Reaction of η^6–Dihydronaphthalene–$Cr(CO)_3$ and η^6-Indene-$Cr(CO)_3$ complexes with iodoarenes under Pd-catalysis

Krishna Gopal Dongol,[a,b] Kouki Matsubara,[a,c] Masataka Watanabe,[a] Shuntaro Mataka,[a] Thies Thiemann[a,d]*

[a]Institute of Materials Chemistry and Engineering, Kyushu University, 6-1, Kasuga-koh-en, Kasuga-shi 816-8580, Japan

[b-d]present addresses:

[b]NK Ingredients Pte Ltd, Singapore

[c]Department of Chemistry, Faculty of Science, Fukuoka University, 8-19-1, Nanakuma, Fukuoka 814-0180, Japan

[d]Department of Chemistry, United Arab Emirates University, Al Ain, PO Box 15551, United Arab Emirates

Abstract: η^6-Dihydronaphthalene tricarbonylchromium(0) complexes and η^6-indene tricarbonylchromium(0) have been prepared and subjected to Pd(0) catalysed reactions with iodoarenes. The reaction of η^6-dihydronaphthalene tricarbonylchromium(0) complexes with iodoarenes under Jeffery conditions leads after decomplexation to triarylated products. The stereo- and regiochemistry of these products could be affirmed by an X-ray crystal structure. The η^6-dihydronaphthalene unit can be part of more complicated structures such as of estrone derived compounds without changing the course of the reaction. The reaction of η^6-indene tricarbonylchromium(0) with iodoarenes, however, leads to benzophenones, where the indene unit is not incorporated.

Keywords: η^6–Dihydronaphthalene–$Cr(CO)_3$ complexes, triarylation, condensed aromatic systems, η^6-indene-$Cr(CO)_3$ complexes, Heck-type reaction, benzophenones

Introduction

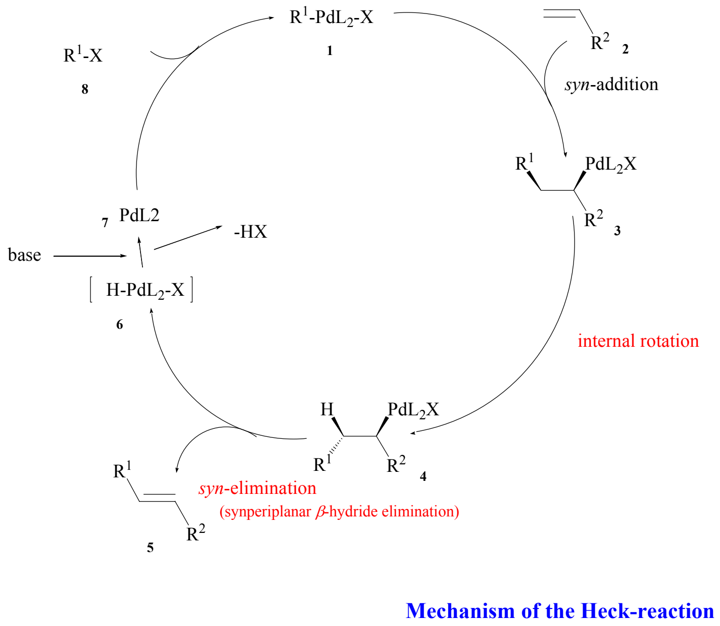
Heck reactions with cycloalkenes are difficult to perform as the mechanism of the transformation necessitates the β-hydride elimination to be *syn*.[1] This requires that a β-hydrogen is positioned *syn*-periplanar to the halopalladium residue. While the initial oxidative addition of the aryl palladium iodide is *syn*, a *syn*-periplanar elimination can be achieved for most linear alkene substrates by internal σ-bond rotation after the addition step (Scheme 1). *Per se*, this rotation is not possible in a cyclic structure of small or medium ring size (Scheme 2). Clearly, when both of the allylic carbons of the initial cyclic alkene can provide a hydrogen in *syn*-position after the addition has taken place, the reaction proceeds normally, regardless of the regiochemistry of the initial addition product. E. Nifant'ev et al. have shown that other pathways can come into play when no β-hydrogen is in *syn*-position such as a slow, thermal epimerization of the carbon carrying the halopalladium residue (Scheme 3).[2]

There are a number of cases known where in the Heck-type conversion of strained alkenes or of electron-poor alkenes with iodoarenes an aromatic C-H insertion within the primary adduct takes place with the formation of a palladacycle instead of a *β*-hydride elimination. This is followed by further oxidative addition of iodoarene and C-C coupling reaction. A final reductive elimination leaves a polyarylated aromatic system as product.[3,4] Some of the more prominent representative transformations of this type are the reaction of enesulfones of type **20** with iodobenzene (**21**) giving **22** as product (Scheme 4) [5] and the reaction of norbonene (**23**) with iodoarenes (Scheme 5) to give compounds **25** – **28** [6].

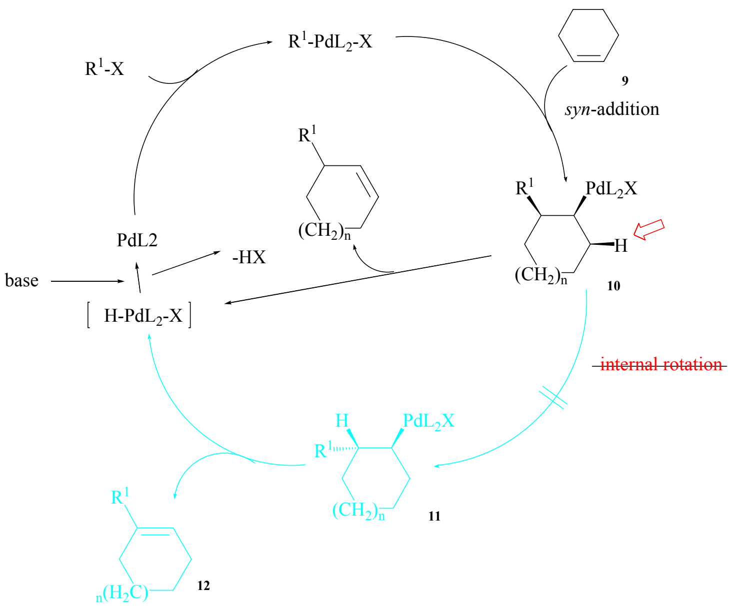
Results and Discussion

Our introduction into this thematic occurred with the desire to link to C7 of the estra-1,3,5(10),6-tetraen-17-one (**29**) via Heck-type reaction an aryl function substituted with a carboxylate function. The reaction, which was run under Jeffery conditions [7], proceeded sluggishly and gave a mixture of Heck products **30** in very low yield (Scheme 6). At the time, it was envisaged that a complexation of the A-ring in the steroid with the electron-withdrawing tricarbonylchromium-(0) moiety would result in greater regioselectivity of the Heck olefination, driving the reaction towards the desired C7-arylated product. At that point, the complexation itself provided a surprise with the π-facial selective production of solely the β-estra-1,3,5(10),6-tetraene tricarbonylchromium complex (**32**). As the *β*-face is the sterically more congested side and estra-1,3,5(10)-diol derivatives themselves are known to give both α- and β-isomers, the π-facial selectivity in the present case was linked to the directive effect of the double bond at C6-C7 [8]. This π-facial selectivity was also found in the reaction of **33** to complex **34**. When the Heck-reaction was run with complex **32** and iodobenzene (**21**) under Jeffery phase transfer catalysis conditions [$Pd(OAc)_2$, n-Bu_4NCl, KOAc, CH_3CN] [7], polyarylated product **35** was isolated (Scheme 6) after decomplexation of the primarily produced complex.

Next, η^6-dihydronaphthalene tricarbonylchromium(0) complexes of type **36** were reacted with iodoarenes under Jeffery conditions [$Pd(OAc)_2$, n-Bu_4NCl, KOAc, CH_3CN], producing after decomplexation of the product complex triarylated compounds **37**. These could easily be dehydrogenated to polycondensed aromatic systems **38** (eg., with DDQ). A single crystal X-ray structure analysis of **37** (R'=H, R=CO_2CH_3) has been carried out [9]. This showed **37** to be the *syn*-adduct. The proposed mechanism of the Heck-type reaction of complexes **36** to the triarylated complexes **45** as the primary products is shown in Scheme 9 [9]. The reaction mechanism is close to the reaction mechanism proposed for the Heck-type arylation of norbornene (**23**, Scheme 5). The iodoarene adds oxidatively to Pd(0). The arylpalladium iodide adds *syn* to the η^6-dihydronaphtalene tricarbonylchromium(0) complex. The palladium undergoes a C-H insertion at the ortho-position of the added aryl group, leading to a palladacycle **B** (Scheme 9). This is opened by the addition of a second aryl iodide (**C** to **D**, Scheme 9). The sequence repeats with the addition of a third aryl iodide.



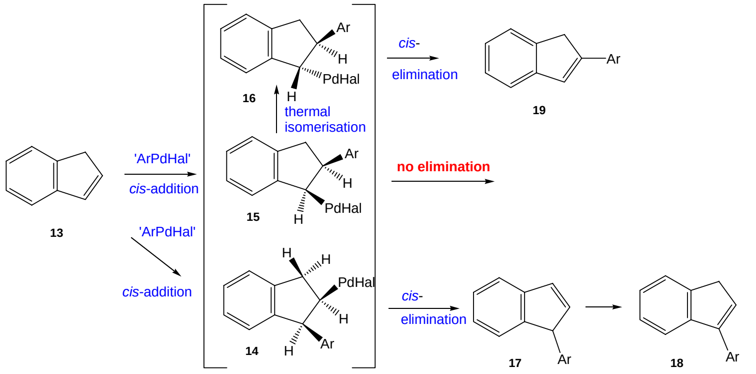
Scheme 1. General mechanism of the Heck reaction



Options for cyclic olefins in the Heck-reaction

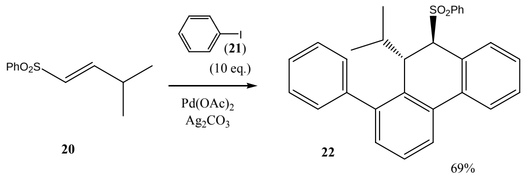
Scheme 2. Difficulties in the Heck olefination with cyclic alkenes

Problems associated with cyclic alkenes in the Heck-reaction
(Example Heck reaction with Indene as Olefin Component)



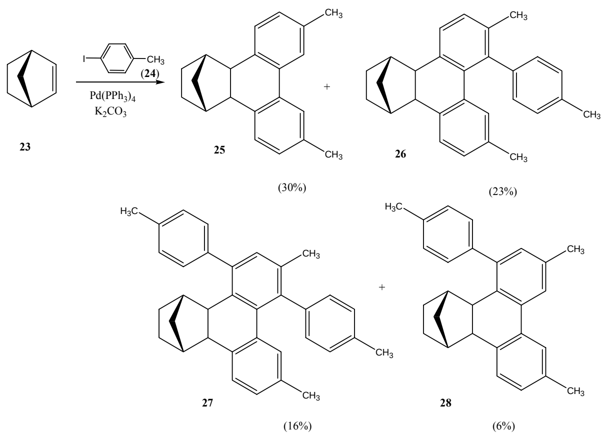
(I. E. Nifant'ev et al. 2000)

Scheme 3. Different outcomes of the Heck reaction with indene as starting material



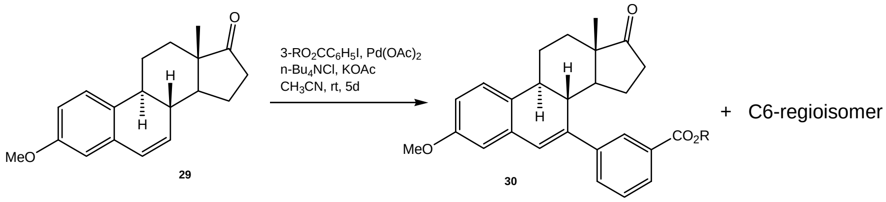
(J. Carretero *et al.* 2001)

Scheme 4. Heck reaction with vinylsulfones

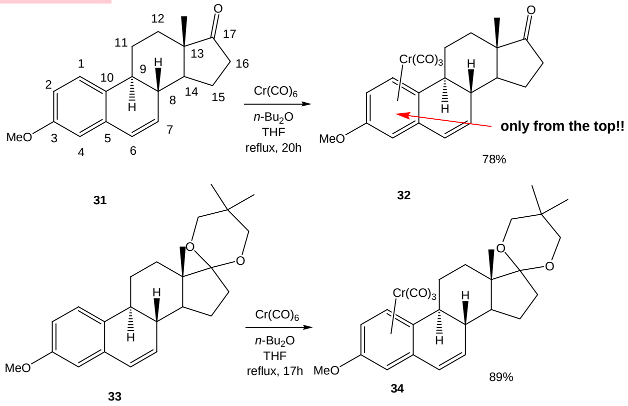


(M. Catellani)

Scheme 5. Oligoarylation in a Heck reaction with norbornene



New Syntheses and Applications from Steroidal Research



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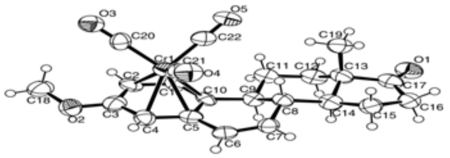
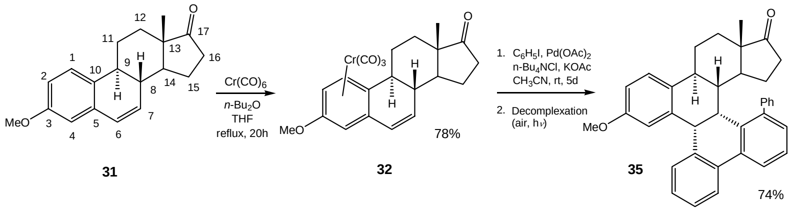


X-ray crystal structure of complex **32**

Change of Reaction Pathway - Example C-C coupling reaction of Estratetraenes with Aryl iodides under Heck reaction conditions (specifically, under Jeffery-conditions)

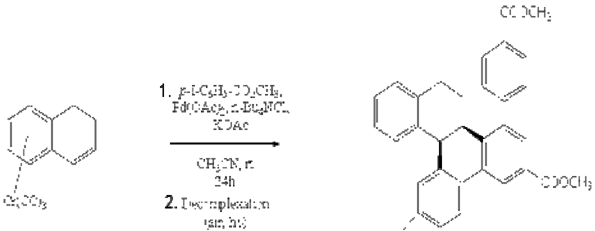


31 **32** **35**

New Syntheses and Applications from Steroidal Research

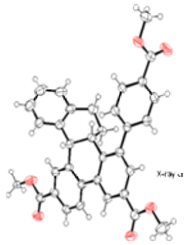
Scheme 6. Preparation of η^6-estra-1,3,5(10),6-tetraen-17-one tricarbonylchromium (0) and its triarylation in a Heck reaction under Jeffery conditions

A Triarylation of the olefin with concomitant ring closure reaction occurs!



(70%)

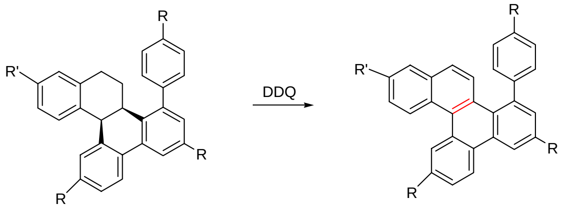
37d



J. Chem. Soc., Chem. Commun. **2002**, 3060

Scheme 7. Triarylation of η^6-dihydronaphthalene tricarbonylchromium (0) in a Heck-type reaction under Jeffery conditions

Towards Polycondensed Aromatic Systems



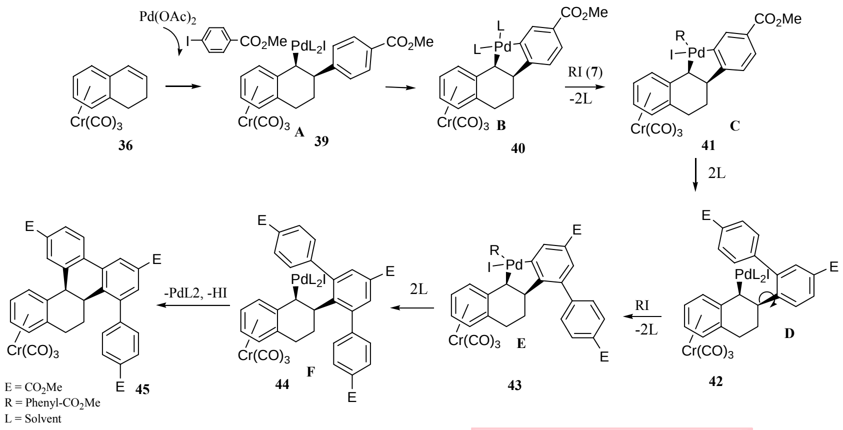
37

37a: R' = OMe, R = CO_2Me
37b: R' = OMe, R = H
37c: R' = H, R = CF_3

38a: R' = OMe, R = CO_2Me (84%)
38b: R' = OMe, R = H (92%)
38c: R' = H, R = CF_3 (73%)

Scheme 8. Dehydrogenation of the primary products to polycondensed aromatic substances

Proposed Mechanism



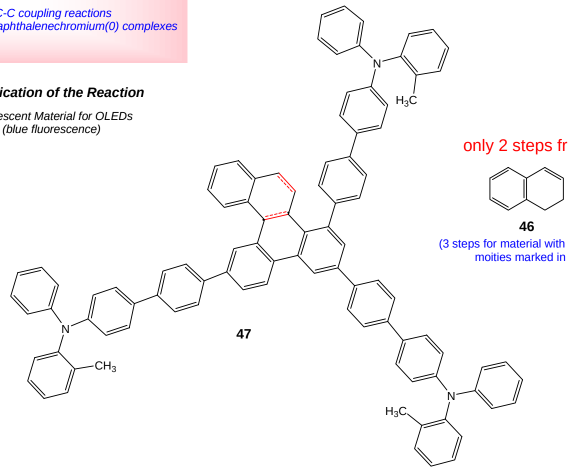
C-C coupling reactions
with dihydronaphthalenechromium(0) complexes

Scheme 9. Proposed Mechanism of the reaction

C-C coupling reactions
with dihydronaphthalenechromium(0) complexes

Application of the Reaction

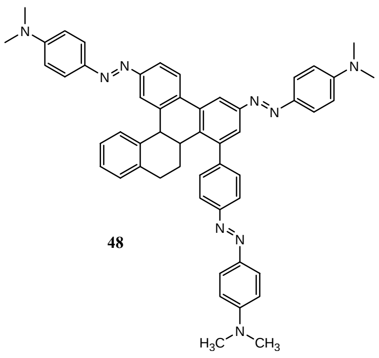
Fluorescent Material for OLEDs
(blue fluorescence)



only 2 steps from

46

(3 steps for material with two olefinic moities marked in red)



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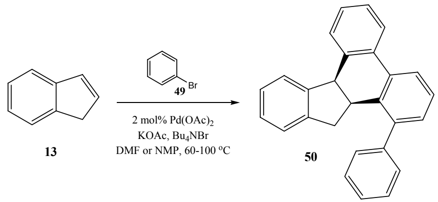
Scheme 10. Expanded pi-systems for electro-optical applications

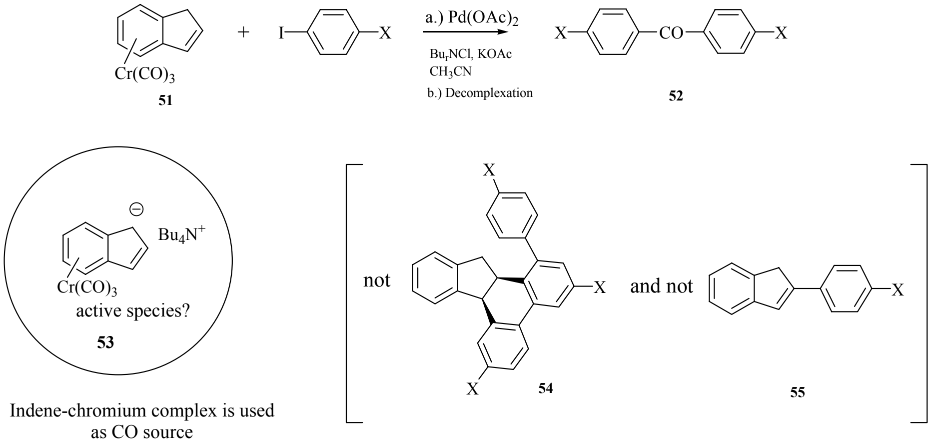
Subsequently, the authors have investigated the course of the reaction with η^6-indene tricarbonylchromium(0). A. de Meijere et al. had shown that indene was of the few cyclic alkenes that could undergo Heck-type oligoarylation [10], albeit with relatively low yield (Scheme 11).



A. de Meijere et al.

Scheme 11. Triarylation of indene under Heck-type conditions (A. de Meijere)

When a deaerated mixture of η^6-indene tricarbonylchromium(0), iodobenzene, tetrabutylammonium chloride (Bu_4NCl) and K_2CO_3 with a catalytic amount of palladium (II) acetate [$Pd(OAc)_2$] was reacted in acetonitrile, benzophenone was isolated in 55% yield after aerating the reaction solution. Neither the expected triarylated product **54** nor the 2-arylated indene **55** was observed (Scheme 12). Clearly, the keto-carbonyl function of the benzophenone stems from the indene tricarbonylchromium(0) complex. Under the conditions described, a number of substituted aryl iodides could be converted to benzophenones with ease (Scheme 13, Table 1). These reactions were carried out at room temperature (rt).



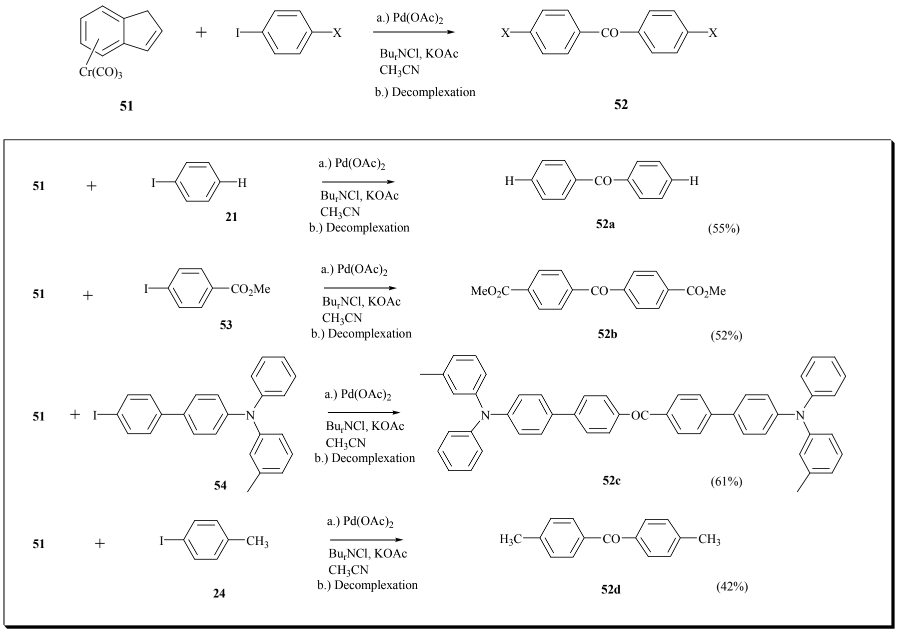
Scheme 12. Outcome of the reaction of η^6-indene tricarbonylchromium(0) with iodoarenes under Heck type conditions

There are precedents for the direct carbonylation of aryl iodides with metal carbonyls to provide symmetric benzophenones, albeit often at higher reaction temperatures. Thus, J.-J. Brunet could show that with a bimetallic pre-catalyst $Fe(CO)_5$-$Co_2(CO)_8$, iodobenzene could be converted to a mixture of benzophenone, benzoic acid, and biphenyl (cat. Bu_4NBr, 20 eq. NaOH, benzene, H_2O, 60 ^oC). [11,12] Also, J.-J. Brunet could show that the reaction of iodobenzene with $Bu_4N^+HFe(CO)_4^-$ in a biphasic medium of benzene and aq. NaOH under a CO atmosphere affords benzophenone. A radical mechanism was proposed initiated by an SET process from $Bu_4N^+HFe(CO)_4^-$ to iodobenzene to give a phenyl radical intermediate. [13] Subsequently, M. Larhead et al. have forwarded a fast microwave-aided synthesis of symmetric benzophenones from aryl iodides from aryl iodides and $Co_2(CO)_8$ in the presence of air. [14] Here, a radical reaction was suggested to happen after the thermal cleavage of $Co_2(CO)_8$ into $Co(CO)_4$, without details given of the reaction steps themselves.

On the other hand, a larger number of carbonylation reactions are known with palladium as a catalyst. Here, however, usually the aryl halide is reacted in presence of an aryl boronic acid or an arylstannane in a Stille type reaction, which gives access also to non-symmetric benzophenones. Often, the reactions are performed in a carbon monoxide atmosphere, although again metal carbonyls have been used either as catalyst or as the supplier itself of the CO functionality. In one case, even a η^6-arene metaltricarbonyl(0) complex has been used. Crucially, the reaction conditions determine the outcome of the transformations as also “normal” coupling reactions have been performed with arene metaltricarbonyl(0) complexes without carbonylation.

Whether the reaction here described operates by an SET initiated process, perhaps from a tetrabutylammonium η^6-indene tricarbonylate, via a radical mechanism and whether the palladium species functions in the role of a redox mediator or whether it possesses a function at all, still needs to be assessed.

The reaction of aryl halide with indene-chromium complex under Heck reaction conditions
- Synthesis of symmetically substituted benzophenones



Scheme 13, Table 1. Benzophenones from the reaction of η^6-indene tricarbonylchromium(0) with iodoarenes under Heck type conditions

Conclusion

The authors could show that Heck–type reaction of η^6-dihydronaphthalene tricarbonylchromium(0) complexes with iodoarenes under Jeffery conditions leads after decomplexation to triarylated products **37**. The stereo- and regiochemistry of these products could be affirmed by X-ray crystal structure of **37d**. The η^6-dihydronaphthalene unit can be part of more complicated structures such as estrone derived **31**/**32** without changing the course of the reaction. The reaction of η^6-Indene tricarbonylchromium(0) with iodoarenes, however, leads to benzophenones without incorporation of the indene structure.

Experimental

General. – Melting point were measured on a Yanaco microscopic hot-stage and are uncorrected. Infrared spectra were measured with a JASCO IR-700 machine. In the text w (weak), m (middle), s (strong) denote qualitatively the band intensities. ^{1}H and ^{13}C-NMR spectra were recorded with a JEOL EX-270 [^{1}H at 270 MHz, ^{13}C at 67.8 MHz], a JEOL 395 [^{1}H at 400 MHz and ^{13}C at 100.4 MHz] or a JEOL JNM-LA 600 (600 MHz [^{1}H] and 150.8 [^{13}C]). The chemical shifts are relative to TMS (solvent $CDCl_3$, unless noted otherwise). Assignments of the signals were aided by DEPT (= Distortionless Enhancement by Polarisation Transfer) measurements; (+) denotes primary and tertiary, (-) secondary and (C_{quat}) quaternary carbon atoms. Mass spectra were measured with a JMS-01-SG-2 spectrometer (EI, 70 eV, unless noted otherwise). Column chromatography was carried out on Wakogel. The solvents were used as supplied. Pyridine (over KOH), methanol (over Mg), dichloromethane (over CaH_2), and chloroform (over $CaCl_2$) were dried according to standard procedures. Dibutyl ether (DBE), tetrahydrofuran (THF) and diethyl ether were dried over sodium ketyl. The η^6-aryl tricarbonylchromium complexes were prepared by reacting the requisite arene (dihydronaphthalene, indene or estra-1,3,5(10),6-tetraen-17-one) with chromium hexacarbonyl in a refluxing solvent mixture of dibutyl ether and THF (10:1 *v*/*v*) under inert atmosphere. The products were purified by column chromatography on silica gel (deaerated hexane-ether).

Triarylation of 36 in a Heck reaction under Jeffery conditions: A mixture of **36** (50 mg, 0.19 mmol), $Pd(OAc)_2$ (21 mg, 0.09 mmol), methyl 4-iodobenzoate (150 mg, 0.6 mmol), KOAc (46 mg, 0.5 mmol) and *n*-Bu_4NCl (105 mg, 0.6 mmol) in acetonitrile was stirred under inert atmosphere for 24h at rt. Thereafter, the solution was aerated and exposed to light. Insoluble material was filtered off, and the concentrated filtrate was subjected to column chromatography on silica gel (hexane/$CHCl_3$ 1:1) to give **37d** (70 mg, 70%) as colorless crystals, mp. 287 ^oC; ν_{max} (KBr/cm^{-1}) 2930, 2854, 1720, 1606, 1490, 1436, 1261, 1243, 1113, 870, 804, 766; δ_H (600 MHz, $CDCl_3$) 1.60 – 1.64 (1H, m), 1.69 – 1.75 (1H, m), 2.58 – 2.66 (2H, m), 3.17 (1H, ddd, J = 13.2 Hz, J = 4.5 Hz, J = 3.5 Hz), 3.82 (3H, s, CO_2CH_3), 3.94 (3H, s, CO_2CH_3), 3.97 (3H, s, CO_2CH_3), 4.20 (1H, d, J = 4.5 Hz), 7.10 (1H, bd, ^3J = 7.3 Hz), 7.22 – 7.28 (3H, m), 7.42 (2H, d, ^3J = 8.5 Hz), 7.46 (1H, brs), 7.92 (1H, d, ^4J = 1.6 Hz), 7.98 (1H, d, ^3J = 7.8 Hz), 7.99 (1H, d, ^3J = 7.8 Hz), 8.09 (2H, d, ^3J = 8.5 Hz), 8.57 (1H, d, ^4J = 1.6 Hz); δ_C ($CDCl_3$, 150.8 MHz) 23.6, 28.3, 36.0, 42.2, 52.0, 52.2, 52.3, 124.5, 125.7, 126.4, 127.4, 127.8, 128.4, 128.5, 128.9, 129.2, 129.4, 129.5, 129.6, 129.8, 130.2, 130.9, 131.5, 133.4, 135.2, 135.8, 137.2, 138.8, 141.0, 143.9, 144.9, 166.7, 166.8, 166.9; MS (EI, 70 eV) *m/z* (%) 532 (M^+, 100), 501 (13), 399 (24), 339 (28), 104 (58). HRMS calcd. for $C_{34}H_{28}O_6$: 532.1886. Found: 532.1889. Calcd. C, 76.67; H, 5.29%. Found: 76.10; H, 5.31%.

Oxidative decomplexation of the triarylated complexes 45: A deaerated solution of **45-OMe(CO_2Me)$_3$** (40 mg, 0.6 mmol), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (60 mg, 0.2 mmol) in benzene (2 mL) was heated at 80 °C for 16 h. Purification of the product by column chromatography (SiO_2, 20 cm, hexane), gave **38a** as a colorless solid in (30 mg, 80 %) as a colorless solid; mp. 229 °C; ν_{max} (KBr/cm^{-1}) 2950 (w), 1722 (s, CO), 1605 (w), 1497 (w), 1435 (m), 1255(s), 1115(m),1043 (w), 763 (w); δ_H (270 MHz, $CDCl_3$) 3.90 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.10 (1H, d, J = 3.0 Hz), 7.24 (1H, dd, ^3J = 6.9 Hz, ^3J = 3.0 Hz), 7.35 (dd, 1H, ^3J = 9.6 Hz, J = 1.6 Hz), 7.42 (dd, 1H, ^3J = 6.9 Hz), 7.48 (d, 1H, ^3J = 9.6 Hz), 7.92 (d, 1H, ^3J = 9.6 Hz), 8.01 (d, 1H, ^3J = 8.3 Hz), 8.06 (d, 1 H, ^3J = 8.6 Hz), 8.25 (dd, 1H, ^3J = 8.3 Hz, J = 1.6 Hz), 8.48 (s, 1H), 8.70 (d, 1H, ^3J = 9.6 Hz), 8.79 (d, 1H, ^3J = 8.6 Hz), 9.33 (s, 1H), 9.41 (s, 1H); δ_C ($CDCl_3$, 67.8 MHz) 52.1, 52.2, 52.5, 55.5, 106.9, 118.1, 123.8, 124.3, 124.5, 125.0, 125.1, 125.7, 125.9, 126.8, 127.2, 127.4, 128.2, 129.1, 129.3, 129.5, 129.7, 130.3, 130.4, 130.5, 131.3, 132.0, 133.9, 135.2, 139.6, 149.0, 158.4, 166.8, 166.9, 167.1; MS (EI, 70 eV) *m/z* (%) = 558 [M $^{+1}$] (100), 529 ($M^{\tilde{+}}$-CHO, 7), 493 ($M^{\tilde{+}}$-CO, -OCH_3, 11), 440 (13), 397 (10), 350 (3), 337 (12), 298 (3), 263 (4), 236 (2), 195 (2), 168 (6), 145 (4), 105 (3), 83 (4), 69 (4). HRMS ($C_{35}H_{26}O_7$): Calcd. 558.1679, Observed 558.1680.

Example of the preparation a benzophenone 52 from η^6-indene tricarbonylchromium(0) (51) and an aryl iodide: 4,4'-dimethylbenzophenone (**52d**). - η^6-Indene tricarbonylchromium(0) (**51**, 106 mg, 0.42 mmol) was added to a deaerated mixture of 4-iodotoluene (**24**, 321 mg, 1.46 mmol), $Pd(OAc)_2$ (9.4 mg, 4.2.10-5 mol), tetrabutylammonium chloride (Bu_4NCl, 292 mg, 1.05 mmol) and K_2CO_3 (174 mg, 1.25 mmol) in dry acetonitrile (1 mL), and the resulting reaction mixture was stirred for 50h at rt. Thereafter, it was poured into water (20 mL) and extracted with chloroform (2 X 15 mL). The organic phase was dried over anhydrous $MgSO_4$, left to stand in daylight for 10 h, and thereafter it was concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel (hexane : ether = 3 – 1) to give 4,4'-dimethylbenzophenone **52d** (64 mg, 42%) as pale yellow prisms; mp. 90 °C [Lit. 90 – 93 °C]; ν_{max} (KBr/cm^{-1}) 1651, 1605, 1315, 1296, 1177, 1148, 1112, 930, 843, 826, 750, 641; δ_H (270 MHz, $CDCl_3$) 2.44 (6H, s, 2 CH_3), 7.27 (4H, d, ^3J = 7.5 Hz), 7.70 (4H, d, ^3J = 7.5 Hz); δ_C (67.8 MHz, $CDCl_3$) 21.6 (2C, CH_3), 128.9 (4C, CH), 130.2 (4C, CH), 135.3 (2C, C_{quat}), 142.9 (2C, C_{quat}), 196.5 (C_{quat}, CO); MS (EI, 70 eV) *m/z* (%) 210 (M^+, 10), 119 (100).

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