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NUCLEOPHILIC SUBSTITUTION OF p-DINITROBENZENE WITH SOME CARBANIONS. FORMATION OF p-SUBSTITUTED NITROBENZENES

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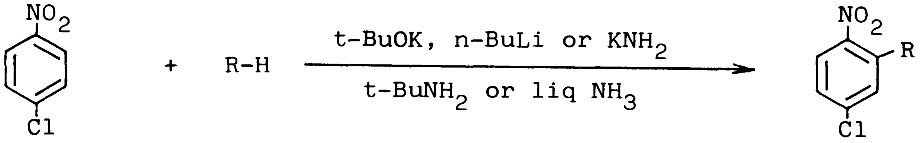
Treatment of p-dinitrobenzene with active methylene compounds of rather weak acidity in the presence of t-BuOK in liq NH_3 at -70 °C leads to nucleophilic substitution of a nitro group, giving p-substituted nitrobenzenes in generally good yields.

Previously, we reported that 4-chloronitrobenzene undergoes nucleophilic substitution of a hydrogen to give 2-substituted 4-chloronitrobenzenes upon treatment with some active methylene compounds in the presence of a strong base in $t\text{-}BuNH_2$ or in liq NH_3 at low temperatures as illustrated below.[1,2]



R: CH_2COMe, CH_2COCMe_3, CH_2COPh, $CH_2COOCMe_3$, CH_2CN etc.

In continuation of this work, we found that the reaction of p-dinitrobenzene (**1**) with active methylene compounds under similar conditions followed another course, i.e., the nucleophilic displacement of a nitro group, to afford p-substituted nitrobenzenes (**2**).

Thus, an active methylene compound (3 equiv.) was added dropwise at -70 °C to a suspension of t-BuOK (4 equiv.) in liq NH_3 and the mixture was stirred for 10 —

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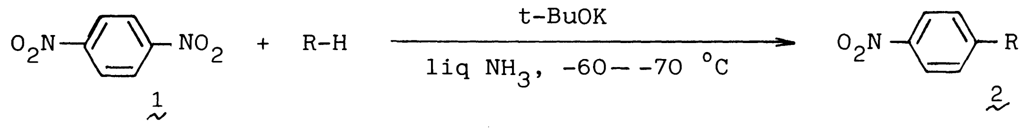
20 min to give a pale yellow solution. When **1** was added in small portions under stirring, the reactants immediately turned dark blue. Stirring was continued for 20 min to 1.5 h at the same temperature to give the corresponding p-substituted nitrobenzene **2** in generally good yields (Table 1).

Table 1. Reactions of p-dinitrobenzene (**1**) with active methylene compounds in the presence of t-BuOK in liq NH_3



Run	R-	Temp/°C	Time	Yield of 2/% a)
1	$-CH_2COMe$	-70	1.5 h	59.2
2	-CH(Me)COEt	-70	1.0 h	97.0
3	-CH(Et)COMe	-70	30 min	85.5
4	$-C(Me_2)COCHMe_2$	-60	30 min	75.4
5	$-C(Me_2)COMe$	-70	1.5 h	43.4
6	$-\overset{\vert}{C}HCO(CH_2)_3-$ b)	-70	40 min	69.4
7	$-\overset{\vert}{C}HCO(CH_2)_4-$ c)	-70	1.5 h	48.6
8	$-CH_2COOEt$	-70	20 min	40.2
9	$-CH_2COOCMe_3$	-60	1.0 h	44.3
10	-CH(Me)COOEt	-60	1.0 h	52.7
11	$-CH_2CN$	-70	40 min	72.7
12	-CH(Ph)CN	-70	20 min	97.6
13	-C(Me)(Ph)CN	-70	1.5 h	18.0
14	$-CH(C_{10}H_7)CN$ d)	-70	30 min	44.2
15	-NHPh	-70	20 min	77.1
16	$-NHC_5H_4$ e)	-70	30 min	77.2

a) Isolated yield based on **1**. b) Cyclopentanone c) Cyclohexanone
d) 1-Naphthylacetonitrile e) 2-Aminopyridine

As shown in Table 1, the reaction proceeded readily with a number of active methylene compounds of rather low acidity; those with highly acidic ones, such as ethyl cyanoacetate, gave no definite products. Aniline and 2-aminopyridine were also found to react with **1** in a similar manner (runs 15 and 16 in Table 1).

Examinations of various conditions demonstrated that the reaction is highly sensitive towards the reaction conditions (Table 2), and the best results were obtained by application of 3 equiv. active methylene compounds and 4 equiv. t-BuOK in liq NH_3. Particularly important is the nature of the solvent. Thus, the reaction with acetonitrile by means of t-BuOK/THF or t-BuOK/t-$BuNH_2$ gave only small amounts of the product (runs 2 and 3 in Table 2), and no products were formed in other attempted reactions using n-BuLi/THF or t-BuOK/THF (runs 4—7 in Table 2). Whereas **1** did not react with cyclohexanone in the presence of t-BuOK in THF, the reaction took place to a small extent when hexamethylphosphoric amide (HMPA, 4 equv.) or N,N,N',N'-tetramethylethylenediamine (TMEDA, 4 equiv.) was added as a cmplexing agent (runs 8 and 9 in Table 2).

Table 2. Reactions of p-dinitrobenzene (**1**) with active methylene compounds (R-H) under various conditions[a)]

Run	R-H (3 equiv.)	Base (4 equiv.)	Solvent	Time	Yield/%
1	MeCN	t-BuOK	liq NH_3	40 min	72.2
2	MeCN	t-BuOK	THF	1.0 h	28.4
3	MeCN	t-BuOK	t-$BuNH_2$	1.5 h	15.8
4	MeCN	n-BuLi	THF	1.0 h	—
5	MeCOMe	t-BuOK	THF	1.0 h	—
6	$MeCOOCMe_3$	t-BuOK	THF	2.0 h	—
7	$OC(CH_2)_5$	t-BuOK	THF	1.0 h	—
8	$OC(CH_2)_5$	t-BuOK/HMPA[b)]	THF	10 min[c)]	15.0
9	$OC(CH_2)_5$	t-BuOK/TMEDA[d)]	THF	10 min	4.3
10	MeCN	$LiNH_2$	liq NH_3	0.5 h	48.1
11	MeCN	$NaNH_2$	liq NH_3	0.5 h	66.4
12	MeCN	KNH_2	liq NH_3	0.5 h	58.4
13	MeCOMe	KNH_2	liq NH_3	5.0 h	trace
14	EtCOEt	KNH_2	liq NH_3	1.0 h	14.6
15	$OC(CH_2)_5$	KNH_2	liq NH_3	3.0 h	52.0
16	$MeCOOCMe_3$	KNH_2	liq NH_3	2.5 h	14.2

a) All reactions were carried out at -70 °C. b) Hexamethylphosphoric amide (4 equiv.) was added. c) A slightly higher yield of 16.8% was obtained from one hour's reaction. d) N,N,N',N'-Tetramethylethylenediamine (4 equiv.) was added.

On the other hand, alkali amide in liq NH_3 was found to be appreciably effective. Thus, the reaction with acetonitrile in liq NH_3 gave the product in fair yields not only by KNH_2 and $NaNH_2$ but also by $LiNH_2$ which was not effective at all in the reaction of p-chloronitrobenzene with active methylene compounds (runs 10—12 in Table 2). The three hours' reaction of **1** with cyclohexanone by means of KNH_2/liq NH_3 gave a slightly better yield (run 15 in Table 2) than the reaction using t-BuOK (run 7 in Table 1), whereas yields of reactions with acetone, diethyl ketone and t-butyl acetate in the presence of KNH_2 were much lower as compared with reactions using t-BuOK/liq NH_3 (runs 13, 14, and 16 in Table 2).

Although it is well documented that an activated aromatic nitro group undergoes displacement with oxygen-, nitrogen- and sulfur-nucleophiles, there have been only few reports on the nucleophilic substitution with carbanions.[3,4] Kornblum et al. reported that active nitro group of some p-substituted nitrobenzenes is replaced with the carbanion of 2-nitropropane.[5] Makosza and his coworkers described that some 4-nitrobenzophenones undergo nucleophilic substitution upon treatment with phenylalkanenitriles in the presence of 50% NaOH and benzyltriethylammonium chloride, giving the 4-substituted benzophenones.[6] They also noticed that the nucleophilic displacement of a nitro group occurrs as a side reaction in the vicarious nucleophilic substitution of p-dinitrobenzene with chloromethyl phenyl sulfone.[7]

As compared with these reactions, the above-mentioned reaction is more general and more useful for synthetic purposes. Further studies are in progress to explore the characteristic features of the reaction and the applicability to other nitroarenes.

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