

A NOVEL SYNTHESIS OF NITRILES FROM SECONDARY AMIDES

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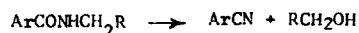
The von Braun reaction (1) in which an N-alkyl amide is converted into an alkyl halide may be used, in some cases, for the preparation of nitriles. No other useful method for the conversion of secondary amides into nitriles has been reported.

We wish to report the transformation of secondary amides RCONHR' into cyanides RCN by chlorotris(triphenylphosphine)rhodium, $\text{RhCl}(\text{PPh}_3)_3$ (2). As an example, a mixture of 4.3 g of N-benzylbenzamide and 225 mg of the rhodium complex was heated for 2 min at 285° and then for 6 hr at 250°. The reaction mixture was distilled under reduced pressure (20 mm) and the distillate separated by vpc (on 10% XE-60 on Chromosorp W) to yield 1.89 g (90%) of benzonitrile and 0.66 g of toluene, together with small quantities of bibenzyl and water.

The reaction could be carried out (in somewhat lower yield) in a high-boiling solvent. N-Benzylbenzamide gives in boiling α -chloronaphthalene, e.g., 62% yield of benzonitrile.

Other results are listed in Table I.

The reaction can be formulated as a simple elimination reaction of a primary alcohol only if the substituent at the nitrogen is alkyl:



N-Benzyl-(or substituted benzyl-) arylamides give both the nitriles derived formally from the acid residue Ar and from the N-benzyl group (exps. 1-4, 6-8, 13, 14). In exp. 4, the nitrile generated from the benzyl group forms an even higher yield than that derived from the acid part of the molecule. 1,3-Shift of the hydrogen in the imidoyl form of the amide,

$\text{Ar}-\text{C}(\text{OH})=\text{N}-\text{CH}_2-\text{Ar}' \rightleftharpoons \text{Ar}-\text{CH}(\text{OH})-\text{N}=\text{CH}-\text{Ar}'$, may be involved in this process and could be catalyzed by $\text{RhCl}(\text{PPh}_3)_3$ (3). Steric hindrance seems to interfere with this isomerization, if one can judge from one example (exp. 1).

In addition to nitriles and water, hydrocarbons are formed in relatively small quantities. In exp. 3, e.g., toluene, *m*-xylene and *p*-chlorotoluene were isolated. These compounds may result,

TABLE I. Conversion of Secondary Amides into Nitriles by $\text{RhCl}(\text{PPh}_3)_3$
(0.02 mole amide, 2.5×10^{-4} mole rhodium complex, 6-7 hr at 250°)

No.	Amide	Nitriles formed (yield, %)
1	N-Benzyl- <u>o</u> -toluamide ^(a)	<u>o</u> -tolunitrile (77); benzonitrile (6)
2	N-Benzyl- <u>m</u> -toluamide	<u>m</u> -tolunitrile (50); benzonitrile (26)
3	N-(<u>p</u> -Chlorobenzyl)- <u>m</u> -toluamide ^(b)	<u>m</u> -tolunitrile (72); benzonitrile (25); <u>p</u> -chlorobenzonitrile (traces)
4	N-(<u>p</u> -Methylbenzyl)- <u>m</u> -toluamide	<u>m</u> -tolunitrile (7.5); <u>p</u> -tolunitrile (61)
5	N-Ethyl- <u>p</u> -toluamide	<u>p</u> -tolunitrile (72)
6	N-Benzyl- <u>m</u> -fluorobenzamide ^(c)	<u>m</u> -fluorobenzonitrile (45); benzonitrile (38)
7	N-Benzyl- <u>m</u> -chlorobenzamide	<u>m</u> -chlorobenzonitrile (35); benzonitrile (25)
8	N-Benzyl- <u>p</u> -chlorobenzamide	<u>p</u> -chlorobenzonitrile (31); benzonitrile (61)
9	N-Ethyl- <u>p</u> -chlorobenzamide	<u>p</u> -chlorobenzonitrile (25); benzonitrile (58)
10	N-Methyl- <u>p</u> -bromobenzamide ^(d)	<u>p</u> -bromobenzonitrile (0.7); benzonitrile (69)
11	N-Methyl- <u>p</u> -bromobenzamide ^{(d)(e)}	<u>p</u> -bromobenzonitrile (52); benzonitrile (5); <u>p</u> -chlorobenzonitrile (0.5)
12	N-Methyl- <u>p</u> -phenylbenzamide ^(f)	4-cyanobiphenyl (71)
13	N-Benzyl- α -naphthamide ^(g)	α -naphthonitrile (45); benzonitrile (5)
14	N-(<u>p</u> -Chlorobenzyl)phenylacetamide ^(h)	benzyl cyanide (42); benzonitrile (traces)

(a) Mp $102-103^\circ$ (from EtOH); Calcd for $\text{C}_{15}\text{H}_{15}\text{NO}$: C, 80.0; H, 6.7; N, 6.2. Found: C, 79.8; H, 6.8; N, 6.2. (b) Mp 148° (from EtOH); Calcd for $\text{C}_{15}\text{H}_{14}\text{ClNO}$: C, 69.4; H, 5.4; Cl, 13.7; N, 5.4. Found: C, 69.1; H, 5.7; Cl, 13.8; N, 5.5. (c) Mp $84-85^\circ$ (from EtOH); Calcd for $\text{C}_{14}\text{H}_{12}\text{FNO}$: C, 73.4; H, 5.2; F, 8.3; N, 6.1. Found: C, 73.6; H, 5.3; F, 8.0; N, 6.2. (d) Mp 162° (from EtOH); Calcd for $\text{C}_8\text{H}_8\text{BrNO}$: C, 44.9; H, 5.7; Br, 37.4; N, 6.5. Found: C, 44.9; H, 3.6; Br, 37.7; N, 6.7. (e) A four-fold amount of purified hexachlorobenzene was used as solvent. (f) Mp 168.5° (from EtOH); Calcd for $\text{C}_{14}\text{H}_{13}\text{NO}$: C, 79.6; H, 6.2; N, 6.6. Found: C, 80.0; H, 6.1; N, 6.6. (g) Mp $118-119^\circ$ (from EtOH); Calcd for $\text{C}_{18}\text{H}_{15}\text{NO}$: C, 81.8; H, 5.8. Found: C, 81.5; H, 5.7. (h) Mp $131-132^\circ$ (from EtOH); Calcd for $\text{C}_{15}\text{H}_{14}\text{ClNO}$: C, 69.4; H, 5.4; Cl, 13.7. Found: C, 69.3; H, 5.1; Cl, 13.7.

TABLE II. Conversion of Primary Amides into Nitriles in the Presence of $\text{RhCl}(\text{PPh}_3)_3$

Amide	Nitriles (yield, %)
Benzamide	benzonitrile (70)
<u>o</u> -Toluamide	<u>o</u> -tolunitrile (46)
<u>m</u> -Toluamide	<u>m</u> -tolunitrile (81)
<u>m</u> -Chlorobenzamide	<u>m</u> -chlorobenzonitrile (72); benzonitrile (6)
<u>p</u> -Chlorobenzamide	<u>p</u> -chlorobenzonitrile (71); benzonitrile (13)
α -Naphthamide	α -naphthonitrile (66)

at least in part, from the benzyl alcohols corresponding to N-benzyl groups in the presence of the rhodium catalyst. Traces of benzyl alcohol were, in fact, isolated in exp. 13.

The catalytic reaction is complicated in chlorine and in particular bromine containing compounds: the halogen atoms are partially abstracted both from the benzyl groups (exps. 13, 14) and from the substituted benzoyl moiety. In exps. 9 and 10 the dehalogenated benzonitrile is even the major product (4). The extent of this halogen abstraction can be reduced by dilution of the reaction mixture with hexachlorobenzene (exp. 12). The process, we assume, proceeds via a free radical mechanism. This assumption is supported by the formation of small quantities of bibenzyl from the N-benzylamides and of p-chlorobenzonitrile (traces) from N-methyl-p-bromobenzamide in hexachlorobenzene.

Experiment 14 indicates that the reaction is not limited to aromatic secondary amides.

Unlike in the von Braun reaction, N,N-dialkyl amides cannot be converted into nitriles, nor do N-aryl amides give positive results. Primary amides are smoothly converted to the corresponding nitriles when heated with or distilled over catalytic amounts of the rhodium complex (Table II). Here, too, elimination of aromatic chlorine atoms (as hydrogen chloride) is observed, but to a smaller extent than with secondary amides.

Chlorotris(triphenylphosphine)rhodium as such is not the true catalyst in this reaction. In fact, no nitrile was formed at all when the reaction mixture was heated in an atmosphere of argon.

If, however, the rhodium complex (in benzene) was treated with air or oxygen for a few minutes or converted into chlorobis(triphenylphosphine)rhodium dimer (5), the amide \rightarrow nitrile conversion could be carried out under argon without difficulty. On the other hand, when oxygen was passed continuously through the reaction mixture, the yield of nitrile was reduced significantly.

A study of the scope and mechanism of the new reaction, using various organometallic catalysts, is now in hand.

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