Anal. Calcd for $C_{30}H_{28}O_4$: C, 79.6; H, 6.24; mol wt, 452. Calcd for $C_{30}H_{28}O_5$: C, 76.90; H, 6.02; mol wt, 468. Found: C, 76.6; H, 6.1; mol wt, 453 in benzene.

Registry No.—**1a**, 31592-22-0; **1b**, 10239-91-5; **2a**, 31592-24-2; **2b**, 31592-25-3; **3a**, 31592-26-4; **3b**, 31592-27-5; **4a**, 31592-28-6; **4b**, 31592-29-7; **5a**, 31592-30-0; **5b**, 31592-31-1; **6a**, 31592-32-2; **6b**, 31592-33-3; **7a**, 31592-34-4; **7b**, 31592-35-5; **8a**, 31592-36-6; **8b**, 31592-37-7; **9**, 31592-38-8; **10**, 31592-39-9; **11**, 31592-40-2; **12a**, 31592-41-3; **12b**, 31592-42-4; **13**, 33189-77-4; **14**, 33189-78-5; **15**, 31592-45-7; **16**, 31592-46-8; **17a**, 31592-47-9; **17b**, 31592-48-0; **18**, 31592-49-1; **19**, 31592-50-4; **20a**, 31592-51-5; **20b**, 31662-33-6; **21**, 31592-52-6; **22a**, 31592-53-7; **22b**, 31592-54-8; **23**, 31592-55-9; **24**, 31592-56-0; **25**, 31592-57-1; **26**, 31592-58-2; **27**, 31592-59-3; **28**, 31592-60-6; **29**, 31592-61-7; **30**, 31592-62-8; **31**, 31592-63-9; **32**, 31592-64-0; **33**, 31592-65-1; **34**, 31592-66-2; **35**, 31592-67-3; phenylmagnesium bromide, 100-58-3; phenyllithium, 591-51-5.

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Reaction of Nitriles with Hydrazine Hydrate and Raney Nickel[1]

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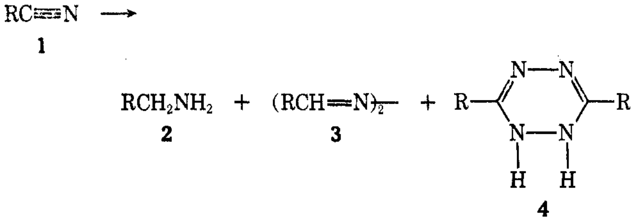
The reaction of ethanolic solutions of nitriles with hydrazine hydrate and catalytic amounts of Raney nickel was investigated as a possible general synthesis of aldehydes (isolated as the aldazines). The types of nitriles investigated were mono-, di-, and trisubstituted acetonitriles, carbocyclic nitriles, aromatic nitriles, α,β-unsaturated nitriles, and some heterocyclic nitriles. Depending upon the structure of the nitrile, it was found that either a primary amine, an aldazine, or a 3,6-disubstituted 1,2,4,5-tetrazine derivative was the major product. The reaction of α,β-unsaturated nitriles is further complicated by reactions of the double bond. Some experiments aimed at elucidating the reaction path were also performed. As a general aldehyde synthesis, the reaction appears to be limited to benzonitrile and substituted benzonitriles.

Hydrazine hydrate and Raney nickel are an effective combination for the reduction of aromatic nitro compounds to amines.[3] These same reagents have been employed by Pietra and Trinchera[4] for the partial reduction of 20 substituted benzonitriles to the corresponding aldazines which upon hydrolysis affords the corresponding aldehydes. We extended the hydrazine–Raney nickel reducing system to 2-(arylmethyl)benzonitriles and obtained aldazines which upon heating with acid give excellent yields of polynuclear aromatic hydrocarbons.[5] Terent'ev, *et al.*,[6] reported that phenylacetonitrile, 3-indoleacetonitrile, and 5-methoxy-2-methyl-1-benzyl-3-indoleacetonitrile are reduced to the primary amines with hydrazine and Raney nickel. In another investigation using these reducing agents, Dallacker[7] reported that the three isomeric cyanopyridines and 3,4-methylenedioxybenzonitrile yield the corresponding 3,6-disubstituted 1,2-dihydro-1,2,4,5-tetrazines. However, it was later reported by Butte and Case[8] that Raney nickel is not necessary for the formation of the tetrazines as had been reported by Dallacker.

In view of the results of the various studies, we undertook an examination of the effect of structure in determining the nature of the product from the reaction of nitriles with hydrazine hydrate and catalytic amounts of Raney nickel.



The results of the reactions of the 34 nitriles studied are tabulated in Table I.

Some nonkinetic methods of investigation were also used to study the course of the reduction of nitriles with hydrazine and Raney nickel. Preparatively, benzaldazine is obtained from benzonitrile by evaporation of the solvent from the reaction mixture followed by addition of aqueous acid to the residual oil. The oil was thought to be either the impure hydrazone or aldazine or a mixture of both. The ultraviolet spectrum of this oil (before acidification) was found to be consistent with that which would be obtained from a mixture of benzaldehyde hydrazone and benzaldazine. The presence of benzaldehyde hydrazone was confirmed by acidifying the oil, thus converting the hydrazone to benzaldazine, and this was observed spectroscopically. The presence of benzylamine (15%) and benzonitrile (a trace) was confirmed by vapor phase chromatograms of the reaction mixture both before and after conversion of the hydrazone to the aldazine.

Robinson and Brown[9] had found that hydrazine–Raney nickel effected the cleavage of N,N'-diacylated hydrazines to produce the corresponding amides. This suggested that the benzylamine found in the reaction

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(1) This work was presented in part at the Second Middle Atlantic Regional Meeting of the American Chemical Society, New York, N. Y., Feb 1967.

(2) Abstracted in part from the M.S. theses of J. F. Siuda, 1964, M. J. Nolan, 1964, and T. M. Santosusso, 1966, Villanova University.

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TABLE I

YIELD OF PRODUCTS FROM THE REACTION OF NITRILES WITH HYDRAZINE HYDRATE AND RANEY NICKEL

No.	**1**, R	Registry no.	Product (yield, %)	No.	**1**, R	Registry no.	Product (yield, %)	Registry no.
1	$CH_3CH_2CH_2-$	109-74-0	**2** (75)	20	$C_6H_5(CH_3CH_2)_2C-$		*a*	
2	$C_6H_5CH_2-$	140-29-4	**2** (75)	21	$CH_3CH_2(C_6H_5)_2C-$		*a*	
3	$4\text{-}C_6H_5\text{-}C_6H_4CH_2-$	31603-77-7	**2** (75)	22	$(C_6H_5)_3C-$		*a*	
4	$C_6H_5CH_2CH_2-$	645-59-0	**2** (75)	23	$CH_2{=}CHCN$	107-13-1	*c*	
5	$C_6H_5CH_2CH_2CH_2-$	2046-18-6	**2** (75)	24	$CH_3CH{=}CHCN$	4786-20-3	*c*	
6	$1\text{-}C_{10}H_7CH_2-$	132-75-2	**2** (75)	25	$C_6H_5CH{=}CHCN$	4360-47-8	**3** (15)[c]	1568-11-2
7	$(CH_3)_2CH-$		*a*	26	*p*-HOC_6H_4-	767-00-0	**3** (74)	5466-23-9
8	$C_6H_5(CH_3)CH-$	1823-91-2	**2** (35)	27	*o*-NCC_6H_4-		*a*	
9	$C_6H_5(CH_3CH_2)CH-$	769-68-6	**2** (30)	28	*p*-NCC_6H_4-		*a*	
10	$(C_6H_5)_2CH-$	86-29-3	**2** (40), **3** (50)					
				29	2-(2′-Methylbenzyl)phenyl	782-13-8	**3** (98)	
11	9-Fluorenyl	1529-40-4	**2** (45), **3** (50)					
12	Cyclopropyl	5500-21-0	*b*	30	9-Phenanthryl	2510-55-6	**2** (66), **3** (10)	
13	3-Methylcyclobutyl	31603-86-8	**2** (5)[b]	31	2-Fluorenyl	2523-48-0	**2** (15)	
14	Cyclopentyl		*a*	32	2-Pyridyl	100-70-9	**4** (61)[d]	1671-86-9
15	Cyclohexyl		*a*	33	3-Pyridyl	100-54-9	**4** (70)[d]	31599-23-2
16	Cycloheptyl		*a*					
17	Bicyclo[2.2.1]heptyl	74-90-8	**2** (10)					
18	$(CH_3)_3C-$		*a*	34	4-Pyridyl	100-48-1	**4** (80)[d]	31599-25-4
19	$(CH_3CH_2)_3C-$		*a*					

[a] >95% of unreacted starting nitrile. [b] Products isolated from ring-opening reactions. [c] Products isolated from additions to the double bond. [d] Raney nickel is not necessary for this reaction; *cf.* ref 8.

mixture might arise as the result of reductive cleavage of benzaldazine or benzaldehyde hydrazone. In order to determine if this were the case, benzaldazine and benzaldehyde hydrazone were each allowed to react with hydrazine–Raney nickel under the reaction conditions. With benzaldazine, it was found that reductive cleavage did occur under these conditions, benzylamine being formed.

In should be noted that the conditions under which this cleavage occurred did not conform exactly to those found in the reduction of benzonitrile. In the cleavage reaction, there were relatively large concentrations of benzaldazine, hydrazine, and fresh Raney nickel simultaneously present, while, in the reduction of benzonitrile, is formed only after decomposition of the hydrazine has begun. Nevertheless, in the reduction of benzonitrile, some benzaldazine is present while hydrazine is undergoing decomposition, and, therefore, it seems likely that some reductive cleavage of the aldazine should occur.

Under the reaction conditions benzaldehyde hydrazone was converted to a mixture of benzaldazine and benzylamine. Because of the ease with which the hydrazone is converted to the aldazine by heat or moist air,[10] it could not be determined by a simple examination of products if the benzylamine found in the reaction mixture were formed directly from the hydrazone or indirectly through the aldazine or from both sources. Similar results were obtained in the investigation of the reaction of 9-cyanophenanthrene. As with benzaldazine, 9-phenanthrenecarboxaldazine underwent reductive cleavage to yield the corresponding amine under the reaction conditions. The extent of the reaction in this case was limited by the relative low solubility of the aldazine in the reaction mixture.

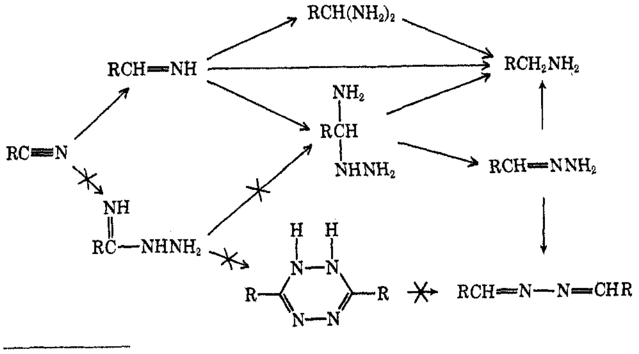
The final part of the investigation dealt with the reaction of benzonitrile with the separate components of the hydrazine–Raney nickel reducing system.

In all cases, benzonitrile remained unreacted. Hydrazine alone did not effect a reduction nor did Raney nickel alone, whether the active catalyst or the modified "reacted" catalyst was used, or whether the ammonia normally found in the reaction mixture was present or not. These results show that reduction of benzonitrile in this system can be accomplished only in the presence of active Raney nickel and excess decomposing hydrazine.

The formation of a hydrazone from an aromatic nitrile by initial nucleophilic attack of hydrazine to give the intermediate amidrazone (proposed by Pietra and Trinchera[4]) seems unlikely in view of the fact that under the usual reaction conditions hydrazine does not react with benzonitrile in the absence of Raney nickel. However, the cyanopyridines seem to exhibit a marked reactivity toward hydrazine, since these nitriles yield the corresponding 3,6-disubstituted 1,2-dihydro-1,2,4,5-tetrazines[7,8] presumably by initial formation of the amidrazone.[11]

The results of our investigation are consistent with a mechanism also proposed by Pietra and Trinchera[4] (Scheme I). In the presence of Raney nickel and de-

SCHEME I



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composing hydrazine, the nitrile is reduced to the aldimine. Addition of hydrazine to the aldimine followed by loss of ammonia yields the hydrazone. However, the present evidence indicates that this description of the course of the reaction should be extended to account for the formation of primary amine from the aldazine which need not be the only source of primary amine, since either direct reduction, as in catalytic hydrogenation, or addition of ammonia to the aldimine or hydrazone followed by reductive cleavage would also yield the primary amine. The relative importance of the different reactions as sources of the primary amine has yet to be determined. Furthermore, this reaction scheme also accounts for the fact that in those cases where primary amine is the major product, no secondary amine formed by reaction of the aldimine and primary amine is obtained.

$$\mathrm{RCH{=}NH + RCH_2NH_2 \longrightarrow RCH(NH_2)NHCH_2R \xrightarrow{H_2} (RCH_2)_2NH + NH_3}$$

In catalytic hydrogenation Schwoegler and Adkins[12] reported that the extent of the reaction between the primary amine and aldimine to form secondary amine could be diminished by conducting the hydrogenation in the presence of ammonia. Since it appears that the hydrazine hydrate reduction of nitriles may also proceed through the aldimine intermediate, the yield of pure primary amine by this method might then be explained as a result of preferential reaction of the ammonia produced by hydrazine decomposition with the aldimine.

One of the original intents of this investigation was to determine the reaction limitations as an aldehyde synthesis. From our results it is obvious that good yields of aldazine can be expected only with benzonitriles providing they do not contain strongly electron-withdrawing groups. It has also been demonstrated that the reaction is useful as a preparative method for converting monosubstituted acetonitriles to the corresponding primary amines.

Experimental Section

Elemental analyses were carried out by Alfred Bernhardt, Mülheim (Ruhr), Germany. Melting points were determined in capillaries in a Thomas–Hoover apparatus and are uncorrected. Infrared spectra were obtained using a Perkin-Elmer Model 337. Ultraviolet spectra were obtained using a Perkin-Elmer Model 202. Nmr spectra were determined on a Varian A-60 nmr spectrometer with tetramethylsilane as an internal standard. Gas chromatographic analyses were carried out on an F & M model 720 using a 6 × $^3/_8$ in. column packed with 5% 20M Carbowax–1% KOH on a Diatoport S support.

The Raney nickel used during this work was prepared by the method of Dominguez, Lopez, and Franco[13] and was periodically tested for activity by running the reaction with benzonitrile and 85% hydrazine hydrate in 95% ethanol.

All the nitriles used were commercially available except for the following, which were synthesized by published procedures: *cis*- and *trans*-3-methylcyclobutanecarbonitrile,[14] 9-cyanofluorene,[15] and 2-(2′-methylbenzyl)benzonitrile.[16]

9-Phenanthrenecarboxaldazine was prepared from 9-phenanthrenecarboxaldehyde and hydrazine hydrate as a yellow solid: mp 239–240° (benzene–ethanol); uv max (DMF) 352 and 366 nm; ir (KBr) 1625 cm^{-1} (C=N); nmr (CDCl$_3$) δ 7.6 (s, 1, -CH=N-).

Anal. Calcd for $C_{30}H_{20}N_2$: C, 88.21; H, 4.94; N, 6.85. Found: C, 88.47; H, 5.07; N, 6.45.

2-(2′-Methylbenzyl)benzaldazine was prepared in 98% yield from the reaction of 2-(2′-methylbenzyl)benzonitrile[16] with hydrazine hydrate and Raney nickel as yellow needles: mp 153–155° (benzene–95% ethanol); uv max (95% ethanol) 309 nm; ir (KBr) 1613 cm^{-1} (C=N); nmr (CDCl$_3$) δ 7.55 (s, 1, CH=N-).

Anal. Calcd for $C_{30}H_{28}N_2$: C, 86.49; H, 6.77; N, 6.73. Found: C, 86.93; H, 6.80; N, 6.44.

Reaction of Nitriles with Hydrazine Hydrate in the Presence of Raney Nickel.—Two general sets of reaction conditions were used in conjunction with several methods of separation, purification, and identification of products (Table II). After filtration to remove the Raney nickel the resulting solution was treated in one of the following ways.

TABLE II

	Method A	Method B
Nitrile	1–2 g	1–2 g
Solvent (95% ethanol)	15 ml	50 ml
Hydrazine hydrate (85%)	5 ml	48 ml
Raney nickel[13]	50 mg	0.50 g
Time of reaction	18 hr	7 hr
Temperature	50–55°	70–80°

(a) The solution was distilled and various fractions were subjected to vapor phase chromatographic analysis. If it was determined that only amine was present it was then isolated and characterized by spectroscopic methods as well as conversion to the benzoyl derivatives.

(b) After removal of volatile material by distillation under reduced pressure the residual oil was acidified with hydrochloric acid. Any solid material which precipitated was collected while the mother liquor was examined by vpc.

The solid residue was treated with dilute sodium hydroxide and then extracted under the ether. When the ether extract was analyzed by glpc and determined to have amine then the amine was isolated as the benzoyl derivative. Any solid aldazine residue was recrystallized and characterized by spectroscopic means and comparison with authentic samples.

Registry No.—Hydrazine hydrate, 7803-57-8; 9-phenanthrenecarboxaldazine, 31603-73-3; 2-(2′-methylbenzyl)benzaldazine, 31603-74-4.

Acknowledgment.—The authors wish to thank Dr. Aldan Josey, E. I. du Pont de Nemours and Co., Wilmington, Del., for the generous sample of 3-methylenecyclobutanecarbonitrile.

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