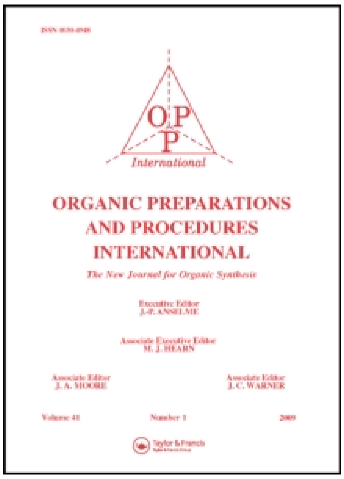

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REDUCTIVE DECYANATION *vs* ADDITION OF GRIGNARD REAGENTS WITH HINDERED NITRILES

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REDUCTIVE DECYANATION *vs* ADDITION OF GRIGNARD REAGENTS WITH HINDERED NITRILES

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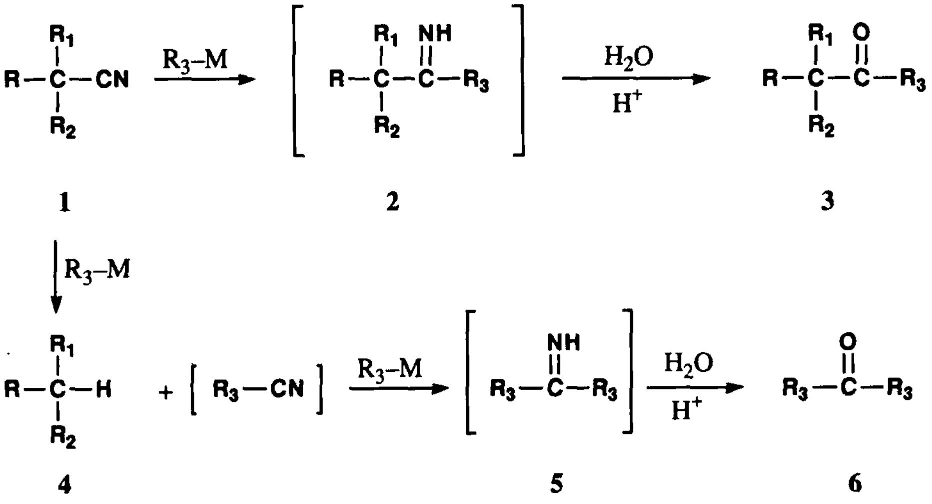
The differences in the rate of hydrolysis of a number of 2,2-disubstituted cycloalkanoneketimines, to the corresponding ketones has been reported.[1] In order to obtain quantified data on related model compounds, we synthesized a series of acetophenonimines by the reaction of phenylmagnesium halides with alkyldiphenylacetonitriles (**1**) in which the alkyl group was methyl, ethyl, butyl, pentyl or isopropyl. The first compound studied was 2,2-diphenylhexanenitrile (**1c**). In the initial experiments, the expected ketimine (**2c**) was not found in the reaction mixture; however, the reductive decyanation product, 1,1-diphenylpentane (**4c**) was isolated along with some benzophenone. Ramart-Lucas and Salmon-Legagneur[2] apparently were the first to discover reductive decyanation (reductive displacement) and reported a 70% yield of the decyanation product by treatment of triphenylacetonitrile with benzylmagnesium chloride. A possible mechanism for this observation was proposed by Kharasch.[3] Although there have been a number of similar isolated cases of reductive decyanation,[3,4] a study of this reaction in our series seemed warranted. Gregory *et al.*



recently showed that several 1-benzyl-1-cyano-1,2,3,4-tetrahydronaphthalenes undergo decyanation with Grignard and lithium reagents.[3]

Our results are summarized in Table 1. In addition to the five alkyldiphenylacetonitriles, we extended the substrate choices to include three more Grignard reactions: mesityldimethylacetonitrile with both phenyl- and methylmagnesium chloride, trimethylacetonitrile and 2,6-dichlorobenzonitrile. Due to the greater reactivity of organolithium reagents,[5] both phenyllithium and methyllithium were also included.

As expected, compounds **1a** and **1b** gave addition products exclusively with PhMgBr. With **1c**-**1f**, the ratio of addition to decyanation decreased. Steric factors appear to dominate the competition results. The last two nitriles (**1e** and **1f**) are not sufficiently hindered to give a preponderance of decyanation. The separation of products in the reaction mixtures was difficult since in addition to the anticipated ketimines and hydrocarbons there were varying amounts of biphenyl, the ketone (from the hydrolysis of the expected ketimine hydrochloride in the work up), benzophenonimine and its hydrochloride and benzophenone.

The hydrolysis of the ketimines to the ketones listed in Table 2 was effectively accomplished in aqueous-dioxane and HCl. In most cases, several hours of reflux gave 80% yields.However, in

TABLE 1. Addition vs Decyanation of Hindered Nitriles

Cmpd	R	R_1	R_2	R_3M	Add 'n	Yields (%) Decyanation	$Ph_2C{=}NH$
1a	Me	Ph	Ph	PhMgBr	~100		
1b	Et	Ph	Ph	PhMgBr	~100		
1c	n-Bu	Ph	Ph	PhMgBr	72		
				PhMgBr[a]		80	
				PhLi			80
1d	n-C_5H_{11}	Ph	Ph	PhMgBr	80		
				PhLi		60	40
1e	Me_2CH	Ph	Ph	PhMgBr	34		
				MeLi		79	
				MeLi[b]		~100	
1f	Mes[c]	Me	Me	PhMgBr	40		
				MeLi		50	
				i-BuMgCl	0	0	0
1g	Me	Me	Me	PhMgBr		63	
	2,6-$Cl_2C_6H_3CN$			PhMgBr	70	4	

a) Solvent inadvertently evaporated allowing reaction temperature to rise to ca. 180°. b) One equivalent of tetramethylethylenediamine added. c) Mes = 2,4,6-$Me_3C_6H_2$.

order to obtain comparable results for the mesityl and trimethylmethyl ketones, 2-3 days of heating were required. The 2,6-dichlorophenyl phenyl ketimine gave only a 25% yield after 3 days under reflux for $t_{1/2}$ = 96 hours. For synthetic purposes, many of these ketones are more readily prepared by alternate approaches.

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EXPERIMENTAL SECTION

Infrared spectra were obtained on a Perkin-Elmer Model 237B instrument. NMR spectra were recorded on a Perkin-Elmer R-24 instrument. Elemental analyses were performed by G. I. Robertson Laboratory, Florham Park, NJ. All spectra were consistent with the assigned structures and superimposable on those of authentic samples where applicable. Most of the compounds reported herein are available from the Aldrich ABC Library of Rare Chemicals. All yields are of isolated products. Nitriles **1b-e** were prepared from diphenylacetonitrile and the appropriate alkyl bromide with lithium cyclohexylisopropylamide as usual and had the following properties: **1b**, bp 153-155/2.5 mm; **1c**, bp 156-158/1 mm; **1d**, bp 155-160/1 mm (mp 47.5-48.5); **1e**, mp 59-60. The yields were typically ~85%. Dimethylmesitylacetonitrile, bp 161/18 mm (mp 45-46 from hexane) was prepared in 84% yield from mesitylacetonitrile[7] by dialkylation with lithium diisopropylamide and methyl iodide. 2,2-Diphenylpropanenitrile (**1a**), trimethylacetonitrile and 2,6-dichlorobenzonitrile were purchased from Aldrich Chemical Company.

Grignard and Related Reactions. General Procedures.- The reactions were carried out at the 0.05 to 0.01 mole level. The Grignard reagents were prepared as usual in ether or purchased. After mixing the Grignard or lithium reagent with the nitrile, the reaction mixture was either refluxed or the lower boiling solvents replaced with higher boiling solvent and heated for the indicated time and worked up in the typical manner. Saturation of dry ether solutions gave the hydrochlorides and distillation separated the other compounds formed as well as unreacted starting nitriles.

Pentyldiphenylacetonitrile (1d).- This substrate was studied the most extensively. Phenyllithium used in three-fold excess gave, after 6 hrs of reflux gave benzophenone (40%), ketimine hydrochloride (60%) and 1,1-diphenylhexane (**4d**), bp. 119°/1 mm, identical with an authentic sample.[8] Traces of biphenyl and benzophenone were found in the distillate. A run with a three-fold excess of phenylmagnesium bromide in refluxing toluene for 8 hrs gave an 80% yield of a mixture containing the ketimine and the corresponding acetophenone (**3d**) formed by hydrolysis in the work up, bp. 180-182°/1 mm.

Butyldiphenylacetonitrile (1c).- This compound with a three-fold excess of phenyllithium in refluxing ether for 6 hrs gave an 80% yield of benzophenone (**6**). With three-fold phenylmagnesium bromide in refluxing toluene for 8 hrs, the major product (72%) was **2c**, hydrochloride mp. 182-184°, bp. 178-179°/1 mm.[9]

Isopropyldiphenylacetonitrile (1e).- This substrate with phenylmagnesium bromide in refluxing toluene for 6 hrs gave **2e** (34%), bp. 145°/1 mm, mp. 55-57° (hydrochloride mp. 243-246°).

Anal. Calcd for $C_{23}H_{24}ClN$ (imine hydrochloride): C, 78.95; H, 6.91; N, 4.01; Cl, 10.13
Found: C, 78.89; H, 6.99; N, 4.06; Cl, 10.24

Compound **1e** reacted with methyllithium.in refluxing ether for 6 hrs to give a 79% yield of **4e**, bp. 170°/16 mm. Repetition of this reaction with 1 eq of tetramethylethylenediamine in THF at room temperature for 2 hrs gave an essentially quantitative yield of 1,1-diphenyl-2-methylpropane (**4e**).

TABLE 2. Ketone and Hydrocarbon Products and their Properties

Cmpd	R	R_1	R_2	R_3	Bp./mm (°C)	mp. (°C)
3a	Me	Ph	Ph	Ph		92.5-93.5
3b	Et	Ph	Ph	Ph		97-98.5
3c	n-Bu	Ph	Ph	Ph	182-185/1	
4c	n-Bu	Ph	Ph		112-128/1	
3d	n-C_5H_{11}	Ph	Ph	Ph	182-185/4	
4d	n-C_5H_{11}	Ph	Ph		116-119/1	
3e	Me_2CH	Ph	Ph	Ph	180-181/1	95.5-97
3e'	Me_2CH	Ph	Ph	Me	145-148/1	
4e	Me_2CH	Ph	Ph		170/16	
3f	Mes[a]	Me	Me	Ph		65-66.5
3f'	Mes[a]	Me	Me	Me	150-151/16	
4f	Mes[a]	Me	Me		116-118/16	
3g	Me	Me	Me	Ph	220-222[b]	
	$2,6-Cl_2C_6H_3(CO)Ph$					82-83
	$1,3-Cl_2C_6H_4$				172	

a) Mes = $2,4,6-Me_3C_6H_2$. b) lit.[6] bp. 220°.

Methyldiphenylacetonitrile (1a) gave only the addition product **2a**, mp. of hydrochloride 220-240°. **Ethyldiphenylacetonitrile (1b)** gave only the addition product **2b** as the only isolable product, free imine, mp. 104-105° (hydrochloride, mp. 243-244°).

Anal. Calcd for $C_{22}H_{21}N$: C, 88.25; H, 7.07; N, 4.68. Found: C, 88.03; H, 7.13; N, 4.60

Dimethylmesitylacetonitrile (1f) with 3 equiv. of PhMgBr and refluxing 3 hrs in ether gave the addition product **2f** in 40% yield, bp. 218-220°/16 mm, mp. 68-70° (petroleum ether); hydrochloride mp. 254-255°.

Anal. Calcd for $C_{19}H_{23}N$: C, 85.99; H, 8.73; N, 5.28. Found: C, 85.80; H, 8.85; N, 5.17

The nitrile with a three-fold excess of methyllithium in refluxing ether gave a 50% yields of addition product **2f**, bp. 155°/16 mm, (hydrochloride mp. 176-180°).

Anal. Calcd for $C_{14}H_{21}N$: C, 82.70; H, 10.41; N, 6.89. Found: C, 82.42; H, 10.42; N, 6.62

Reaction of **1f** with isobutylmagnesium chloride in refluxing ether for 6 hrs gave only recovered starting material.

Pivalonitrile (1g) with a three-fold excess PhMgBr at 90° for 6.5 hrs gave a 63% yield of addition product **2g**, (hydrochloride, mp. 200-225°).

2,6-Dichlorobenzonitrile was refluxed with a three-fold excess PhMgBr in ether for 6 hrs and gave a 70% yield of the ketimine, mp. 68.5-69.5° (petroleum ether), hydrochloride mp. 250-252° and 4% *m*-dichlorobenzene, bp. 172°.[6]

Ketones.- The hydrolysis to the compounds in Table 2 was accomplished in aqueous dioxane/HCl.[2] The reflux time was typically 3-6 hrs and the yields were around 80%. Longer reaction times were required for the mesityl compounds **3f** (2 days) and **3f'** (3 days) for comparable yields. 2,6-Dichlorobenzophenone was obtained from its ketimine in only 25% yield after 3 days under reflux.

Compound 3b

Anal. $C_{22}H_{20}O$: C, 87.96; H, 6.71. Found: C, 88.06; H, 7.03

Compound 3c

Anal. $C_{24}H_{24}O$: C, 87.76; H, 7.37. Found: C, 88.02; H, 7.35

Compound 3d

Anal. $C_{25}H_{26}O$: C, 87.67; H, 7.66. Found: C, 87.61; H, 7.53

Compound 3e

Anal. $C_{23}H_{22}O$: C, 87.90; H, 7.01. Found: C, 87.81; H, 7.09

Compound 3f

Anal. $C_{19}H_{22}O$: C, 85.73; H, 8.33. Found: C, 85.81; H, 8.45

Compound 3f'

Anal. $C_{14}H_{20}O$: C, 82.32; H, 9.87. Found: C, 82.03; H, 9.71

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9. During one run of this reaction, a stopper became dislodged and the unattended reaction proceeded at elevated temperatures, possibly 180-190°, for several hours and gave some biphenyl, a trace of benzophenone and an 80% yield of 1,1-diphenylpentane (**4c**), bp. 112-118°/1 mm, identical with an authentic sample.[8]

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