracted with benzene. The residue obtained on removal of solvent was either distilled in vacuum or filtered and recrystallized.

2. *Reaction of 2-phenylbutyronitrile with 2,4-dichloronitrobenzene*

The reaction was carried out essentially as above. The product was extracted and purified by distillation in vacuum (bp. 186°/0·2) giving mixture of isomers, total yield 81%. Distillate was separated by column chromatography on alumina giving **3a** and **3b** (Table 1 No. 28 and 29).

3. *Nitroarylation of diphenylacetonitrile with o-chloronitrobenzene in DMSO*

Diphenylacetonitrile (9·7 g, 0·05 mole) and *o*-chloronitrobenzene (7·9 g, 0·05 mole) were dissolved in DMSO (25 ml). To this soln powdered KOH (6 g) was added with stirring, resulting in an exothermic reaction. The reaction was carried out at 60° for 2 h, then the mixture was poured on cold water and extracted with benzene, the extracts washed with water and solvent evaporated. The residue was recrystallized from MeOH (Table 1 No. 10).

4. *Reaction of phenylalkanenitriles with p-nitrobenzophenones* (Table 2).

The nitrobenzophenone (0·015 mole), nitrile 1 (0·025 mole), TEBA (0·1 g) and 50% NaOH aq (10 ml) were stirred at 50–60° for 3 h. The mixture was diluted with water and extracted with benzene, organic layer washed, dried, the solvent evaporated and the residue purified by distillation in vacuum and/or recrystallisation.

With nitrile 1 (R = iso-C_3H_7) dilution of the mixture after reaction resulted in formation of solid products which were filtered and purified by crystallisation from DMF to give azoxybenzophenone derivatives (see Scheme 9)

X = H, mp. 200°, lit.[25] mp. 200°
X = Cl, mp. 290°, lit.[25] mp. 291°; Analysis*
X = Br, mp. 288°; Analysis*
X = CH_3, mp. 220°; Analysis*

Aqueous filtrates were extracted with benzene and the solvent evaporated. Analysis by GLC together with the preparation of the 2,4-dinitrophenylhydrazone (mp. 160°) established the presence of iso-butyrophenone.

5. *Reaction of diphenylacetonitrile with aromatic nitro compounds in methanol*

Synthesis of nitrones **6** (Table 3). Diphenylacetonitrile (9·7 g, 0·05 mole) and aromatic nitro compound (0·05 mole) were added to solution of NaOMe in MeOH (3 g Na in 50 ml of MeOH). The intensely coloured mixture was kept at 50° for 2 h then diluted with water and extracted with benzene. The solvent was evaporated and the residue diluted with MeOH. The first crop of crystalline product (tetraphenylsuccinonitrile in variable amounts) was filtered off, the filtrate concentrated, the product filtered and recrystallized.

*Satisfactory elemental analysis were obtained.

6. *Cycloaddition of nitrones* **6** *to phenylisocyanate* (Table 5).

The nitrone **6** (2 g) and phenylisocyanate (1 g, an excess) were dissolved in benzene and the soln boiled under reflux for 1 h. After cooling the soln deposits crystalline adduct **8**.

7. *Oxidative hydrolysis of nitrones* **6** *to azoxycompounds* **7**

The nitrone **6** (0·02 mole) dissolved in benzene was shaken with 20% HCl for 0·5 h. Benzene layer was evaporated and residue recrystallized from MeOH. Benzophenone was isolated from the filtrate.

8. *Reaction of 2-phenylpropionitrile with nitrobenzene*

a. In methanol. 2-Phenylpropionitrile (13·1 g, 0·1 mole) and nitrobenzene 8·2 g (0·066 mole) were added to soln of NaOMe (3 g Na in 50 ml of MeOH). The mixture was gradually heated to 70°C, kept at this temp for 3 h, diluted with water, extracted with benzene and the extracts steam distilled. GLC analysis of the steam distillate (11·5 g after evaporation of benzene) showed presence of acetophenone (40%), nitrobenzene (28%) and 2-phenylpropionitrile (32%). The residue from the steam distillation was recrystallized from MeOH giving **7** (Table 4). The experiment was repeated and the residue reduced with Sn/HCl giving 2 - phenyl - 2 - (p - aminophenyl)propionitrile, yield 11 g, 50% based on starting nitrile.

b. In THF-ether mixture. Sodium derivative of 2-phenylpropionitrile was obtained from 13·1 g (0·1 mole) of the nitrile and 4 g of $NaNH_2$ in liquid ammonia. To this soln dry THF was added and then ammonia evaporated. The resulting suspension was diluted with Et_2O, cooled to −35° and nitrobenzene 12·3 g (0·1 mole) in THF (30 ml) was added dropwise, the temperature being maintained at −25–35°. After the addition was completed the mixture was stirred for 15 min then treated with water, the organic material extracted with ether and the solvent evaporated.

The residue was distilled in vacuum giving two fraction (a) bp. 95–105°/10 mm Hg (7·7 g); (b) 180–200°/0·5 mm Hg (7·5 g). Fraction (a) analyzed by GLC consists of nitrobenzene (49%) 2-phenylpropionitrile (35%) and acetophenone (16%). Fraction (b) is almost equimolar mixture of *p*-nitroaryl- and *p*-aminoaryl-derivatives of 2-phenylpropionitrile which were separated by treatment with HCl aq. Isolated compounds (total yield 32%) have mp, IR and NMR spectra identical with authentic samples.

Reactions with other nitroaromatic compounds as well as with 2-phenylbutyronitrile were carried out under similar conditions.

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