PINACOLIC COUPLING OF AROMATIC ALDEHYDES AND KETONES PROMOTED BY AQUEOUS TITANIUM TRICHLORIDE IN BASIC MEDIA.

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Summary.Aromatic aldehydes and ketones, which are not effected by aqueous titanium trichloride in acidic media, undergo rapid one-electron reduction to pinacols in basic media under very simple experimental conditions. The increase in the reducing power of the redox system with increasing the pH is discussed, and the stereoselectivity observed is shown in terms of Ti(IV) bridging control.

In these last years three separate research groups observed that low-valent titanium species, Ti(0) and Ti(II), prepared by reduction of anhydrous TiCl₃ with either LiAlH $_{\lambda}^{1}$ or reactive metals²⁻⁴, reductively couple aldehydes and ketones to olefins, diols being the reaction intermediates. For some time, now, we have been carrying out investigations regarding the species Ti(III), and have recently shown⁵ that aqueous $TiCl_{2}$, certainly a milder reducing agent (E[°]= -0.1 V), effectively couples, in acidic media (pH= 1), carbonyl compounds activated towards reduction by an electron-withdrawing group such as -CN, -COOR, -COOH, and 2- or 4-pyridyl residues.

We wish to report herein our preliminary studies and results on the reducing power of aqueous $TiCl_{q}$ in basic media (pH= 10-12) which considerably extend the scope and effectiveness of the pinacolic coupling reaction promoted by the Ti(III) species.

Simple aromatic aldehydes and ketones (benzophenone, acetophenone, and benzaldehyde) are recovered unchanged when allowed to react with $TiCl_{1}$ in aqueous acidic solution, but undergo rapid one-electron reduction with formation of bimolecular products in alkaline aqueous solution, according to the stoichiometry of equation in Scheme 1.

$$2 \text{ Ph-}_{C}^{R} + 2 \text{ Ti}^{3+} + 6 \text{ OH}^{-} \longrightarrow \text{Ph-}_{C}^{R} + 2 \text{ TiO}_{2} + 2 \text{ H}_{2} \text{O}_{OH} + 2 \text{ H}_{2} \text{O}_{OH}$$

R= H, CH₂, Ph Scheme 1 The results obtained are given in Table.

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Substrate	Dimer (%) ^{a)}	Alcohol (%) ^{a)}	Overall yield (%) ^{b)}	Ratio d1/meso
Benzophenone	53	47	95	-
Acetophenone	87	13	95	2.7 ^{c)}
Benzaldehyde	88	12	quantitative	1.3 ^{d)}
3-acety1pyridine	83	17	73	_ e)

m., 1, 1

- a) determined by ¹H N.M.R. spectroscopy, except for benzophenone (column chromatography, silica gel, eluant hexane/ethylacetate : 7/3);
- b) based on the starting substrate (isolated yield);
- c) determined by a height comparison of the two methyl proton peaks⁶;
- d) determined by a height comparison of the two benzylic proton peaks';
- e) the relative height of the two methyl proton peaks gave a ratio of 2 but any attempt to separate the two isomers, and therefore to assign their configurations, was unsuccessful.

The reducing power of Ti³⁺/Ti⁴⁺ system is strongly pH dependent according to the equation⁸: E= 0.029 - 0.236 pH - 0.0591 log $[Ti^{3+}]$

for the reaction in which insoluble TiO₂ is formed.

The increase in the reducing power by increasing the pH is therefore required to make the reduction of the substrates in Table thermodynamically possible. The behaviour of acetylpyridine isomers is rather revealing: the 2- and 4- isomers are effectively coupled by aqueous TiCl₃ in acidic media ⁵ while the 3- isomer is dimerized to the corresponding pinacol only in basic media in accord with the redox potentials which show the 3- isomer to be the least reducible. The experimental conditions are very simple. All the reactions were carried out by dropwise addition of 15% aqueous acidic TiCl, solution to the substrate in MeOH and enough 30% NaOH solution to keep the pH= 10-12 at the end of addition, and performed under N_2 at room temperature. A sharp colour change from white to dark-blue indicated the end of the reactions which were completed within few minutes. Usual workup afforded the products of Table which displayed satisfactory spectral data (¹H N.M.R., M.S., and I.R.). The data reported deserve some more comments. The high yield of benzhydrol (47%) is due to subsequent cleavage of benzophenone pinacol, in alkaline media, to benzhydrol and benzophenone: this cleavage proceeds rapidly enough to be of both synthetic¹⁰ and analytical¹¹ value. The successful pinacolization (53% yield) here reported depends on the very short reaction time, not more than 5 min. The acetophenone and benzaldehyde pinacols are not interconverted and are stable under the alkaline reaction conditions.

The reduction of acetophenone and benzaldehyde shows some stereoselectivity:

- the ratio dl/meso of 2.7 for acetophenone is similar to those observed in its photochemical and electrochemical ¹³ bimolecular reduction in alkaline solution;
- the ratio dl/meso of 1.3 for benzaldehyde is somewhat higher than that obtained by its electrodimerization, which is close to 1⁷.

The hydrodimerization of aromatic carbonyl compounds in alkaline media occurs^{12,14,15} via coupling of the radical anion (I) and the neutral ketyl radical (II) according to Scheme 2.

Scheme 2

The dl/meso ratio obtained in the electrochemical route was interpreted in terms of the influence of interspecies hydrogen bonding between (I) and (II) at the time of coupling leading to higher proportion of the dl isomer^{7,13}. The influence of interspecies hydrogen bonding in solvents capable of forming strong hydrogen bonds, e.g. C_2H_5OH , H_2O , was questioned and alternate mechanisms were proposed involving absorption of reactants at mercury cathodes¹⁶ or surface orientation¹⁵ of the radical anions about to dimerize in basic media.

In our reaction, the electron transfer step may involve an initial coordination between the carbonyl group and the Ti(III) species^{17,20} according to Scheme 3.

Ph-C=0---Ti³⁺
$$\longrightarrow$$
 Ph-C-0-Ti⁴⁺ $\xrightarrow{+ H^+}$ (II) ; (III) + (II) $\xrightarrow{+ H^+}$ dimer
R (III)

Scheme 3

Because of the great affinity of titanium species for oxygen, radical (II), in the dimerization step, will be most likely oriented to maximize the electrostatic interaction with the titanium ion of (III), or with the titanium ion of a contact ion pair readily formed between (I) and Ti⁴⁺. There are three possibilities (1, 2, and 3 in Scheme 4) for the coupling step involving bridging by Ti(IV) species. Of these, 2 will be more favoured since it minimizes interaction between the aromatic rings, and will explain the clear preference for the formation of the dl isomers for both acetophenone and benzaldehyde.

In the absence of Ti(IV) bridging, the meso configuration will be much more important since $\frac{4}{2}$ is the only possible conformation that minimizes interaction between like groups; besides it is



known from the literature^{18,19} that radicals, for which steric and polar effects appear to be important, lead predominantly to the meso dimers.

A very recent report²⁰ on the mechanism of the Ti(0)-induced coupling of ketones supports our interpretation, in fact E.S.R. measurements show the benzophenone anion radical bonded to titanium.

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