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One-Pot Conversion Of α-Substituted Arylacetaldehydes Into α-Dicarbonyl Compounds

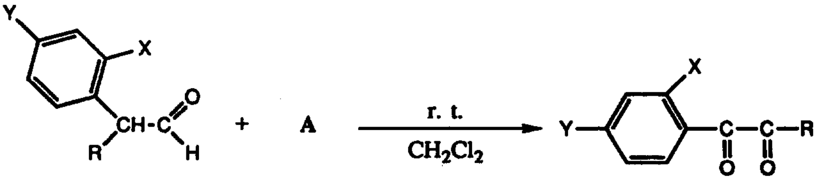
Luigi Lopez ,[a*] *Giuseppe Mele*,[a] *Angelo Nacci*,[a] *Luigino Troisi* [b]

[a] *CNR. Centro "M.I.S.O." Dipartimento di Chimica Università di Bari, via Amendola 173 70126 Bari Italy*
[b] *Laboratorio di Chimica Organica, Dipartimento di Biologia Università di Lecce, via Monteroni 73100 Lecce Italy*

Abstract: α-dicarbonyl compounds **7-12** can be easily prepared by reaction of methylene chloride solutions of several α-substituted arylacetaldehydes **1-6** with a slight excess of tris-(o,p-dibromophenyl) ammoniumyl hexachloro antimonate **A**.

The direct introduction of a ketone α to a carbonyl group is an important functional group transformation which has many applications in natural product synthesis.[1] Many of the existing methods for the synthesis of α-keto carbonyl systems are of limited use due to the rough reaction conditions employed. For example, conventional reagents for oxidizing ketones to α-diketones, such as selenium dioxide[2] or alkyl nitrites in acid or base,[3] often lead to further oxidation or side reactions because of the inherently strong reaction conditions. More indirect methods, such as α-halogenation, or α-oxygenation of the starting ketone followed by further oxidation may be applied to the most simple ketonic systems.[4] Instead, the dye-sensitized photooxygenation of a series of enamino ketones, a general procedure for the synthesis of α-diketones, is limited by the low overall yields of the starting materials.[5] A recent interesting report by Page and co-workers introduces a new procedure for the synthesis of symmetrical and unsymmetrical α-diketones.[6]

In connection with ongoing researches on the thermal-induced generation and evolution of cation radicals from different classes of organic substrates,[7] we disclose here that tris-(o,p-dibromophenyl) ammoniumyl hexachloro antimonate $[(o,p\text{-}Br_2C_6H_3)_3N^{+\cdot}\ SbCl_6^{-}]$ (E^{red} = 1.66 V. vs S.C.E.)[8] **A** is a reagent suited to the conversion of several aldehydes **1-6** into α-diketones **7-12** under mild conditions eq.1



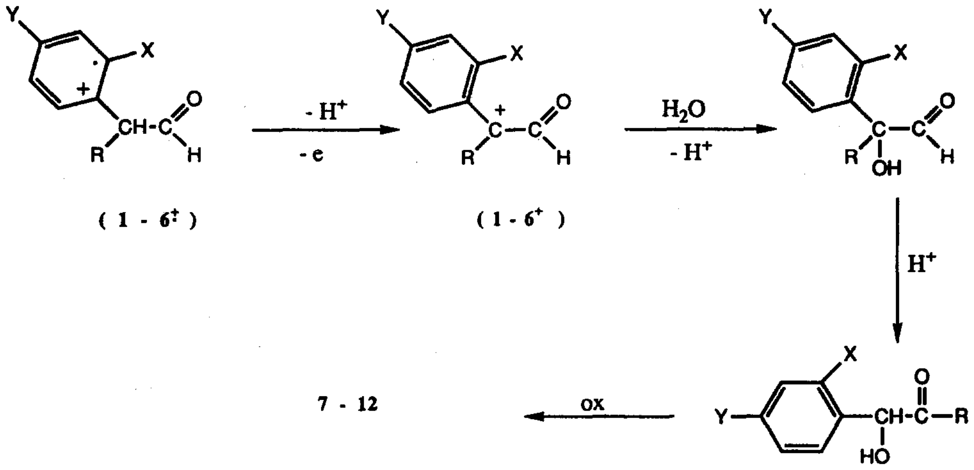
1 - 6 **7 - 12**

1: X,Y = H, R = C_6H_5; **2**: X = H, Y = CH_3, R = 4-$CH_3C_6H_4$; **3**: X = H, Y = OCH_3, R = 4-$CH_3OC_6H_4$;
4: X = H, Y = Cl, R = 4-ClC_6H_4; **5**: X = Cl, Y = H, R = 4-ClC_6H_4; **6**: X, Y = H, R = CH_3

The starting materials, with the exception of 6 (commercial samples from Aldrich Co.) have been synthesized by isomerization of commercial 5a,[9] or synthesized stilbene oxides 1a-4a[10] with borontrifluoride etherate,[13] as well as with catalytic amounts of A, or tris-(p-bromophenyl) ammoniumyl hexachloroantimonate B.[7a,14,15] Typical experimental conditions for the conversion of α-substituted arylacetaldehydes into α-diketones are illustrated in the following procedure for the synthesis of 8. 0.2 mmol, 44.8 mg of 2 are dissolved under stirring in freshly distilled methylene chloride (10 ml), at room temperature under air atmosphere, and then a slight excess of A (0.22 mmol, 235 mg) is added. The intensely green colour of the solution fades within 15 min., and the following gc/ms analysis reveals the formation of a new main product (>90%) together with the corresponding amine. The solvent is removed in vacuo and the reaction product 8, isolated by column chromatography (silica gel, petroleum ether / diethyl ether 95 / 5 v / v), 41 mg (90%) yield, has been fully identified by physical, spectral data and by comparison with a synthesized sample.[17] These experimental results have been confirmed for 1,3-5, affording high yields of the corresponding α-dicarbonyl compounds. However, the conversions of diphenylacetaldehyde 1 and D,L-2-phenylpropionaldehyde 6, into benzil 7 and 1-phenyl-1,2-propanedione 12, also afford not negligible amounts (10%) of chlorine containing derivatives. These reaction products have been characterized by gc/ms spectroscopy as the corresponding α-chloro-diphenylaceldehyde 13 and 2-chloro-2-phenylpropionaldehyde 14.[18]

Despite the neat synthetic outcome, the conversion of aldehydes into α-diketones presents some mechanistic incognita, mainly due to the actual stoichiometry of the process, requiring, on the basis of our experimental observations, more than two equivalents of one electron oxidizing agent (scheme1).

Scheme 1



Photoelectron spectroscopy has revealed that π electrons of the aromatic rings,[19] sentitive to substitution,[20] are easily oxidizable. Thus, the powerful oxidant would induce electron-transfer reactions on substrates 1-6 with the formation of the corresponding amine and cation radicals (1-$6^{+\cdot}$). These latter, by loss of an electron and a proton, would afford carbonium ions, easily trapped by traces of water with formation α-hydroxyacetaldeyde intermediates. The fast acid-catalyzed isomerization into benzoin derivatives, a well known process,[21] followed by subsequent oxidation to benzils would complete the process.[22]

The chemical proofs, accounting for such a mechanism, are the following: (a) the involvement of water in the whole process has been tested carrying out similar reaction on **2** in the presence of trace amounts of 18-oxygen labeled water (20 %), and analyzing the reaction product by gc/ms spectroscopy. The slower reaction (2 h.), the lower conversion of the starting material (60 %),[23] and the incorporation of 18-oxygen into the marked α-diketone **8*** support our hypothesis. These experimental results have been confirmed for all starting materials; (b) the inhibition, from total to partial, observed in three different reactions carried out on **1**, in the presence of progressively reduced amounts of 1,4-diazabicyclo [2,2,2]-octane **DABCO** ($E^{ox} = 0.64$ V. vs SCE),[24] substantiates that the inhibition could be due to an easier electron-transfer between **DABCO** and **A**. Thus, this would inhibit or reduce, depending on **DABCO** concentration, the formation of the primary cation radicals ($\mathbf{1}$-$\mathbf{6}^{+}$); (c) the involvement of oxygen into the reaction process has been ruled out by running similar reactions under an inert atmosphere (nitrogen or argon). In fact, the conversions occur with the same rate, affording the same reaction products; (d) the stoichiometry of the process has been confirmed by treatment of a methylene chloride solution of **1**[15] with an equivalent amount of antimonium pentachloride, in the same solvent.

This reaction, affording **7** (50%) together with unreacted starting material, further substantiates that antimonium pentachloride can act as a one electron oxidizing agent.[25]

Although further detailed investigations in the area are warranted, we believe the preliminary results reported herein provide one more attractive procedure for the conversion of carbonyl compounds into α-diketones

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10) The *m*-chloroperbenzoic acid **MCPBA**-oxidations of *trans*-stilbene, *trans*-4,4'-dimethylstilbene and trans-4,4'-dichlorostilbene lead to the corresponding oxirane **1a**, **2a**, **4a**, showing physical and spectral

data consistent with those reported in the literature.[11] The epoxidation of olefins *trans*-4,4'-dimetoxy stilbene, yielding acid-sensitive epoxides **3a**, are typically conducted in the presence of a buffer such as sodium bicarbonate.[12]

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14) The starting material **2**, as similar, has been isolated by silica gel chromatography, petroleum ether/diethylether 95/5 v/v as eluant and characterized spectroscopically. i.r. (KBr) υ = 3024, 2922, 2858, 2724, 1725, 1513, 811 cm^{-1}; ms (m/e %) 224 (2), 195 (100), 180 (32), 165 (44), 152 (7), 215 (6), 89 (11), 77 (8), 63 (6), 51 (6), 39 (8); ^{1}H n.m.r. (CDCl$_3$) δ= 9.92 (s,1H, J= 2.4 Hz), 7.00–7.40 (m, 8H), 4.82 (d, 1H, J=2.4 Hz), 2.36 (s, 6H) ppm; ^{13}C n.m.r. (CDCl$_3$) δ= 21.07, 63.39, 128.98, 129.66, 133.37, 137.28, 198.91 ppm.

15) The isomerization of **1a-3a** with catalytic amounts of the powerful aminium salt **A** leads to the expected **1-3**, together with not negligible amounts of the corresponding substituted-benzaldehydes (10-15%) This is an intriguing reaction because it involve cleavage of a carbon-carbon single bond with the formation of ring opened cation radicals.These transient cation radicals are decomposed rapidly by strong nucleophiles, as for example water, to afford the corresponding carbonyl compounds, see ref.16. In the presence of 18-oxygen labeled water (20%), incorporation of 18-oxygen into the marked aldehydes has been observed.

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17) **8** i.r. (KBr) υ = 3063, 3033, 2921, 2853, 1661, 1605, 1572, 1222, 1208, 850, 830, 782, 742 cm^{-1}; ms (m/e %) 238 (10), 119 (100), 91 (27), 65 (13); ^{1}H n.m.r. (CDCl$_3$) δ= 7.85 (d, 4H, J= 8.5 Hz), 7.29 (d, 4H, J= 8.5 Hz), 2.42 (s, 6H) ppm; **8*** 18-oxygen labeled ms (m/e %) 240 (6), 238 (9), 121 (20), 119 (100), 91 (27), 65 (12)

18) The gc mass fragmentation patterns of **13**, **14** respectively are: ms (m/e %): 203 (24 = M$^+$ - 29), 202 (12), 201 (81), 167 (27), 166 (33), 165 (100), 152 (13); ms (m/e %):141 (31 = M$^+$- 29), 140 (14), 139 (100), 105 (21), 104 (12) 103 (62)

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