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HOMOLYTIC AROMATIC ACETYLATION. A NEW SUBSTITUTION REACTION OF ARENEDIAZONIUM SALTS

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Summary. The homolytic decomposition of arenediazonium salts induced by thermal, photochemical or redox (iron(II) salts or copper) sources in the presence of biacetyl gives substituted acetophenones with complete positional selectivity by a free-radical chain or a redox chain process.

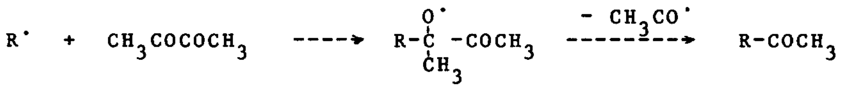
The homolytic replacement of the diazonium group (dediazoniation) by a variety of functional groups (i.e. hydrogen, halogen, pseudohalogen, aromatic, matals, sulfur and arsenic containing groups, etc.) is a well established reaction type of arenediazonium salts[1]. In all these substitutions the basic interaction is the one-equivalent reduction of arenediazonium ion by nucleophiles or reducing agents which affords aryl radicals via the intermediate unstable[2] aryldiazenyl radicals (eq. 1)

$$ArN_2^+ \xrightarrow{+e} ArN_2^{\cdot} \xrightarrow{-N_2} Ar^{\cdot} \qquad 1)$$

The reaction of the aryl radical with an appropriate substrate gives the final dediazoniation product, often in a chain process (i.e. Sandmeyer, Meerwein reactions, etc.).

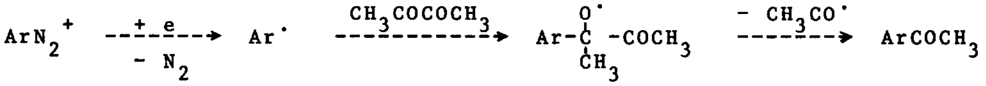
There is some analogy between the reactions given by aryl radicals and those of alkyl radicals, despite their different reactivity and sensibility to steric, electronic and polar effects[3]. So, most of the functionalizations obtained in dediazoniation reactions in the aromatic series have a counterpart in the aliphatic series in reactions which use a suitable source of alkyl radicals.

The last ones are known to give an acetylation reaction by addition-elimination with biacetyl (eq. 2), using thermal[4], photochemical[4] and redox[5] sources.



$$R^{\bullet} + CH_3COCOCH_3 \longrightarrow R-\underset{CH_3}{\overset{O^{\bullet}}{C}}-COCH_3 \xrightarrow{-\,CH_3CO^{\bullet}} R-COCH_3 \qquad 2)$$

Now, we have found that aryl radicals arising from photochemical, thermal and redox decomposition of arenediazonium tetrafluoborates in the presence of biacetyl give an analogous acetylation reaction (eq. 3), which, besides the mechanistic interest, can have some synthetic potentiality (see Table).



$$ArN_2^{+} \xrightarrow[-\,N_2]{+\,e} Ar^{\bullet} \xrightarrow{CH_3COCOCH_3} Ar-\underset{CH_3}{\overset{O^{\bullet}}{C}}-COCH_3 \xrightarrow{-\,CH_3CO^{\bullet}} ArCOCH_3 \qquad 3)$$

Among the various reducing agents tested, powdered copper in DMSO, acetone or water and ferrous sulfate in DMSO[6] were found to be effective in promoting the reaction. Dimethyl sulfoxide was the preferred solvent owing to its high solvent properties for both biacetyl and organic or inorganic salts, its low reactivity in hydrogen atom abstraction by aryl radicals[7] and its stabilizing effect towards ionic decomposition of arenediazonium salts.[8]

A representative experimental procedure is as follows. copper powder (0.190 g, 3 mmol) was added to a magnetically stirred solution of 4-methoxybenzenediazonium tetrafluoborate (2.21 g, 10 mmol) in biacetyl (10 ml) and DMSO (5 ml) at 10°C under N_2. The reaction mixture was kept 60 min. at 10°C and 2 hrs at 40°C. The biacetyl was distilled at 100 mmHg. Flash chromatography[9] of the residue (pentane eluent) efforded 4-methoxyacetophenone (m.p. 38°C, 98% purity by g.l.c. (glass column (2m) packed with SP 2250 3% on Chromosorb AW-DMCS, iso. 130°C), 1.02 g, 68% yield).

The data in the Table indicate that the reaction is general with yields increasing at high biacetyl concentration. The photochemical and redox experiments indicate that a free-radical chain is sustained by the following step (eq. 4)

$$CH_3CO^{\bullet} + ArN_2^{+} \xrightarrow{k_1} CH_3CO^{+} + ArN_2^{\bullet} \xrightarrow{-\,N_2} Ar^{\bullet} \qquad 4)$$

TABLE - Decomposition of $X\text{-}C_6H_4\text{-}N_2^+\ BF_4^-$ in the presence of biacetyl

X (mmol)	biacetyl (mmol)	solvent (ml)	Initiator (mmol)	X-Acetophenone (Yield %)
4-OCH_3 (10)	100	DMSO (5)	Cu (3)	68
4-OCH_3 (1)	10	Acetone(1.5)	Cu (0.3)	64
4-OCH_3 (1)	10	H_2O (10)	Cu (0.3)	55
4-OCH_3 (1)	10	DMSO(0.5)	$FeSO_4$ $7H_2O$(1)	49
4-OCH_3 (1)	50	DMSO(0.5)	$FeSO_4$ $7H_2O$(1)	65
4-OCH_3 (3)	70	DMSO(1.5)	hν*	70
4-OCH_3 (3)	70	DMSO(1.5)	Δ**	53
H (1)	10	DMSO(2.5)	Cu (1)	35
H (1)	10	DMSO(2.5)	$FeSO_4$ $7H_2O$(1)	33
4-Cl (1)	10	DMSO (0.3)	"	25
4-Cl (1)	100	DMSO (0.9)	"	50
3-Cl (1)	10	DMSO (0.9)	"	10
2-Cl (1)	10	DMSO (0.3)	"	23
4-$COCH_3$(1)	10	DMSO (0.7)	"	19
4-NO_2 (1)	10	DMSO (1.5)	"	10
4-CH_3 (1)	10	DMSO (0.5)	"	48

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[*] The irradiation was performed using a Rayonet RPR 100, equipped with 16 low pressure mercury lamps for 3 hrs at room temperature (10% of diazonium salt was present at the end).

[**] The homogeneous solution of arenediazonium salt, biacetyl and DMSO was poured in a thermostated bath at 70°C (± 1) for 2 hrs.

This behaviour is in agreement with our recent results concerning the addition of acyl radicals to arenediazonium ions[6,10].

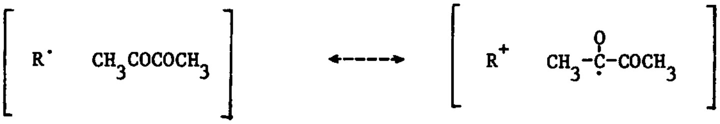
Ferrous salt and copper metal can be used in catalytic amount either because the same free-radical chain is working or because a redox chain, sustained by the steps of eqs. 5 and 6, is present.

$$CH_3CO^{\cdot} + Fe^{3+}(Cu^{2+}) \xrightarrow{k_2} CH_3CO^{+} + Fe^{2+}(Cu^{+}) \qquad 5)$$

$$ArN_2^{+} + Fe^{2+}(Cu^{+}) \longrightarrow Ar^{\cdot} + N_2 + Fe^{3+}(Cu^{2+}) \qquad 6)$$

The relative importance of the two chain processes is strictly related to the values of k_1 and k_2.

Biacetyl appears to be a less effective trap for aryl radicals than for alkyl radicals. This fact, together with the substituent effect (yields increased by electron-releasing groups and decreased by electron-withdrawing groups), suggests that polar effects play a significant role in the interaction of aryl radicals with biacetyl, as previously suggested[5] for alkyl radicals.



$$\left[R^{\cdot} \quad CH_3COCOCH_3 \right] \longleftrightarrow \left[R^{+} \quad CH_3-\overset{O}{\underset{\cdot}{C}}-COCH_3 \right]$$

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