5672 *J. Org. Chem.* **1998,** *63,* 5672−5674

Oxidation by Molecular Oxygen: One-Pot Synthesis of Diaryl Ketones Complexed to Tricarbonylchromium[†]

Sunil K. Mandal and Amitabha Sarkar*

Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune-411008, India

Received February 23, 1998

We have recently observed[1] that a number of commonly employed bases can bring about facile cleavage of the Ar−$SiMe_3$ bond at room temperature if the aromatic ring is complexed with a tricarbonylchromium moiety. Potassium hydride, in the presence of a catalytic quantity of 18-crown-6, effected rapid (1−2 h) and complete desilylation in diethyl ether. Uncomplexed arylsilanes remain unaffected (>24 h) under these conditions. Following desilylation, anionic aryl species stabilized by $Cr(CO)_3$ were trapped by electrophiles to afford regiospecifically functionalized products (Scheme 1).

In the present work, we have extended this methodology to offer a convenient and general synthesis of diaryl ketones wherein one aromatic ring is predictably complexed with tricarbonylchromium. In this protocol, three consecutive reactions, viz. desilylation of $(CO)_3Cr{-}Ar{-}SiMe_3$ to generate a stable aryl anion, reaction of the anion with aromatic or heteroaromatic aldehydes to generate a carbinol, and autoxidation of the latter to a diaryl ketone, take place in a single-step, one-pot operation. A remarkable feature of this reaction is that the chromium complex survives such oxidative conditions.

Results and Discussion

When desilylation was carried out in DMF using 1.0−1.2 equiv of KH and 10 mol % of 18-crown-6 in the presence of an aromatic aldehyde under *an atmosphere of dry argon,* the major product was the expected carbinol (70−87%) contaminated with a small amount (5−15%) of the protiodesilylated product (Scheme 2, Table 1). No formyl derivative was observed though DMF was used as solvent.[2] Reactions of aromatic aldehydes with *ortho*-substituted arylsilanes (substrates **1c**, **1d**) were moderately diastereoselective[3] (diastereomeric ratios in **2e**, **2f** are 5:1, 4.5:1, respectively). In all cases, diastereoisomers were separable by column chromatography.

Table 1

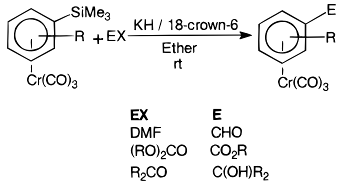
entry	sub-strate	R	Ar	condi-tions	time (h)	product	yield (%)[a]
1	**1a**	H	4-Me-C_6H_4	A	0.5	**2a**	70 (10)
				B	0.75	**3a**	90 (6)
2	**1a**	H	2-thienyl	A	0.5	**2b**	80 (6)
				B	0.5	**3b**	78 (9)
3	**1a**	H	2-pyridyl	A	0.5	**2c**	80 (<5)
				B	0.5	**3c**	77 (13)
4	**1b**	4-OMe	4-OMe-C_6H_4	A	0.5	**2d**	70 (10)
				B[c]	0.5	**3d**	70 (10)
5	**1c**	2-OMe	C_6H_5	A[d]	0.5	**2e**[b]	80 (10)
				B	0.75	**3e**	80 (<5)
6	**1d**	2-Cl	C_6H_5	A	0.5	**2f**[b]	87 (<5)
7	**1a**	H	ferrocenyl	B	0.5	**3f**	77 (10)
8	**1a**	H	4-NO_2-C_6H_4	B	0.25	**3g**	90 (<5)

[a] Numbers in parentheses indicate percent yield of protiodesilylated products. [b] Mixture of two diastereoisomers, which were separated by column chromatography; yields mentioned for two diastereoisomers together. [c] In a separate experiment when cesium fluoride was used instead of potassium hydride, the carbinol **2d** was obtained in 72% yield, whereas the yield of the corresponding ketone was less than 5%, even after stirring for 10 h. [d] In a separate experiment, when equivalent amounts of ethyl benzoate and 2,2,2-trifluoroacetophenone were added, in addition to benzaldehyde, there was no other product except **2e**.

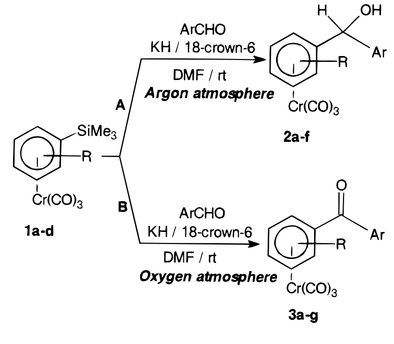
Table 2

substrate	Ar	conditions	time (h)	product	yield (%)
2a	4-Me-C_6H_4	C	0.25	**3a**	72
2a	4-Me-C_6H_4	D	4.5	**3a**	69
2b	2-thienyl	C	0.25	**3b**	83
2b	2-thienyl	D	5.5	**3b**	78
2c	2-pyridyl	C	0.25	**3c**	90
2c	2-pyridyl	D	6.0	**3c**	82

Scheme 1



Scheme 2



However, when the same reaction was carried out with 2.0−2.2 equiv of potassium hydride under *an atmosphere of dry oxygen*, the major product was a diaryl ketone (70−90%) instead of a carbinol (Scheme 2, Table 1).

In a typical procedure, potassium hydride suspension in diethyl ether was added dropwise to a solution of the substrate, the aldehyde, and a catalytic amount of 18-crown-6 in DMF at room temperature under a blanket of dry oxygen. In most of the reactions (Table 1, entries 1−6, 8), a deep blue-green color developed instantly on addition of the potassium hydride suspension, which

---

* E-mail: sarkar@ems.ncl.res.in. Phone/FAX: 91-212-335153.

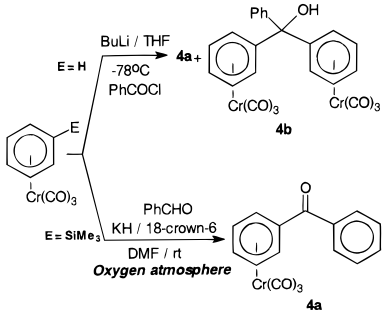
[†] NCL Communication No. 6439.

(1) Mandal, S. K.; Sarkar, A. *J. Org. Chem.* **1998**, *63*, 1901.

(2) (a) Choice of DMF as solvent was governed by a precedent: Effenberger, F.; Schollkopf, K. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 226. (b) In aqueous hydroxide mediated reactions, only desilylation was observed—no reaction with aldehyde was detected. This observation rules out any role of adventitious water in DMF.

(3) Direct *ortho*-lithiation of anisole and chlorobenzene complexes and subsequent reaction of the aryl anions with benzaldehyde were reported to provide an approximately 60:40 mixture of diastereoisomers. In comparison, the present diastereoselectivities appear respectable, which may be a consequence of a counterion effect, cf.: Semmelhack. M. F.; Bisaha, J. J.; Czarny, M. *J. Am. Chem. Soc.* **1979**, *101*, 768.

Scheme 3



persisted for a few minutes before changing to the deep red color of the ketone complex. When Ar was ferrocene (entry 7), no blue-green color was observed, which was probably masked by the intense color of the aldehyde. The rate of this reaction was comparatively slow in diethyl ether or THF in which appreciable amounts of decomplexation of both the starting material and the product were observed. The reactions in DMF, on the other hand, were complete in less than an hour with minimal oxidative decomplexation.

This method has certain advantages over the existing ones reported in the literature. For instance, direct thermal complexation of biaryl methanols and biaryl ketones following the Pauson–Mahaffy method[4] always produces a mixture of all possible mono- as well as bis-tricarbonyl chromium complexes.[5] Using our method, it is possible to control tricarbonylchromium complexation to a desired aromatic ring.

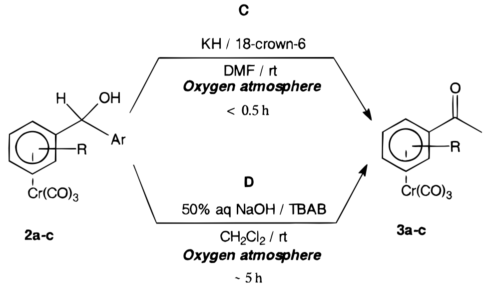
Second, we observed that lithiation of benzene tricarbonylchromium followed by quenching with benzoyl chloride resulted in a mixture of two products (Scheme 3). The major product was **4a** (80%) and the minor product was identified as the carbinol **4b** (20%) (generated from an additional equivalent of lithiated species on complex **4a**). Formation of the side product was avoided following our method of tandem desilylation–nucleophilic addition–oxidation.

The third and significant advantage of this method is that the desilylated species can tolerate sensitive groups such as NO_2 (Table 1, entry 8). Grignard or organolithium reagents are not compatible.[6] In an earlier attempt, Top and Jaouen failed to prepare complex **3g** from 4-nitrobenzophenone by applying direct thermal complexation.[5] The mild conditions of the present reaction affords **3g** readily in 90% yield.

Desilylated species can also react chemoselectively with the aldehyde function in the presence of ketone or ester functionalities. To illustrate this, when substrate **1c** was separately subjected to the reaction conditions A in the presence of equivalent amounts of benzaldehyde, ethyl benzoate, and 2,2,2-trifluoroacetophenone, only **2e** was obtained in 78% yield.

The likely mechanism appears to involve potassium hydride as a *nucleophile* in the desilylation step[1] and as a *base* in the autoxidation reaction.[7] Sodium hydride worked equally well. While aqueous alkali metal hydroxides were able to effect desilylation, the desilylated aryl species underwent proton quench in aqueous medium before reacting with an electrophile. The reaction using cesium fluoride produced a very small amount (<5%) of ketone after 10 h (Table 1, entry 4).

Scheme 4



It appears that the ability of the base to abstract the benzyl proton of the carbinol is crucial for triggering autoxidation, and the basicity of fluoride ion may not be adequate for the purpose. The complexed carbinols **2a–c** afforded the corresponding ketone complexes when treated with 1.0–1.2 equiv of potassium hydride under an *oxygen atmosphere* (Scheme 4, Table 2). The deep blue-green color developed instantly on addition of the potassium hydride suspension and ultimately turned to red. Biphasic autoxidation of carbinols could also be effected with 50% aqueous sodium hydroxide in the presence of tetrabutylammonium bromide (TBAB) as phase transfer catalyst, albeit with a lesser efficiency (Scheme 4, Table 2). When fluoride ion was used as base, a trace amount of ketones was obtained even after 10 h.

Oxidative processes involving reactions of molecular oxygen with organic substrates is well-known. But, autoxidations are not often used for preparative purposes since they frequently result in a complex mixture of products.[8] However, the autoxidation described above is a preparatively useful reaction. Mild conditions and short reaction times permit the tricarbonylchromium group to stay, even in the presence of oxygen. Although the base-catalyzed autoxidation of benzohydrol to benzophenone was studied[7] with a catalytic quantity of anthraquinone and a stoichiometric amount of aluminum *tert*-butoxide, little is known about the autoxidation of diarylmethanols and their synthetic utility in general.

Conclusions

We have described a facile and regioselective synthesis of diarylmethanol and diaryl ketone complexes of tricarbonylchromium using both the basic and nucleophilic behavior of potassium hydride. The strategy permits total control of tricarbonylchromium complexation to a desired aromatic ring and promises synthetic entry into a large number of polyfunctional diarylmethanol and diaryl ketone analogues. The high points of this reaction sequence are the mildness of the conditions and the high functional group tolerance, features that complement normal aryl–metal reactions to attain sensitive targets.

Experimental Section

All reactions except autoxidations were performed under an inert atmosphere of argon, using freshly distilled, degassed solvents. Autoxidations were performed under a dry atmosphere

---

[4] Mahaffy, C. A. L.; Pauson, P. L. *Inorg. Synth.* **1979**, *19*, 154.

[5] Top, S.; Jaouen, G.*J. Organomet. Chem.* **1979**, *182*, 381.

[6] March, J. *Advanced Organic Chemistry*, 4th ed; Wiley-Interscience: New York, 1992; p 927.

[7] Sosnovsky, G.; Zaret, E. H. Base-Catalysed Autoxidation In *Organic Peroxides*; Swern, D., Eds.; Wiley-Interscience: New York, 1970; Vol. 1, p 517–560.

[8] Ref 6, p 705–706 and references therein.

of oxygen. DMF was purified by distillation over calcium hydride under reduced pressure. Diethyl ether and THF were freshly distilled over sodium benzophenone ketyl. Aromatic aldehydes and 18-crown-6 were purchased from Aldrich, and used as received. Potassium hydride and sodium hydride were also purchased from Aldrich and washed with portions of hexane and anhydrous diethyl ether prior to use. *n*-BuLi in hexane (ca. 1.5 M) was prepared using standard procedure and titrated prior to use.[9] For descriptions of analytical instruments, spectral data formats, and standard calibrations see ref 11.

General Procedure for the Preparation of Carbinols (2a−f) from Arylsilanes (1a−d). To a solution of the complexed arylsilane (*n* mmol), aromatic aldehyde (*n* mmol), and 18-crown-6 (10 mol %) in DMF (5*n* mL) was added a suspension of KH (1.0−1.2*n* mmol) in diethyl ether (3*n* mL) dropwise with stirring at room temperature. After completion of the reaction (TLC), the reaction mixture was quenched with degassed methanol at ice-cold temperature, followed by addition of water, and finally extracted with ether. The crude complex obtained after evaporation of solvents was purified by column chromatography. Some products have been reported earlier: viz. complexes **2d**,[10] **2a**,[2] and **2e**, **2f**.[3]

Complex 2b: yellow crystalline solid; mp 98−100 °C (dec); ^{1}H NMR ($CDCl_3$) 2.59 (d, 1H, $J = 5.7$ Hz), 5.29 (m, 3H), 5.40 (m, 1H), 5.69 (m, 2H), 6.97 (m, 2H), 7.26 (d, 1H, $J = 5.2$ Hz); ^{13}C NMR ($CDCl_3$) 70.60, 89.90, 91.7, 92.4, 92.7, 125.7, 126.4, 127.1, 145.7, 232.9; IR ($CHCl_3$) 3400−3600 (br), 1970, 1890 (br) cm^{-1}. Anal. Calcd for $C_{14}H_{10}O_4SCr$: C, 51.54; H, 3.09; S, 9.83. Found: C, 51.56; H, 3.16; S, 9.93.

Complex 2c: yellow crystalline solid; mp 112−114 °C (dec); ^{1}H NMR ($CDCl_3$) 4.70 (brs, 1H), 5.23 (d, 1H, $J = 6.4$ Hz), 5.32 (t, 2H, $J = 6.4$ Hz), 5.43 (brs, 1H), 5.62 (d, 1H, $J = 6.4$ Hz), 7.29 (t, 1H, $J = 7.4$ Hz), 7.47 (d, 1H, $J = 7.4$ Hz), 7.75 (t, 1H, $J = 7.4$ Hz), 8.56 (d, 1H, $J = 5.6$); ^{13}C NMR ($CDCl_3$) 73.40, 91.75, 92.16, 92.54, 93.11, 121.55, 123.64, 137.45, 148.66, 158.97, 232.82; IR ($CHCl_3$) 3400−3600 (br), 1970, 1890 (br) cm^{-1}. Anal. Calcd for $C_{15}H_{11}O_4NCr$: C, 56.08; H, 3.45; N, 4.36. Found: C, 56.11; H, 3.65; N, 4.34.

Procedure for the Attempted Functionalization of Arylsilanes (1a−c) Using 50% Aqueous NaOH/TBAB. To a solution of the complexed arylsilane (*n* mmol), aromatic aldehyde (*n* mmol), and tetrabutylammonium bromide (TBAB) (10 mol %) in CH_2Cl_2 (5*n* mL) was added 50% aqueous NaOH (1.5−2*n* mmol) dropwise with stirring at room temperature. There was no reaction with aldehyde; only desilylated product was obtained. After completion of the reaction (TLC), the reaction mixture was diluted with degassed water and extracted with dichloromethane. Yield of the desilylated products comparable as reported[1] earlier.

General Procedure for the Preparation of Complexed Ketones (3a−g) from Arylsilanes (1a−c). The procedure was the same as in the preparation of carbinols except that 2.0−2.2 equiv of potassium hydride was used. Instead of using an argon atmosphere, reactions were performed under an atmosphere of dry oxygen.

Several of the diaryl ketone complexes have been reported earlier: viz. complexes **3d**, **3f**,[10] **3a**.[5]

Complex 3b: red crystalline solid; mp 100−102 °C; ^{1}H NMR ($CDCl_3$) 5.36 (t, 2H, $J = 6.8$ Hz), 5.62 (t, 1H, $J = 6.8$ Hz), 6.13(d, 2H, $J = 6.8$ Hz), 7.23 (dd, 1H, $J = 5.2$, 3.6 Hz), 7.76 (d, 1H, $J = 3.7$ Hz), 7.90 (d, 1H, $J = 5.2$ Hz); ^{13}C NMR ($CDCl_3$) 90.03, 94.65, 95.20, 98.6, 128.36, 133.8, 134.53, 140.97, 184.34, 230.96; IR ($CHCl_3$) 1990, 1920, 1640 cm^{-1}. Anal. Calcd for $C_{14}H_8O_4SCr$: C, 51.86; H, 2.49; S, 9.89. Found: C, 51.79; H, 2.47; S, 9.80.

Complex 3c: red crystalline solid; mp 60 °C; ^{1}H NMR ($CDCl_3$) 5.32 (t, 2H, $J = 6.8$ Hz), 5.70 (t, 1H, $J = 6.8$ Hz), 6.78 (d, 2H, $J = 6.8$ Hz), 7.51 (m, 1H), 7.92 (dd, 1H, $J = 7.5$, 5.5 Hz), 8.06 (d, 1H, 7.6 Hz), 8.70 (d, 1H, $J = 5.4$ Hz); ^{13}C NMR ($CDCl_3$) 89.03, 94.58, 95.32, 97.68, 124.28, 126.65, 137.28, 148.04, 154.45, 189.63, 230.77; IR ($CHCl_3$) 1990, 1920, 1670 cm^{-1}. Anal. Calcd for $C_{15}H_9O_4NCr$: C, 54.56; H, 2.62; N, 4.39. Found: C, 54.59; H, 2.69; N, 4.40.

Complex 3e: orange crystalline solid; mp 115 °C; ^{1}H NMR ($CDCl_3$) 3.65 (s, 3H), 4.95 (t, 1H, $J = 6.4$ Hz), 5.10 (d, 1H, $J = 6.5$ Hz), 5.70 (t, 1H, $J = 6.5$ Hz), 5.90 (d, 1H, $J = 6.5$ Hz), 7.45 (t, 2H, $J = 7.8$ Hz), 7.55 (t, 1H, $J = 7.8$ Hz), 7.90 (d, 1H, $J = 7.8$ Hz); ^{13}C NMR ($CDCl_3$) 56.00, 72.22, 83.13, 94.63, 96.62, 96.76, 128.36, 129.48, 133.25, 137.31, 141.70, 191.54, 231.61; IR ($CHCl_3$) 1995, 1925, 1670 cm^{-1}. Anal. Calcd for $C_{17}H_{12}O_5Cr$: C, 58.63; H, 3.47. Found: C, 58.68; H, 3.45.

Complex 3g: red crystalline solid; mp 115 °C; ^{1}H NMR ($CDCl_3$) 5.35 (t, 2H, $J = 6.5$ Hz), 5.70 (t, 1H, $J = 6.5$ Hz), 6.00 (d, 2H, $J = 6.5$ Hz), 7.90 (d, 2H, $J = 8.4$ Hz), 8.40 (d, 2H, $J = 8.4$ Hz); ^{13}C NMR ($CDCl_3$) 89.80, 94.10, 95.34, 95.64, 124.01, 129.47, 142.22, 149.87, 192.42, 230.24; IR ($CHCl_3$) 1970, 1900, 1650, 1520 cm^{-1}. Anal. Calcd for $C_{16}H_9O_6NCr$: C, 52.91; H, 2.50; N, 3.86. Found: C, 52.88; H, 2.50; N, 3.79.

Procedure for the Attempted Autoxidation Using Cesium Fluoride. Reactions were performed following the reported procedure[2a] under a dry atmosphere of oxygen.

General Procedure for the Autoxidation of Complexed Carbinols (2a−c) to Complexed Ketones (3a−c): Using KH/18-crown-6. To a solution of the complexed carbinol (*n* mmol) and 18-crown-6 (10 mol %) in DMF (5*n* mL) was added a suspension of KH (1.0−1.2*n* mmol) in ether (3*n* mL) dropwise with stirring at room temperature. After completion of the reaction (TLC), the reaction mixture was quenched with degassed methanol at ice-cold temperature, followed by addition of water, and finally extracted with ether.

Using 50% Aqueous NaOH/TBAB. To a solution of the complexed carbinol (*n* mmol) and tetrabutylammonium bromide (TBAB) (10 mol %) in CH_2Cl_2 (5*n* mL) was added 50% aqueous NaOH (1.5−2*n* mmol) dropwise with stirring at room temperature. After completion of the reaction (TLC), the reaction mixture was diluted with degassed water and extracted with dichloromethane.

Reaction of Tricarbonyl[η^6-benzene]chromium(0), with *n*-BuLi and Benzoyl chloride: *n*-Butyllithium (1.56 M, 0.7 mL, 1.0 mmol) was added dropwise to a cooled (−78 °C) THF solution of benzene tricarbonylchromium (214 mg, 1.0 mmol) and the mixture stirred at −78 °C for 2 h. Benzoyl chloride (168 mg, 1.2 mmol) was added and stirring continued (−78 °C, 2 h). Degassed methanol (5 mL) was slowly added to quench the reaction and the mixture was allowed to attain room temperature. Solvents were evaporated to afford crude mixture of products that were separated by column chromatography to yield **4a**[10] (242 mg, 80%) and **4b**[5] (48 mg, 18%).

Acknowledgment. One of us (S.K.M.) thanks CSIR, New Delhi, India, for a research fellowship.

JO980332A

---

(9) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem*. **1976**, *41*, 1879. Lipton, M. F.; Sorensen, C. M.; Sadler, A. C.; Shapiro, R. H. *J. Organomet. Chem*. **1980**, *186*, 155.

(10) Ceccon, A.; Gobbo, A.; Venzo, A.. *J. Organomet. Chem*. **1978**, *162*, 311.

(11) Chowdhury, S. K.; Samanta, U.; Puranik, V. G.; Sarkar, A. *Organometallics* **1997**, *16*, 2618.