Reactions of Copper(II) β -Diketonates under Free Radical Conditions. II. Diazonium Salts as Aryl Radicals Source in the Arylation of β -Diketones

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Abstract.- Copper complexes of 2,2,6,6-tetramethylheptane-3,5-dione and other ρ -diketones afford α -aryl- ρ -diketones when treated with arenediazonium tetrafluoroborates and copper powder in dichloromethane

Introduction.- We have previously reported that the reactions of cobalt(II) and copper(II) β -diketonates with free radicals result in the binding of the single electron bearing group to the central Car position of the β -diketone.¹ Thus, radicals such as 1-adamantyl and benzoyloxy have been incorporated, among others, into several diketones. The benzoyloxy radical incorporated prior to decomposition into CO₂ and phenyl radical, thus aborting what could have been the birth of a method of arylating diketones.^{1f} The cyclic mechanism of our copper(II) and cobalt(II) mediated reactions of β -diketones, as applied to alkyl halides and acetylacetonates, is represented in Scheme 1.² We decided to examine the possibility of effecting the arylations by generating the aryl radicals from aryldiazonium salts and copper powder.³

SCHEME 1

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Arylation of organic compounds is an important synthetic goal which attracts considerable attention.⁴ Some methods of arylating active methylene compounds have been reported and a useful review can be found in a paper by Novi and associates.⁵ Most of the methods are based on halides as leaving groups, the use of diazonium salts in arylation of β -diketones being limited in scope. Thus, in 1983, Citterio and Ferrario reported a free-radical chain arylation of pentane-2,4-dione,⁶ the free aryl radicals being generated from arenediazonium salts. This work dealt only with that simple diketone and was based on the presence of the enol form to a large extent. Indeed, the reaction was interpreted as a Meerwein arylation of the C=C bond of the enol form of the diketone that acts also as solvent. The more recent work by Novi and associates⁵ describes the arylation of the potassium salt of pentane-2,4-dione with aryl diazosulfides by the S_{RN}1 mechanism. Tenfold excess of the potassium salt was required and the method was only applied to pentane-2,4-dione.

<u>Results</u>.- Our method is summarized in Scheme 2 and in Table 1. $CuBF_4$ and Cu^I complexes 10 were not isolated, their presence in Scheme 2 is a working hypothesis. The formation of 10 is assumed on the basis of the recovery of half the starting diketone upon working up.

Run	<u>1-4</u>	<u>5</u>	Ratio <u>1-4/5/Cu</u>	<u>6-9</u>	Yieldb	Other products isolated (%) ^b or identified (GC-MS or NMR)
1	1	5a	1:1:1	6a	9	d
2	1	5a	1:2:2	6a	21	d
3	1	5b	1:1:1	6b	24	d
4	1	5b	1:2:2	6b	41	d
5	1	5b	1:2:10	6b	21	d
6 ^C	1	5b	4:1:2	6b	6	11b, 14b
7 ^a	1	5b	4:1:2	6b	6	11b, 14b
8 ^a	1	5b	1:8:4	6b	20	
9	1	5d	1:2:2	6d	21	
10	1	5f	1:1:1	6f	20	
11	1	5f	1:2:2	6f	38	
12 ^c	1	5f	4:1:2	6 f	2	11f (76)
13 ^a	1	5f	4:1:2	6 f	7	11f (40)
14	2	5b	1:2:2	7Ъ	21	$PhCOCH_2COCH_3$ (72)
15	3	5b	1:2:2	8b	35	(PhCO) 5CH2 (54)
16	4	5b	1:2:2	9b	34	2 ² d
17	4	5c	1:2:2	9c	31	$(t-BuCO)_2CH_2$ (56)
18	4	-5d	1:2:2	9d	25	$(t-BuCO)_{2}CH_{2}^{2}$ (40), 13d
19	4	-5e	1:2:2	9e	34	(t-BuCO) ₂ CH ₂ (56), 13e
20	4	5f	1:2:2	9f	10	$(t-BuCO)_{2}^{2}CH_{2}^{2}$ (47), 12f

Table 1.- Reactions of complexes 1-4 with diazonium salts 5 and Cu powder^a

^a [1-4] was 0.17-0.20M but in runs 7, 8 and 13 ([1] = 0.90, 0.08 and 0.90 respectively); ^b yields based on diketone, yields according to stoichiometry of Scheme 2 are twice as much; ^c Addition of 5 was made slowly in four portions during 10 h; ^d not studied.



SCHEME 2

In the presence of copper powder several reaction pathways are opened to diazonium salts (Scheme 3). Thus, the generated diazenyl radicals 15^3 can fragment into aryl radicals 16 that either dimerize to biphenyls 13, couple with diazenyl radicals to give azocompounds 14 or react with complexes 1-4 (Scheme 1) to give the arylated diketones 6-9. Indeed, all these reactions were observed when diazonium salts 5a-f reacted with copper complexes 1-4 in the presence of copper powder.



SCHEME 3

First, we studied the reaction of copper(II) pentane-2,4-dionate 1 with benzenediazonium tetrafluoroborate 5b in order to find out the best experimental conditions. Runs 3-8 summarize the results. It was clear soon that yields of 6-9 based on the diketone ligand were never higher than 50% and this we attribute to the inherent mechanistic features of the reaction. Thus, the generated aryl radicals 16 react with copper complexes 1-4 as indicated in Scheme 4 to afford intermediates 17. This step is equivalent to the third initiation step of our general mechanistic scheme (Scheme 1). Copper(III) intermediates 17 give aryldiketones 6-9 and copper(I) diketonates 10 (Scheme 4), in a mechanistic step that is the counterpart of the first propagation step in Scheme 1. Since no Ar-X is present in our reactions, a cyclic mechanism, such as the one represented in Scheme 1 for alkylation reactions cannot operate here. Attempts to force the cyclic mechanism failed. Thus, the addition of iodobenzene did not lead to 18 in what could have been the parallel of the second propagation step of Scheme 1. Using forcing conditions (evaporating the solvent and heating at 140°C) the boron difluoride complex of **6b** was formed, but the overall yield of phenylated compounds was not higher than 50% with respect to the initial diketone. Also, a model reaction of **10** ($\mathbb{R}^1 = \mathbb{R}^2 = \mathbb{M}e$)⁷ with iodobenzene did not afford **6b**. Other attempts using other solvents (butanone, 1,2-dichloroethane, acetonitrile, t-butanol) or adding Cu_20^8 to the reaction mixture did not improve the yields. We therefore focused our attention on finding out the best ratios of reagents, on extending the reaction to diketones other than pentane-2,4-dione, in particular to 2,2,6,6-tetramethylheptane-3,5-dione (dipivaloylmethane) and to other arenediazonium salts and on the recovery of the remaining 50% of the diketone.



10 + PhI
$$\longrightarrow$$
 (R¹COCHCOR²)Cul-Ph \longrightarrow Cu(acac) + PhI
18 10 (R¹=R²=Me)

SCHEME 4

After some experimentation we found that the best molar ratio 1-4/5/Cu was 1:2:2. On the other hand, portionwise addition of 5 has no beneficial effect (compare runs 6 and 7 and 12 and 13). The method could be extended to 1-phenyl-1,3-butanone, 1,3-diphenyl-1,3propanone and 2,2,6,6-tetramethylheptane-3,5-dione (complexes 1-4) as well as to a broad selection of arenediazonium tetrafluoroborates 5, bearing either electron-attracting or electron-withdrawing groups, and the yields according to the stoichiometry of Scheme 2 range from reasonable to good. More important, the non-consumed diketone can be easily recovered. This point was studied in the dipivaloylmethane arylations (Runs 17-20). In conclusion, the results of Table 1 indicate that the method herein constitutes a good alternative to reported procedures for arylating diketones.

Experimental

PMR and CMR spectra were recorded at 80 and 20 MHz respectively, chemical shifts are given in δ units and coupling constants in Hz. Mass spectra were registered at 70eV.

Arenediazonium tetrafluoroborates **5a-f** (mp 137-8, 120, 141, 122, 126 and 140°C respectively) were prepared according to reported general procedures.⁹ Complexes 1-4 (mp

>300, 191-2, >300 and 198°C (Lit.¹⁰ mp 198°C) respectively) were prepared by the standard method, either from copper(II) acetate in methanol-water (for 1-3) or copper(II) chloride in ethanol-water (for 4). Diketones 6 exist as the enols, 7a appears to be a keto-enol mixture and diketones 8-9 are in the diketonic form (see PMR spectra). Minor products 11-14 were identified in chromatographic fractions (IR, NMR, MS or GC-MS and no attempts were made to purify them.

4-(4-Fluoropheny1)-2,2,6,6-tetramethylheptane-3,5-dione, 9c. (Run 17. General procedure)

Complex 4 (4.00 g, 9.3 mmol), diazonium salt 5c (3.90 g, 18.6 mmol), copper powder (1.18 g, 18.6 mg atom) and dichloromethane (50 mL) were added in that order to a three-necked 250 mL round-bottomed flask. Formation of nitrogen was observed immediately after the addition of solvent. The mixture was magnetically stirred for 64 h, then more dichloromethane (100 mL) was added and the organic solution partitioned with 1N HC1 (3 x 100 mL). The solvent was evaporated and the residue distilled to recover 2,2,6,6-tetramethylheptane-3,5-dione (0.864 g). The distillation residue was chromatographed through a silica-gel column (hexane-dichloromethane as eluent) to obtain 1.07 g of 2,2,6,6-tetramethylheptane-3,5-dione (56% overall recovering) and 1.61 g of 9c (62% according to the actual stoichiometry, 31% with respect to the initial diketone), mp 101-2°C (from hexane); IR(KBr): 1717, 1685 cm⁻¹; PMR(CDCl₃): 1.04 (s, 18H), 5.65 (s, 1H), 6.80-7.24 (m, 4H); CMR(CDCl₃): 27.0, 45.0, 59.6, 115.2 (d, J = 21.5), 129.3 (d, J = 3.4), 131.1 (d, J = 8.1), 162.1 (d, J = 246.6), 207.3. Calculated for $C_{17H_23}FO_2$: C, 73.35; H, 8.33. Found: C, 73.32; H, 8.30.

All the other compounds 6-9 were prepared by the same general method.

4-Phenyl-2,2,6,6-tetramethylheptane-3,5-dione, 9b.

Mp 97-8°C (hexane-dichloromethane); IR(KBr): 1716, 1664 cm⁻¹; PMR(CDCl₃): 1.12 (s, 18H), 5.74 (s, 1H), 7.17-7.33 (m, 5H); CMR(CDCl₃): 27.1, 45.1, 60.6, 127.4, 128.4, 129.5, 133.5, 207.3.

Calculated for C17H2402: C, 78.42; H, 9.29. Found: C, 78.04, H, 9.65.

4-(4-Chloropheny1)-2,2,6,6-tetramethylheptane-3,5-dione, 9d.

Mp 133-4°C (hexane); IR(KBr): 1718, 1688 cm⁻¹; PMR(CDCl₃): 1.12 (s, 18H), 5.75 (s, 1H), 7.13, 7.22, 7.27 and 7.37 (AA'BB' system, 4H); CMR(CDCl₃): 26.9, 45.0, 59.6, 128.4, 130.7, 132.0, 133.3, 207.0; MS(m/e): 294 (M, 1), 85(22), 57(100). Calculated for C₁₇H₂₃ClO₂: C, 69.26; H, 7.86. Found: C, 68.98; H, 8.24.

4-(4-Bromophenyl)-2,2,6,6-tetramethylheptane-3,5-dione, 9e.

Mp 147-8°C (hexane); IR(KBr): 1717, 1687 cm⁻¹; PMR(CDCl₃): 1.12 (s, 18H), 5.71 (s, 1H), 7.06, 7.18, 7.42, 7.53 (AA'BB' system, 4H); CMR(CDCl₃): 27.0, 45.0, 59.7, 121.6, 131.0,

131.4, 132.5, 206.8. Calculated for C₁₇H₂₃BrO₂: C, 60.18; H, 6.83. Found: C, 59.98; H, 7.00.

4-(4-Nitropheny1)-2,2,6,6-tetramethylheptane-3,5-dione, 9f.

Mp 154-5°C (hexane-dichloromethane); IR(KBr): 1717, 1686, 1515, 1364 cm⁻¹; PMR(CDCl₃): 1.14 (s, 18H), 5.72 (s, 1H), 7.35, 7.46, 8.13, 8.23 (AA'BB' system, 4H); CMR(CDCl₃): 26.8, 45.2, 60.0, 123.3, 130.1, 140.5, 147.1, 205.9. Calculated for C_{17H23}NO₄: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.95; H, 7.93; N, 4.71.

3-(4-Methoxyphenyl)pentane-2,4-dione, 6a.

Mp 35°C (hexane-dichloromethane) (Lit.⁶ mp: 70°C); IR(KBr): 1609 cm⁻¹; PMR(CDCl₃): 1.90 (s, 6H),3.83 (s, 3H), 6.84, 6.96, 7.03, 7.14 (AA'BB' system, 4H), 16.61 (s, 1H); CMR(CDCl₃): 23.7, 54.9, 114.0, 114.3, 128.9, 131.8, 158.8, 190.7; MS(m/e): 178(2), 135(100), 107(18), 92(13), 77(31).

3-Phenylpentane-2,4-dione, 6b

Mp 58-60°C (hexane-dichloromethane) (Lit.⁶ mp: 59-60°C); IR(film): 1601 cm⁻¹; PMR(CDCl₃): 1.88 (s, 6H), 7.06-7.58 (m, 5H), 16.63 (s, 1H); CMR(CDCl₃): 23.8, 115.1, 127.3, 128.6, 130.9, 136.9, 190.6; MS(m/e): 176(M, 100), 161(71), 133(36), 77(14), 55(59), 43(62).

3-(4-Chlorophenyl)pentane-2,4-dione, 6d.

Mp 85-6°C (hexane-dichloromethane) (Lit.⁶ mp 90-1°C); IR(KBr): 1591 cm⁻¹; PMR(CDCl₃): 1.92 (s, 6H), 7.12, 7.22, 7.39, 7.49 (AA'BB' system, 4H), 16.75 (s, 1H); CMR(CDCl₃): 24.0, 114.0, 129.0, 132.4, 133.6, 135.5, 190.6; MS(m/e): 210(M, 76), 195(63), 167(44), 115(17), 103(17), 55(57), 43(100).

3-(4-Nitrophenyl)pentane-2,4-dione, 6f.

Mp 117-8°C (hexane-dichloromethane) (Lit.⁶ mp 119°C); IR(KBr): 1597, 1523, 1346 cm⁻¹; PMR(CDCl₃): 1.91 (s, 6H), 7.36, 7.47, 8.24, 8.36 (AA'BB' system, 4H), 16.76 (s, 1H); CMR(CDCl₃): 23.9, 113.5, 123.8, 132.1, 144.0, 147.3, 190.3; MS(m/e): 221(M, 63), 206(94), 179(19), 161(14), 132(50), 131(23), 103(19), 43(100).

1,2-Diphenyl-1,3-butanedione, 7b.

Mp 84-6°C (hexane-dichloromethane) (Lit.¹¹ mp 75-9°C); IR(KBr): 1693 cm⁻¹; PMR(CDCl₃): keto form: 2.28 (s, 3H), 5,71 (s, 1H), 7.05-8.13 (m, 10H), enol form: 2.05 (s, 3H), 7.05-8.13 (m, 10H), 17.40 (s, 1H); CMR(CDCl₃): keto + enol forms: 26.0, 29.0, 67.8, 114.2, 127.0, 127.3, 127.8, 128.4, 128.5, 128.6, 128.8, 129.1, 129.6, 130.0, 131.6, 133.2, 134.5, 136.0, 136.7, 182.9, 196.0. 1,2,3-Tripheny1-1,3-propanedione, 8b.

Mp 147-9²C (hexane-dichloromethane) (Lit.¹² mp 148-9²C); IR(KBr): 1695, 1669 cm⁻¹; PMR(CDCl₃): 6.61 (s, 1H); 7.05-7.69 (m, 11H), 7.85-8.10(m, 4H); CMR(CDCl₃): 62.8, 127.5, 127.8, 128.6, 128.7, 129.9, 133.1, 133.1, 136.0, 193.9.

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