POLAR EFFECTS IN FREE-RADICAL REACTIONS. A NEW TYPE OF HOMOLYTIC AROMATIC ALKYLATION BY SILVER CATALYZED OXIDATION OF ACETONE BY PEROXYDISULPHATE IN THE PRESENCE OF OLEFINS.

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<u>Abstract</u>. Silver catalyzed peroxydisulphate oxidation of acetone in the presence of olefins and protonated heteroaromatic bases leads to compound I via addition of acetonyl radical to the olefin and scavenging of the resulting radical adduct by the aromatic base.

Homolytic alkylation in acidic medium is a significant reaction of heteroaromatic bases¹. Polar effects, related to the nucleophilic character of the alkyl radical, and the electrondeficiency of the aromatic substrate are considered the main cause of the synthetic interest^{1,2}.

The addition of electrophilic radicals to olefins provides a general and versatile source of nucleophilic radicals. Thus, the alkylation according to the sequence :

$$S \longrightarrow X'$$

$$x^{+} \downarrow C = C \swarrow x^{-1} \downarrow C^{-1}$$

$$x^{-1} \downarrow -1 \downarrow C + ArH_{2}^{+} \longrightarrow x^{-1} \downarrow -1 \downarrow C^{-1}$$

can involve, in principle, a wide variety of electrophilic radicals (X'), which for polar reasons do not add to the aromatic substrate but easily add to the olefin.

We now report a new simple example of homolytic alkylation which can be included in this general scheme. When acetone is oxidized by peroxydisulphate under Ag^+ catalysis in the presence of olefins and protonated heteroaromatic bases, selective alkylation occurs to give compound I in high yield on converted base.

$$\operatorname{ArH}_2^+$$
 + $\operatorname{CH}_3\operatorname{COCH}_3$ + $\operatorname{CH}_2=\operatorname{CH-R} \xrightarrow{\operatorname{Ag}^+/\operatorname{S}_2\operatorname{O}_8^{2^-}}$
Ar- $\operatorname{CH-CH}_2\operatorname{CH}_2\operatorname{COCH}_3$
I

Acetyl (Ar-COCH₃, II) and β -hydroxyalkyl derivatives (Ar-CH-CH₂OH, III) were detected in minor amounts.

Compound I was not observed in the absence of Ag⁺ catalysis under similar conditions.

A typical experiment was as follows : a solution of 1-octene (3.02 ml, 20 mmol) in acetone (80 ml) was added to a mixture of 4-methylquinoline (2.64 g, 20 mmol), conc. H_2SO_4 (1.1 ml, 20 mmol) and $AgNO_3$ (0.72 g, 4 mmol) in water (60 ml). The mixture was heated at reflux and a solution of $Na_2S_2O_8$ (7.2 g, 30 mmol) in water (40 ml) was added in 1 h. The reaction was run for 4 h, then distilled until 50°C. The residue was added to a mixture of 10% NH₃ (60 ml) and CH_2Cl_2 (50 ml) under stirring. The water was separated and extracted with CH_2Cl_2 (2 x 30 ml). The combined organic extracts were washed with water, dried and concentrated. The residue was chromatographed on SiO_2 (hexane : ethyl acetate 8:2) to give 5-[2-(4-methylquinolyl)] undecan-2-one (I) (2.8 g, 45% yield): ¹H-NMR (CDCl₃) : 7.4-8.2 (4H, m, Ar), 7.12 (1H, s, H₃), 2.98 (quintet, 1H, CH-), 2.63 (3H, s, Ar-CH₃), 1.7-2.4 (4H, m, CH₂CH₂CO-), 1.96 (3H, s, COCH₃), 1.1-1.4 (10H, m, aliph.), 1.78 (3H, t, CH₃); IR (liquid film) : 1715 cm⁻¹ (C=O); M.S. m/e : 311 (M⁺⁺, 5), 310 (6),309 (4), 268 (55), 254 (80), 240 (81), 196 (57),182 (70), 170 (100), 157 (50), and 143 (41).

Quantitative g.l.c. analysis of the reaction residue gave : 4-methylquinoline (60% conversion) undecan-2-one (6% yield), I (80% yield on converted base), 2-acetyl-4-methylquinoline (II) (5%), 2-[2-(4-methylquinolyl)]octan-1-ol (III) (14%).

Besides the synthetic interest, the reaction shows interesting mechanistic features. Since the reaction occurs only in the presence of silver ions, we suggest that Ag^{2+} is involved in the oxidation of acetone according to the following sequence, which determine a catalytic cycle.

$$s_2 o_8^{2^-} + 2 Ag^+ \longrightarrow 2 so_4^{2^-} + 2 Ag^{2^+}$$

 $cH_3 cocH_3 + Ag^{2^+} \longrightarrow cH_3 cocH_2 + Ag^+ + H^+$

On the basis of the known specific interactions of Ag^{2+} ions with alcohols³ or carboxylic acids⁴,

$$R-OH + Ag^{2+} \longrightarrow R-O' + Ag^{+} + H^{+}$$

$$R-COOH + Ag^{2+} \longrightarrow R-COO' + Ag^{+} + H^{+}$$

we suggest that the enol form of acetone is involved in the oxidation.

$$CH_3 - C = CH_2 + Ag^{2+} \longrightarrow Ag^{+} + H^{+} + CH_3 - C = CH_2 \leftrightarrow CH_3 - C - CH_2$$

Acetonyl radicals could be alternatively formed by oxidation of the enol form by electrontransfer with initial formation of a radical cation.

$$CH_3 \xrightarrow{-C=CH_2} + Ag^{2+} \xrightarrow{-} Ag^{+} + CH_3 \xrightarrow{-C-CH_2} \xrightarrow{-} CH_3 \xrightarrow{-C-CH_2} \xrightarrow{-} CH_3 \xrightarrow{-} CH$$

The electrophilic properties of the acetonyl radical (X $^{\circ}$) determine its easy addition to the olefin, as previously observed in the oxidation of ketones by transition metal salts in high oxidation state⁵

$$ch_3 coch_2$$
 + $ch_2 = ch - c_6 h_{13}$ \longrightarrow $ch_3 coch_2 ch_2 ch - c_6 h_{13}$

The nucleophilic alkyl radical adduct $(X- \overset{\downarrow}{C}-\overset{\downarrow}{C}-\overset{\downarrow}{C})$ attacks the heteroaromatic ring efficiently giving rise by rearomatization to the compound I.



The β -hydroxyalkyl derivative (II) is formed by competitive electron-trasfer oxidation of the olefin according to a process previously reported by us⁶.

$$c = c \left(\xrightarrow{Ag^{2+}}_{(\text{or so}_4^{-})} \right) c - c \left(\xrightarrow{H_2^0}_{H^+} \right) c - c \left(\xrightarrow{H_2^0}_{OH} \right) c - c \left(\xrightarrow{ArH_2^+}_{OH} \right) Ar - c \left(\xrightarrow{H_2^-}_{OH} \right) Ar -$$

Actually, by using olefins, such as cyclohexene (I.P. = 8.94 eV), with lower ionization potential than 1-octene (I.P. = 9.46), the yield of I decreases (26% on converted base) and compound II increases (69% on converted base).

The small amounts of acetyl derivatives (III) observed can be related to the formation of nucleophilic acetyl radicals, which are trapped by the heteroaromatic base. They probably arise from the oxidation of α -hydroxyacetone (a side-product of the oxidation), according to a route recently reported⁷.

$$CH_{3}-C-CH_{3} \xrightarrow{S_{2}O_{8}^{2^{-}}/Ag^{+}} CH_{3}-CO-CH_{2}OH$$

$$CH_{3}COCH_{2}OH + Ag^{2^{+}} \xrightarrow{Ag^{+}} Ag^{+} + H^{+} + CH_{3}COCH_{2}O' \longrightarrow CH_{3}CO' + CH_{2}O$$

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