

Aqueous organometallic chemistry: synthesis and characterization of γ , δ unsaturated alkynyl substituted Fischer carbene complexes of group 6 transition metals

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A number of γ , δ unsaturated alkynyl substituted carbene complexes $[(CO)_5M=C(OCH_3)CHR(CH_2C\equiv CH)]$, 4–7 (4: M = Cr, R = $CH_2C\equiv CH$; 5: M = Mo, R = $CH_2C\equiv CH$; 6: M = W, R = $CH_2C\equiv CH$ and 7: M = W, R = $CH(CH_2)_2CH_3$) have been synthesized from group 6 metal–carbene complexes $[(CO)_5M=C(OCH_3)CH_3]$, 1–3 (1: M = Cr, 2: M = Mo, 3: M = W) under biphasic reaction conditions. The alkoxy group has been readily replaced by amino groups in 6 as rotamers 8a–b and 9a–b (*syn* and *anti* isomers), $(CO)_5WC(NHR')-CH(CH_2CCH)_2$, [8a–b: R' = CH_3 ; 9a–b: R' = CH_2Ph]. Further, when a CH_2Cl_2 solution of 4–6 was stirred at room temperature in the presence of trimethylamine-*N*-oxide for 30 min, the ester derivative $CO(OCH_3)CH(CH_2CCH)_2$ was formed. UV–Vis spectra have been recorded for both alkoxy and amino carbene complexes, 4–8, which showed the gradual hypsochromic shift of metal-to-ligand charge transfer bands from Cr to W. Compounds 4–9 have been isolated as yellow oils in moderate to good yields and they have been characterized by IR, 1H , ^{13}C NMR spectroscopic analysis.

Keywords: Aqueous organometallic chemistry, biphasic reaction, transition metals, unsaturated alkynyl carbene complex.

THE usefulness of Fischer carbene complexes has been extensively established during past two decades and they are among the most versatile organometallic reagents for organic synthesis^{1–9}. The number and utility of different types of reactions of these complexes that have been reported since their discovery are far too numerous to list¹⁰. Since the most common route to these complexes involves reaction of organolithium or organomagnesium reagents with metal hexacarbonyl, sensitive functionalities are incompatible with such a procedure. Therefore, alkylation of the acidic α -carbon in alkylcarbene complexes is often a method of choice to prepare functionalized Fischer carbene complexes^{11,12}. Alkylations are usually carried out in tetrahydrofuran using *n*-butyllithium as a base. However, certain limitations are encountered with this protocol^{13–15}. In this communication, we describe the

synthesis of γ , δ unsaturated alkynyl Fischer carbene complexes 4–7 in a biphasic medium mediated by a phase-transfer catalyst. This procedure allows efficient dialkylation with reactive electrophiles and secondary centres can be alkylated in high yield.

All the operations were conducted under Ar atmosphere using standard Schlenk techniques and Glove Box. Solvents were distilled and degassed prior to use under argon. $Cr(CO)_6$, $Mo(CO)_6$, $W(CO)_6$, propargyl bromide, tetrabutylammonium bromide and *n*-BuLi purchased were of analytical grade and used without further purification. MeLi was prepared according to the procedure mentioned in the literature¹⁶. MeI, methylamine and benzylamine were purchased and freshly distilled prior to use. Group 6 Fischer carbene complexes, $[(CO)_5M=C(OMe)Me]$ (M = Cr, Mo, W) were prepared according to the procedure mentioned in the literature¹⁷. Chromatography was carried out on 3 cm of silica gel in a 2.5 cm dia column. Thin layer chromatography was carried on 250 mm dia aluminum-supported silica gel TLC plates (MERCK TLC plates). NMR spectra were recorded on 400 and 500 MHz Bruker FT-NMR spectrometer. Infrared spectra were obtained on a Nicolet 6700 FT-IR spectrometer. UV–Vis spectra were recorded using the JASCO V-650 spectrophotometer.

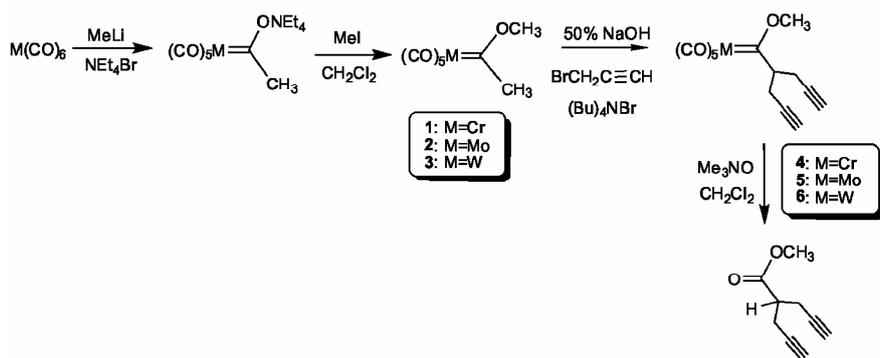
For the synthesis of 4–6, the CH_2Cl_2 (15*n* ml) solution of 1–3 (*n* mmol) was treated with 50% aqueous NaOH and propargyl bromide (3–5*n* mmol) in the presence of tetrabutylammonium bromide (0.1*n* mmol). The resulting mixture was stirred at room temperature until the starting material was consumed (verified by TLC). The colour of the solution changed from dark yellow to reddish-brown. The reaction mixture was diluted with water and extracted with dichloromethane, dried over sodium sulphate and the solvent removed under reduced pressure. The crude product was subjected to flash column chromatography. Elution with hexane: CH_2Cl_2 (80 : 20 v/v) yielded yellow 4–6.

4 (35%): 1H NMR (400 MHz, $CDCl_3$, 22°C): δ = 2.01 (t, 2H), 4.40 (p, 1H), 2.35–2.42 (m, 4H), 4.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 22°C): δ = 362.67 (Cr=C), 223.06 (CO), 215.9 (CO), 80.49 (C \equiv C), 65.73 (C \equiv C), 70.86 (OCH₃), 68.05 (CH), 29.85 (CH₂); IR (hexane): ν (CO) 2064, 1976, 1931, 3291 (C=C–H), 2294 (C \equiv C) cm^{-1} .

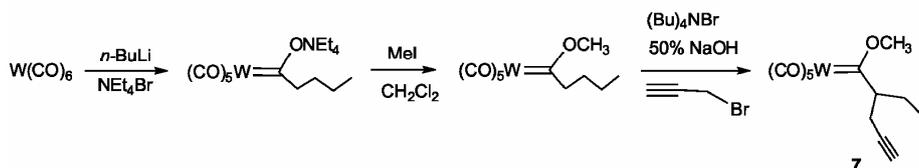
5 (20%): 1H NMR (400 MHz, $CDCl_3$, 22°C): δ = 2.01 (t, 2H), 4.37 (p, 1H), 2.32–2.49 (m, 4H), 4.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 22°C): δ = 352.28 (Mo=C), 205.80 (CO), 201.12 (CO), 78.81 (C \equiv C), 69.48 (C \equiv C), 74.97 (OCH₃), 71.94 (CH), 29.81 (CH₂); IR (hexane): 2068, 2017, 1902 ν (CO), 3295 (C \equiv C–H), 2252 (C \equiv C) cm^{-1} .

6 (40%): 1H NMR (400 MHz, $CDCl_3$, 22°C): δ = 2.02 (t, 2H), 4.37 (p, 1H), 2.32–2.49 (m, 4H), 4.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 22°C): δ = 336.05 (W=C), 203.25 (CO), 196.98 (CO), 80.51 (C \equiv C), 67.92 (C \equiv C), 71.01 (OCH₃), 70.65 (CH), 20.19 (CH₂); IR (hexane): 2071, 2046, 1916 ν (CO), 3309 (C=C–H), 2149 (C \equiv C) cm^{-1} .

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Scheme 1. Synthesis of dialkynyl substituted Fischer carbene complexes, 4–6.



Scheme 2. Synthesis of mono alkynyl substituted Fischer carbene complex, 7.

For the synthesis of **7**, the (*n*-butyl(methoxy)carbene)-tungsten complex (0.23 mmol) and tetrabutylammonium bromide (0.023 mmol) in dichloromethane (15 ml) was treated with 50% aqueous NaOH and propargyl bromide (0.47 mmol). The resulting mixture was stirred at room temperature until the starting material was consumed (TLC). The colour of the solution changed from dark yellow to reddish-brown. The reaction mixture was diluted with water and extracted with dichloromethane, dried over sodium sulphate and the solvent removed under reduced pressure. The crude product was subjected to flash column chromatography to yield the pure product (45%). Elution with hexane : CH₂Cl₂ (90 : 10 v/v) yielded yellow **7**.

7 (45%): NMR (400 MHz, CDCl₃, 22°C): δ = 4.20 (m, 1H), 4.63 (s, OCH₃), 2.18–2.37 (m, 2H), 1.96 (t, 1H), 1.26–1.60 (m, 7H); ¹³C NMR (100 MHz, CDCl₃, 22°C): δ = 340.22 (W=C), 203.34 (CO), 197.30 (CO), 81.60 (C≡C), 70.19 (C≡C), 70.13 (OCH₃), 70.71 (CH), 34.15 (CH₂), 20.76 (CH₂), 20.25 (CH₂), 14.51 (CH₃); IR (hexane): 2071, 2010, 1919 ν (CO), 3422 ν (N–H), 2350 ν (C≡C) cm⁻¹.

For the aminolysis of **6**, to a solution of **6** (*n* mmol) in CH₂Cl₂ (10*n* ml) amine (methyl and benzyl) (1.5*n* mmol) was added at 0°C and the reaction mass stirred at 0°C for 15 min. The colour of the solution changed from yellow to yellowish-green. The reaction mixture was dried over sodium sulphate and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography using 35% CH₂Cl₂ : hexane mixture as eluent to yield pure **8–9**.

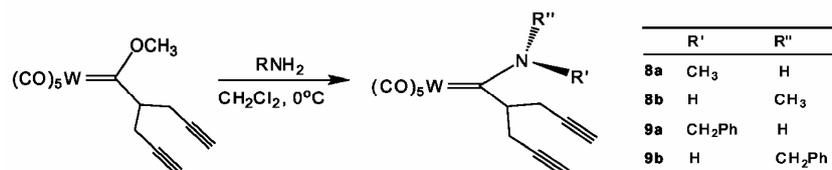
8a–b (30%) (combined NMR): NMR (400 MHz, CDCl₃, 22°C): δ = 9.13–9.31 (s, 1H), 3.16–3.81 (m, 1H), 2.61–2.64 (m, 4H), 2.0–2.07 (t, 2H), 3.23–3.70 (d, 3H); ¹³C NMR (100 MHz, CDCl₃, 22°C): δ = 267.52–265.21

(W=C), 200.92–201.10 (CO), 198.27–198.48 (CO), 80.33–80.56 (C≡C), 71.03–71.94 (NCH₃), 72.02–72.09 (C≡C), 58.65 (CH), 24.65–27.85 (CH₂); IR (hexane): 2063, 1980, 1895 ν (CO), 3448 ν (N–H), 2345 ν (C≡C) cm⁻¹.

9a–b (24%) (combined NMR): NMR (400 MHz, CDCl₃, 22°C): δ = 9.09–9.25 (s, 1H), 7.35–7.49 (m, 5H), 4.85–5.01 (d, 2H), 3.26–3.83 (m, 1H), 2.61–2.65 (m, 4H), 1.98–2.09 (t, 2H); ¹³C NMR (100 MHz, CDCl₃, 22°C): δ = 260.96–266.89 (W=C), 200.77–202.30 (CO), 197.79–198.29 (CO), 80.05–80.50 (C≡C), 127.95–129.69 (Ph), 58.60–60.68 (C≡C), 71.12–72.11 (CH₂Ph), 50.60–54.07 (CH), 134.12 (C–Ph), 29.70 (CH₂); IR (hexane): 2062, 1990, 1891 (CO), 3449 ν (N–H), 2385 ν (C≡C) cm⁻¹.

Let us now consider the isolation and characterization of mono and dialkynyl Fischer carbene complexes, **4–7**. As shown in Schemes 1 and 2, when the complexes **1–3** in dichloromethane were treated with excess of propargyl bromide in the presence of 50% aqueous NaOH and 10 mol% of tetrabutylammonium bromide at room temperature, **4–7** were isolated in good yields. The biphasic reaction conditions were found to be highly suitable for functionalizing the Fischer carbene complexes by facile C–C bond formation, i.e. C-alkylation. It was observed that the alkylation of **1–3** with propargyl bromide proceeded efficiently with K₂CO₃ as the base and 18-crown-6 as the phase transfer catalyst, to give the dipropargylated Fischer carbene complexes **4–6**. However, the isolated yield using aqueous NaOH in dichloromethane was more than that obtained with non-aqueous medium.

Compounds **4–7** have been characterized spectroscopically. The IR absorption spectra of compounds **4–7** are distinguished by the presence of a series of bands in the region of 1700–3500 cm⁻¹. The absorption band positioned at 2149–2350 cm⁻¹ can be attributed to the presence



Scheme 3. Synthesis of amino dialkynyl substituted Fischer carbene complexes.

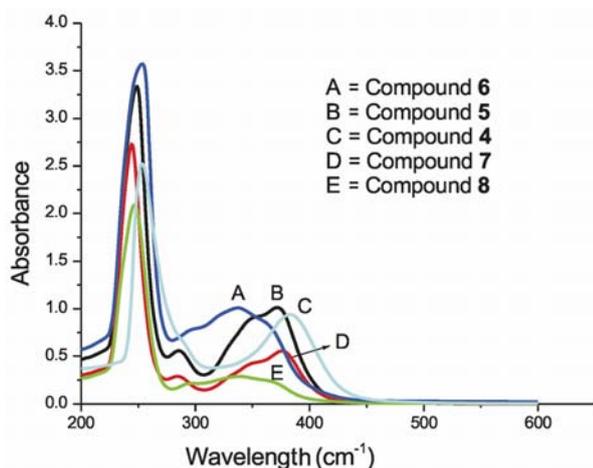


Figure 1. UV-visible spectra of **4–8** in CH₂Cl₂.

of two C≡C moieties. Likewise, the absorption band at 3270–3300 cm⁻¹ can be assigned to the acetylenic hydrogen (–C≡C–H). The acetylenic hydrogen has been confirmed by ¹H NMR, which shows the characteristic peak in the region δ = 1.91–2.12 ppm. ¹³C NMR further confirms the presence of both acetylenic and carbene carbon atoms which appeared in the region 70–82 and 260–365 ppm respectively. The IR spectrum in the carbonyl region shows three terminal carbonyl frequencies in the range 1910–2089 cm⁻¹, which are assigned to M(CO)₅ fragments (M = Cr, Mo and W). ¹³C NMR also shows the presence of metal carbonyl ligands at δ = 195–223 ppm. Although all our attempts to obtain suitable analysis for **4–7** failed, the spectroscopic data satisfactorily support the composition and structure of **4–7**, as shown in Schemes 1 and 2.

As shown in Scheme 1, chemical modification of **4–6** by removing the M(CO)₅ fragment by rapid oxidation using 1 equiv of trimethylamine-*N*-oxide (TMNO) in dichloromethane resulted in the clean formation of carboxylic ester derivative [CO(OCH₃)CH(CH₂CCH)₂] in good yield¹⁸.

Displacement of the alkoxy group of a carbene complex by an amine to produce aminocarbene complexes are versatile starting material for the synthesis of nitrogen-containing heterocycles^{19–22}. Such a reaction permits the attachment of diverse organic groups to a metal–carbene complex²³. For instance, the synthesis of peptides and the R-amino function of amino acids has been protected in the reaction with alkoxy-carbenes to give aminocarbene-labelled peptides²⁴. More recently, this reaction has been

used for protein labelling²⁵ and design of bioactive surfaces for protein immobilization²⁶. As shown in Scheme 3, aminolysis of **6** with methyl amine and benzyl amine at 0°C in CH₂Cl₂ furnished amino dialkyne carbene complexes **8a–b** and **9a–b** as rotamers (*syn* and *anti*).

Compounds **8a–b** and **9a–b** have been isolated in 30% and 24% collective yield from the reaction mixture. The IR spectrum of **8a–b** is distinguished by the presence of one absorption band in the region 3441–3449 cm⁻¹, attributable to the presence of the N–H bond. All the characteristic peaks for CO and –C≡C–H stretching are also observed in the IR spectra. The presence of acetylenic hydrogen has been confirmed by ¹H NMR that shows the characteristic peak at δ = 1.98–2.05 ppm. ¹H NMR shows the presence of *N*-methyl and *N*-benzyl protons at δ = 3.45 and 4.82 ppm respectively. The N–H resonance appeared at 9.15–9.18 ppm. A multiplet at 7.48 ppm appeared in the ¹H NMR due to the presence of a benzene ring in **9a–b**. The presence of all the above characteristic peaks was further supported by ¹³C NMR spectroscopy, which shows the carbene carbon of **8a–b** and **9a–b** at 266.3 and 268 ppm respectively. The chemical shifts of the amino carbene carbon appear at comparatively up field than the carbene carbon of alkoxy analogs¹⁸.

The differences between alkoxy and amino Fischer carbene complexes are of interest. Since the energy of the π*_{C–N} orbital is fairly close to that of π*_{C–O} (carbonyl on the metal), π bond character is delocalized toward the M–C_{carbonyl} creating a partial double-bond character of the C–N bond in the amino carbene complexes. As amino-carbene complexes have a higher barrier to rotation of the C–N bond, we expected that some distinction between features of the *syn* and *anti* conformers should be apparent in their room-temperature NMR spectra. The ¹H NMR and ¹³C NMR spectra of aminocarbene complexes (**8** and **9**) indeed showed the presence of rotamers (*syn* and *anti* conformers) at ambient temperature²⁷. In an attempt to calculate the coalescence temperature and activation energy, we recorded the variable-temperature ¹H NMR of the isomers (**9a–9b**). Upon increasing the temperature the N–H resonances become sharpens, which may be due to the rapid interconversion. Further, on heating the solution at 100°C the peak disappeared, which may be due to the substantial decomposition of the amino carbene complexes.

The study of the UV–Vis spectra between alkoxy and amino carbene complexes is particularly important for gaining insight into how the group-6 metals play a significant role in affecting the charge transfer. The monometallic

carbene complexes **4–8** are strongly coloured, ranging from yellow to deep yellow. Thus, the charge transfer bands in the UV–Vis region of the carbene complexes have been recorded in order to verify if they showed any behaviour compatible with other alkoxy and amino carbene complexes reported in the literature²⁸. As shown in Figure 1, compounds **4–8** exhibit two major absorption bands in the visible region. The absorption bands appeared around ca. 400 nm, which may be attributed to the metal-to-ligand charge transfer, consistent with earlier findings on related Fischer carbene complexes²⁸. The less intense absorption band at ca. 383 nm for **4** shifted slightly blue in molybdenum complex **5** (371 nm), which shifted further in tungsten complex **6** (ca. 336 nm). On the contrary, the sharper and more intense band, arising from $\pi-\pi^*$ transition of the alkyne moieties in **4–8**, does not change substantially in different substituents.

We have described the synthesis of a number of γ , δ unsaturated alkynyl substituted Fischer carbene complexes in good yield under biphasic reaction conditions. Further, the displacement of the alkoxy group of the carbene complexes was performed by amines to synthesize amino carbene complexes, which are versatile starting materials for the synthesis of nitrogen-containing heterocycles.

- Dötz, K. H., Carbene complexes in organic synthesis. *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 587–608.
- Wulff, W. D., Abel, E. W. and Stone, F. G. A., Transition metal carbene complexes: cyclopropanation. In *Comprehensive Organometallic Chemistry II* (ed. Wilkinson, G.), Pergamon Press, Oxford, UK, 1995, vol. 12.
- Hegedus, L. S., Abel, E. W. and Stone, F. G. A., In *Comprehensive Organometallic Chemistry II* (ed. Wilkinson, G.), Pergamon Press, Oxford, UK, 1995, vol. 12.
- Doyle, M., Abel, E. W. and Stone, F. G. A., In *Comprehensive Organometallic Chemistry II* (ed. Wilkinson, G.), Pergamon Press, Oxford, UK, 1995, vol. 12.
- Harvey, D. F. and Sigano, D. M., Carbene–alkyne–alkene cyclization reactions. *Chem. Rev.*, 1996, **96**, 271–288.
- Huang, J., Wang, H., Wu, C. and Wulff, W. D., Intramolecular cyclohexadienone annulations of Fischer carbene complexes: model studies for the synthesis of phomactins. *Org. Lett.*, 2007, **9**, 2799–2802.
- Merlic, C. A., You, Y., McInnes, D. M., Zechman, A. L., Miller, M. M. and Deng, Q., Benzanulation reactions of Fischer carbene complexes for the synthesis of indolocarbazoles. *Tetrahedron*, 2001, **57**, 5199–5212.
- Hegedus, L. S., Chromium carbene complexes in the synthesis of molecules of biological interest. *Pure Appl. Chem.*, 1990, **62**, 691–698.
- Roy, P. and Ghorai, B. K., One-pot three-component synthesis of quinoxaline and phenazine ring systems using Fischer carbene complexes. *Beilstein J. Org. Chem.*, 2010, **6**, No. 52.
- Fischer, E. O. and Maasböl, A., On the existence of a tungsten carbonyl carbene complex. *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 580–581.
- Casey, C. P., *Reactive Intermediates*, Wiley, New York, 1985, vol. 3, p. 109.
- Casey, C. P., Metal carbene complexes in organic synthesis. In *Transition Metal Organometallics in Organic Synthesis* (ed. Alper, H.), Academic Press, New York, 1976, p. 189–233.
- Xu, Y. C. and Wulff, W. D., Alkylations of tetracarbonyl (phosphine)chromium and pentacarbonylchromium carbene complexes and their reactions with selected acetylenes. *J. Org. Chem.*, 1987, **52**, 3263–3275.
- Gander, J. R. and Bernasconi, C. F., Proton transfer from (methoxymethylcarbene)pentacarbonylchromium(0) in aqueous solution. *Organometallics*, 1989, **8**, 2282–2284.
- March, J., In *Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, Wiley, New York, 1992, 4th edn, p. 251.
- Lusch, M. J., Phillips, M. V., Sieloff, W. V., Nomura, G. S. and House, H. O., Preparation of low-halide methyl lithium. *Org. Synth.*, 1990, **7**, 346.
- Aumann, R. and Fischer, E. O., Übergangsmetall-Carben-Komplexe, IV. Addition von Isonitrilen an Methylmethoxycarben-pentacarbonyl-chrom(0). *Chem. Ber.*, 1968, **101**, 954–962.
- Mathur, P., Ghosh, S., Sarkar, A., Satyanarayana, C. V. V. and Puranik, V. G., Chemical modification of the metal–carbene appendage in new, trimetallic adducts of $\text{Fe}_2(\text{CO})_6(\mu\text{-EE}')$ (E = S, Se and E' = Se, Te) and alkynyl Fischer carbene complexes $(\text{CO})_5\text{M}=\text{C}(\text{OEt})(\text{C}=\text{CPh})$ (M = Cr, W). *Organometallics*, 1997, **16**, 4392–4398.
- Borel, C., Hegedus, L. S., Krebs, S. and Satoh, Y., Synthesis of amino- β -lactams by the photolytic reaction of imines with pentacarbonyl[(dibenzylamino)carbene]chromium(0). *J. Am. Chem. Soc.*, 1987, **109**, 1101–1105.
- Dötz, K. H., Schaffer, T. and Harms, K., Synthesis of nitrogen heterocycles by diastereoselective intramolecular aminocarbene annelation. *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 176–177.
- Klabunde, U. and Fischer, E. O., Two new chromium–carbonyl–carbene complexes. *J. Am. Chem. Soc.*, 1967, **89**, 7141–7142.
- Rahm, A., Wulff, W. D. and Rheingold, A. L., Preparation, characterization, and reactions of the first parent acetylene Fischer carbene complexes. *Organometallics*, 1993, **12**, 597–599.
- Weiss, K. and Fischer, E. O., Übergangsmetall-Carben-Komplexe, Pentacarbonyl(organylcarben)chrom- und -wolfram-Reste als Amino-Schutzgruppen für Peptid-Synthesen. *Chem. Ber.*, 1976, **109**, 1868–1886.
- Weiss, K. and Fischer, E. O., Übergangsmetall-Carben-Komplexe, Der Pentacarbonyl(phenylcarben)chrom(0)-Rest als Amino-Schutzgruppe für Peptid-Synthesen. *Chem. Ber.*, 1973, **106**, 1277–1284.
- Samanta, D., Sawoo, S., Patra, S., Ray, M., Salmain, M. and Sarkar, A., Synthesis of hydrophilic Fischer carbene complexes as organometallic marker and PEGylating agent for proteins. *J. Organomet. Chem.*, 2005, **690**, 5581–5590.
- Sawoo, S., Dutta, P., Chakraborty, A., Mukhopadhyay, R., Bouloussa, O. and Sarkar, A., A new bio-active surface for protein immobilisation via copper-free ‘click’ between azido SAM and alkynyl Fischer carbene complex. *Chem. Commun.*, 2008, 5957–5959.
- Amin, Sk. R., Nandi, M., Sathe, K. M., Jayaprakash, K. N. and Sarkar, A., Direct observation of orthogonal orientation of an aromatic ring attached to the carbene carbon in Fischer carbene complexes in solution: diastereotopicity of benzyl protons as a stereochemical probe. *Organometallics*, 1996, **15**, 3528–3533.
- Lage, M. L., Fernandez, I., Mancheno, M. J. and Sierra, M. A., Electronic structure of alkoxychromium(0)carbene complexes: A joint time dependent density functional theory/experimental study. *Inorg. Chem.*, 2008, **47**, 5253–5258.

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