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MIXED CARBONYL COUPLING INDUCED BY AQUEOUS TITANIUM TRICHLORIDE. SOME COMMENTS ON THE MECHANISM.

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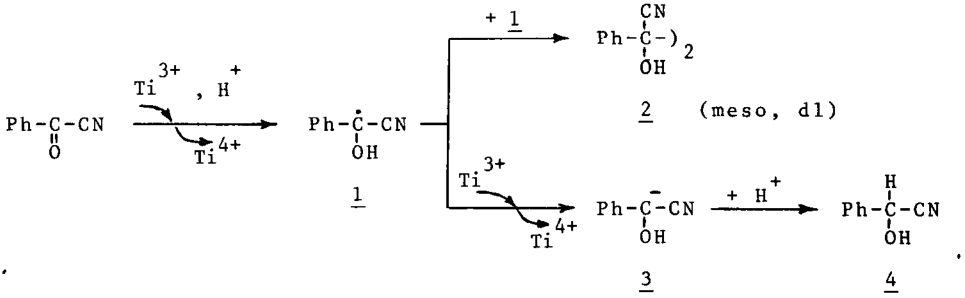
Summary : Aqueous titanium trichloride promotes reductive dimerization of benzoylcyanide in acetic acid and mixed pinacol reaction in acetone medium. A mechanism is proposed to account for this.

We have recently reported[1,2] that aqueous titanium trichloride promotes reductive decyanation and dehalogenation of cyano- and halopyridines to pyridine by two electron transfer. Besides, we have found[2] that this reducing agent easily couples pyridinealdehydes and -ketones to the corresponding symmetric pinacols in very good yields by one electron transfer.

The study of the reduction of benzoylcyanide by aqueous titanium trichloride was undertaken with the aim to determine whether simple dimerization (as for pyridine aldehydes and ketones) or decyanation (as for cyanopyridines) would occur.

Dropwise addition of a 15% aqueous titanium trichloride solution (20 mmol) to a benzoylcyanide solution (10 mmol) in acetic acid (10 ml) at room temperature under nitrogen atmosphere resulted in partial discharge of the dark blue color of titanium(III) and formation of a white suspension after 1 hr. Extractive work up yielded benzyldicyanohydrin 2, mandelonitrile 4, along with unreacted substrate and benzoic acid (formed by hydrolysis of the substrate in acidic medium) according to Scheme 1.



In this process there is produced both the radical 1 by one electron uptake and the anion 3 by two electron uptake from titanium(III).

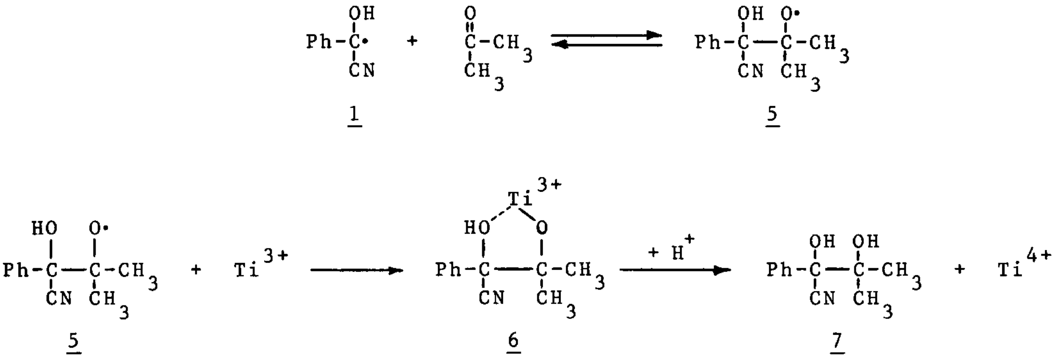
Radical 1 (75% yield) dimerizes to compound 2[3] while the anion 3 is converted to mandelonitrile 4 (6% yield) by hydrogen ion abstraction from the solvent.

By carrying out the reaction in acetone, instead of acetic acid, 2-methyl-3-phenyl-3-cyano-2,3-propanediol 7 was surprisingly formed along with compounds 2 and 4. Screening the data of Table it should be remarked that yields of adduct 7 increase with the increase of both the quantity of acetone used and the molar ratio $TiCl_3/PhCOCN$ while the relative amount of adduct 7 and dimer 2 depends on the quantity of acetone only.

The stoichiometry of the reaction, determined by back-titration of Ti(III) excess, is in accord with a two electron transfer per mole of adduct 7 formed.

We exclude that the mixed pinacol reaction of acetone with benzoylcyanide is a radical coupling process because the reduction potential of benzoylcyanide is ca. 0.9 Volt less negative than that of acetone[4], and a mild reducing agent such as Titanium(III) is able to reduce only carbonyl groups bearing strong electron-withdrawing substituents[2].

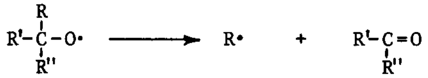
An alternate mechanistic hypothesis consistent with our data is depicted in Scheme 2.



1 5 1)

5 6 7 2)

The radical addition of 1 to the carbon atom of the carbonyl group of acetone is a reversible process. In fact, Eq. 1) is at least formally the reverse of the well demonstrated decomposition of the t-alkoxyl radical[5]:



$$R'-\underset{R''}{\overset{R}{C}}-O\cdot \longrightarrow R\cdot + R'-\underset{R''}{C}=O$$

Table : Reaction of PhCOCN with aqueous $TiCl_3$ in the presence of CH_3COCH_3 or CH_3COOH. Products (moles %) distribution.

$TiCl_3$/PhCOCN molar ratio	Solvent	Dimer 2[a)]	Adduct 7[b)]	Mandelonitrile 4	7/2 molar ratio	Yield[c)] based on PhCOCN	Yield[d)] based on $TiCl_3$
1	10 ml CH_3COCH_3	15.5	17.4	1.0	1.5	50	68
1	40 " "	9.0	24.0	1.0	2.7	43	68
1	60 " "	4.4	26.4	1.5	6.0	38	65
1.5	60 " "	6.6	37.0	2.5	5.6	53	62
2	60 " "	9.3	54.0	2.8	5.8	75	66
2	40 " "	12.2	34.0	2.4	2.8	60	50
1	10 ml CH_3COOH	25.5	-	5.0	-	56	61
2	10 " "	37.5	-	6.0	-	81	43

a) Dimer 2 was directly recovered by filtration from the reaction medium. After recrystallization from ether it melted at 175-6 C. (decomp.)[7]. Spectroscopic data: ^1H N.m.r. (CD_3COCD_3, 90 MHz, TMS as internal standard), δ(ppm) 7.1 (2H, 2OH, s, exchanged with D_2O), 8.5 (10H, Ar-H, m); I.r. (nujol), ν_{max} 3360 (OH, s) and 2250 (CN, w)[7]; M.s. (70 eV), m/e 210 (M^+ -2HCN), 133,105 (major peak), 77, 27.

b) Adduct 7 after recrystallization from ether/light petroleum (1/2) melted at 105-6 C.(uncorr.). Spectroscopic data: ^1H N.m.r. ($CDCl_3$, 90 MHz, TMS as internal standard), δ(ppm) 1.1 (3H, CH_3, s), 1.4 (3H, CH_3, s), 2.7 (1H, OH, s, exchanged with D_2O), 4.3 (1H, OH, s, exchanged with D_2O), 7.3-7.7 (5H, Ar-H, m); I.r. (nujol), ν_{max} 3400 (OH, s) and 2240 (CN, m); M.s. (70 eV), m/e 164 (M^+-HCN), 106, 105, 77, 59 (major peak), and 27.

c) Overall yield (moles %) is referred to starting benzoylcyanide (10 mmol) which is recovered either as unreacted or as benzoic acid. Yields of products 2, 4, and 7, based on starting benzoylcyanide, have been determined by G.l.c. analysis with the internal standard method for comparison with authentic samples.

d) The excess of reducing agent, estimated by back-titration against standard $FeCl_3$ sol. using KSCN sol. as indicator, is in agreement with the theoretical yield based on starting $TiCl_3$.

Therefore, the mechanism of Scheme 2 seems reasonable only if the formation of a Ti(III)-complex 6 is invoked. Formation of 6 would both shift the equilibrium of Eq. 1) to the right and favour the reduction of alkoxyl radical 5 to the corresponding anion. Besides, knowing the ability of Ti(III) to complex electron-donor groups[6] such as ketones and alcohols, an initial complexation of Ti(III) with acetone cannot be discarded. This further complexing effect, enhancing the electrophilicity of the carbonyl group, makes easier tha addition of radical 1 to acetone.

To the best of our knowledge this is the first time that the addition of a free carbon radical to acetone is reported.

We wish to reserve a more detailed discussion of our studies for a full paper to be published later.

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