En Suite Generation of Chromium Carbonyl Arene Complex Substituted Propargylic Cation and Anion Intermediates in Side-Chain Functionalizations†

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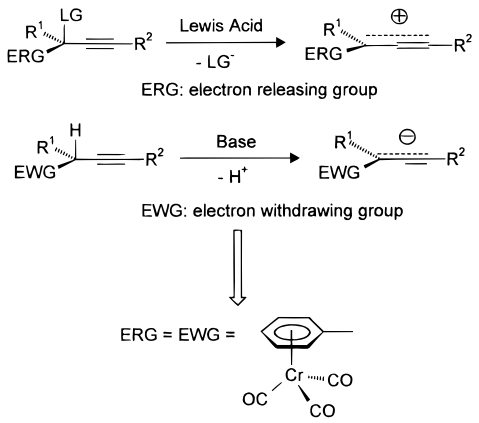
Summary: The (phenyl)Cr(CO)$_3$ substituent efficiently stabilizes both propargyl cations and anions. In subsequent trapping reactions of the anionic species that can be spectroscopically studied, the regioselectivity depends on the hardness of the attacking electrophile.

The advent of chromium carbonyl complexation of arenes has significantly enriched the synthetic repertoire in aromatic chemistry by opening new complementary ways of nucleophilic addition and substitution reactions on the benzoid core[1] as well as on the side chain.[2] Due to the space-filling nature of the chromium carbonyl tripod and the inherent planar chirality of *o*- or *m*-disubstituted arene complexes, diastereo- and enantioselective transformations can be conducted in excellent selectivities. In the past this has been impressively documented in comprehensive methodological studies and in natural product syntheses.[3] Electronically, the amphoteric nature of (arene)Cr(CO)$_3$ complexes, i.e., the stabilization of both anionic *and* cationic charge in benzylic position,[2,4,5] represents their most interesting feature and sets the stage for more sophisticated side-chain functionalizations. Here we communicate preliminary results on the successive generation of a (phenyl)Cr(CO)$_3$-stabilized propargyl cation and anion.

Recently, we showed that (arene)Cr(CO)$_3$-substituted propargyl cations are stable at low temperatures and can be regio- and diastereoselectively trapped with numerous nucleophiles.[6,7] However, the concept of the pronounced amphoteric nature of (arene)Cr(CO)$_3$ substituents[5] suggests that the stabilization of both propargyl cations and anions should be feasible upon applying the same (phenyl)Cr(CO)$_3$ group as electron-releasing (for propargyl cations) and as electron-withdrawing functionality (for propargyl anions) (Scheme 1). As a crucial factor, the functional group needs not to be altered to achieve two complementary effects.

Scheme 1



Thus, starting from a arene complex substituted propargyl acetate **1**, a complete ionization with boron trifluoride etherate is easily accomplished at −78 °C in dichloromethane to furnish a deep purple solution of the propargyl cation **2** (Scheme 2).[6a] This ambident organometallic electrophile is regioselectively trapped with anisole as a nucleophile to give the propargyl compound **3** with excellent *para*-selectivity.[8] After purification this

† This contribution is dedicated to Prof. Dr. Rudolf Knorr on the occasion of his 65th birthday.

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(5) For recent computational studies on the DFT level of theory see, for example: (a) Pfletschinger, A.; Dargel, T. K.; Bats, J. W.; Schmalz, H.-G.; Koch, W. *Chem. Eur. J.* **1999**, *5*, 537. (b) Merlic, C. A.; Walsh, J. C.; Tantillo, D. J.; Houk, K. N. *J. Am. Chem. Soc.* **1999**, *121*, 3596.

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(7) Müller, T. J. J.; Ansorge, M.; Polborn, K. *Organometallics* **1999**, *18*, 3690.

(8) **Synthesis of propargyl compound 3**: To a solution of 1.00 g (2.59 mmol) of acetate **1** in 15 mL of dichloromethane was added at −78 °C 1.4 equiv of boron trifluoride diethyl etherate, and the mixture was stirred for 55 min before a solution of 0.56 mL (5.18 mmol) of anisole in 0.4 mL of dichloromethane was added. After 115 min of stirring at −78 °C successively 20 mL of diethyl ether and 20 mL of water were added and the external cooling was removed. After extraction with diethyl ether and evaporation of the organic solvents in a vacuum the residue was crystallized at −20 °C from a mixture of diethyl ether/pentane to give 0.79 g (70%) of pale yellow microcrystals. Mp: 135 °C. ^{1}H NMR ([D$_6$]DMSO, 400 MHz): δ = 3.72 (s, 3H), 5.11 (s, 1H), 5.61−5.67 (m, J = 6.5 Hz, 2H), 5.74 (t, J = 6.2 Hz, 1 H), 5.88 (d, J = 6.3 Hz, 1H), 5.93 (d, J = 6.4 Hz, 1H), 6.92 (d, J = 8.7 Hz, 2H), 7.37−7.39 (m, 3H), 7.47 (d, J = 8.7 Hz, 2H), 7.49−7.51 (m, 2H). ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 40.13 (CH), 55.10 (CH$_3$), 84.67 (C$_{quat.}$), 88.41 (C$_{quat.}$), 93.01 (CH), 94.07 (CH), 94.28 (CH), 94.54 (CH), 95.13 (CH), 114.21 (CH), 115.45 (C$_{quat.}$), 122.33 (C$_{quat.}$), 128.53 (CH), 128.55 (CH, double intensity), 131.38 (CH), 132.78 (C$_{quat.}$), 158.63 (C$_{quat.}$), 233.67 (C$_{quat.}$, CO). MS (70 eV), *m*/*z* (%): 434 (M$^+$, 7), 350 (M$^+$ − 3 CO, 100), 298 (M$^+$ − Cr(CO)$_3$, 21). IR (KBr): $\tilde{\nu}$ = 1957 cm^{-1}, 1904, 1868. UV/vis (DMSO): λ_{max} (ϵ) = 317 nm (10200). Anal. Calcd for C$_{25}$H$_{18}$CrO$_4$ (434.41): C, 69.12; H, 4.18. Found: C, 69.13; H, 4.29.

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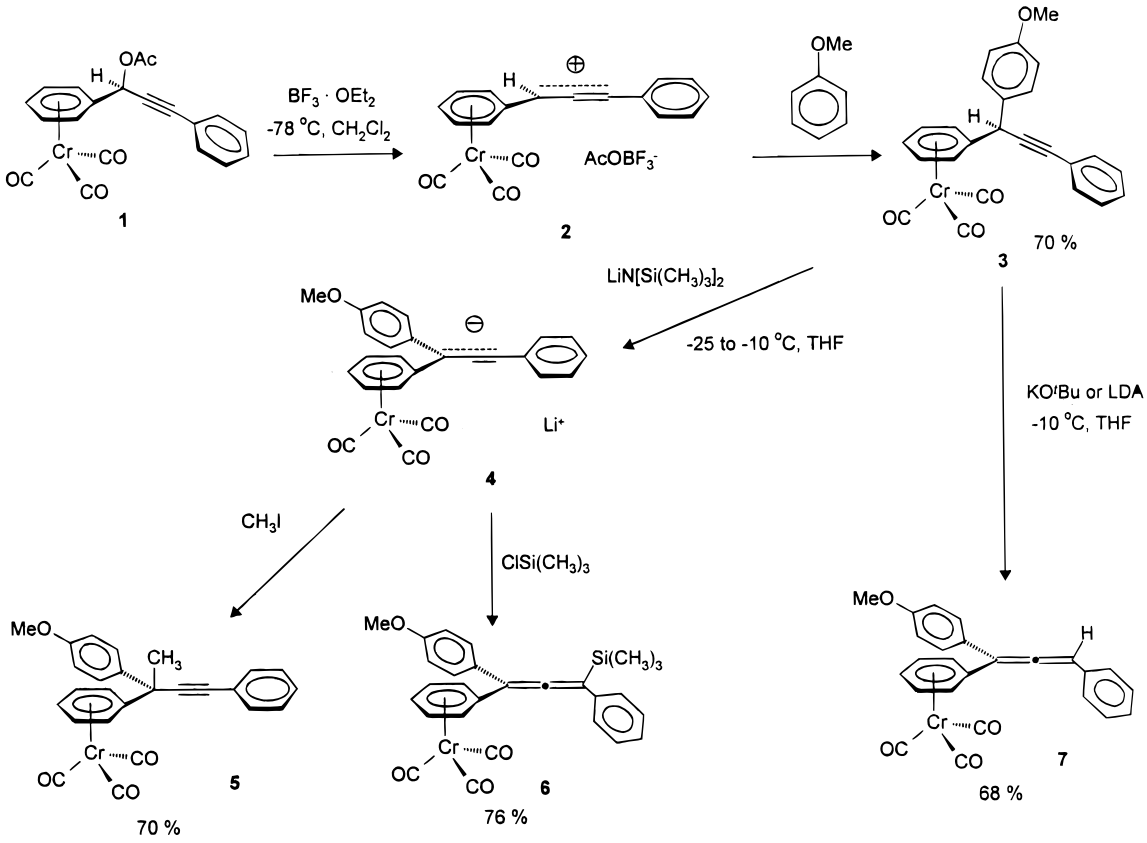
Scheme 2



propargyl derivative can be irreversibly deprotonated with lithium hexamethyl disilazane[9,10] (LiHDMS) at −25 °C in THF to give a deep red solution of the propargyl anion **4** (Scheme 2). The structural assignment is strongly supported by the UV/vis (−23 °C) and ^{13}C NMR (−55 °C) spectra of this intermediate. In the UV/vis spectrum (Figure 1) the appearance of two intense red-shifted absorption bands at 378 and 467 nm indicates the formation of a species with extended π-conjugation.

Characteristically, in the ^{13}C NMR spectrum (Figure 2) the downfield shift of the carbonyl resonance upon deprotonation (**3**, δ 234.5; **4**, δ 239.4; $\Delta\delta = +4.9$) follows from the generation of a delocalized negative charge in the side chain that exerts a strongly electron releasing effect on the chromium carbonyl arene fragment.[11] Furthermore, the most significant shifts can be observed for the resonances of the propargyl moiety[12] (Table 1). Upon deprotonation, the α-resonance (**3**, δ 42.5; **4**, δ 72.7) is shifted downfield by $\Delta\delta = +30.2$, in agreement with a change of hybridization at this center from sp^3 to sp^2. Together with the smaller ionization shifts for the β- (**3**, δ 88.7; **4**, δ 101.9; $\Delta\delta = +13.2$) and γ-carbon resonances (**3**, δ 85.8; **4**, δ 92.1; $\Delta\delta = +6.3$) a pronounced localization of the negative charge at the α-center or propargylic center can be deduced. Surprisingly, the ionization shift ($\Delta I = -4.4$) of the quaternary methoxy carbon resonance in the anisole core (*para* with respect to the propargylic charge) is considerably smaller compared to the *para* carbon resonance ($\Delta I = -9.4$) of the γ-phenyl group. Thus, the negative charge is predominantly stabilized by the arene chromium carbonyl substituent and the propargyl allenyl resonance (assisted by the aromatic γ-substituent) and only to a minor extent by the anisyl substituent.

This propargyl anion **4** can be trapped with electrophiles[13] such as methyl iodide to give the corresponding propargyl derivative **5**[14,15] and with trimethylsilyl chloride to furnish the allenyl compound **6**[16] (Scheme 2). In the ^{13}C NMR spectrum of the propargyl compound **5** the characteristic alkynyl carbon resonances can be detected, whereas for the allene **6** the indicative signal of the central allenyl carbon atom is found at δ 206.8. Besides steric effects the softness and hardness of the trapping electrophiles seem to play an important role in the regioselectivity of electrophilic attack. The soft electrophile

(9) Bartsch, R.; Dorst, C.; Klingebiel, U. In *Synthetic Methods of Organometallic and Inorganic Chemistry (Hermann/Bauer)*; Herrmann, W. A., Ed.; Georg Thieme Verlag: Stuttgart, 1996; Vol. 2, p 15.

(10) The use of KO^{t}Bu or LDA, suitable for the deprotonation of related toluene complexes, results only in the isolation of the isomeric allene (vide infra) and cannot be applied for the generation of a persistent propargyl anion **4**.

(11) For the electronic influence of ring substituents on the ^{13}C NMR carbonyl shifts see, for example: (a) Gansow, O. A.; Schexnayder, D. A.; Kimura, B. Y. *J. Am. Chem. Soc.* **1972**, *94*, 3406. (b) Brown, D. A.; Chester, J. P.; Fitzpatrick, N. J.; King, I. J. *Inorg. Chem.* **1977**, *16*, 2497. (c) Hunter, A. D.; Mozol, V.; Tsai, S. D. *Organometallics* **1992**, *11*, 2251.

(12) For a ^{13}C NMR and MNDO study on related propargyl anions see, for example: Dem'yanov, P. I.; Styrkov, I. M.; Krut'ko, D. P.; Vener, M. V.; Petrosyan, V. S. *J. Organomet. Chem.* **1992**, *438*, 265.

(13) **Electrophilic trapping reactions with 4**: To a cooled solution (−25 to −10 °C) of 105 mg (0.24 mmol) of **3** in 6 mL of THF was added a solution of 0.28 g (1.7 mmol) of LiHDMS in 3 mL of THF. This intense orange-red solution was stirred for 10−15 min at −25 to −10 °C. After an excess of the trapping electrophile (2.5 mmol) had been added neat to the reaction mixture a color change from red to orange was observed. After stirring at that temperature for 10−15 min 10−20 mL of water was added and the cooling was removed. After extraction with dichloromethane and removal of the solvents the residues crystallized from diethyl ether to give the alkyne **5** and the allene **6**, respectively, as yellow solids.

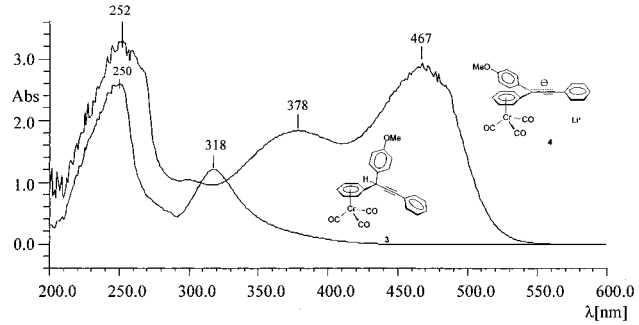


Figure 1. UV/vis spectra of **3** (λ_{max} at 250 and 318 nm) and **4** (λ_{max} at 252, 378, and 467 nm) at −25 °C in THF.

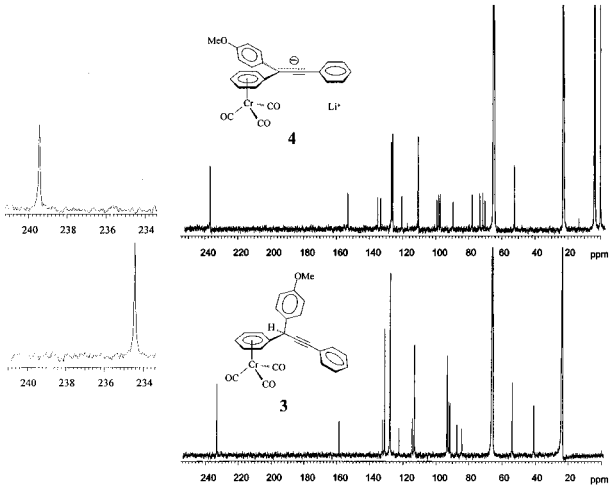
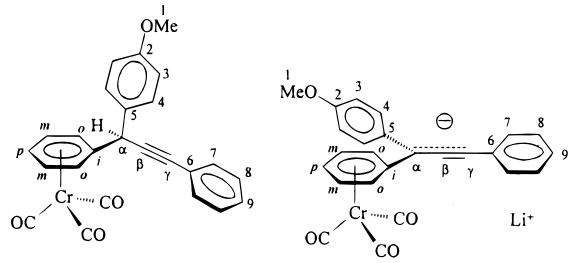


Figure 2. ^{13}C NMR spectra (THF-d_8, −55 °C, 100 MHz) of **3** (bottom) and **4** (top); inset of carbonyl resonances (left).

methyl iodide attacks the center with the highest orbital coefficient, and the hard trimethylsilyl chloride approaches the γ-position. This observation is also supported by the thermodynamically driven base-catalyzed isomerization of the propargyl compound **3** with either KO^{t}Bu or LDA, where the hard proton attacks at the γ-position to give the isomeric allene **7**[17] (Scheme 2).

Table 1. Assignments and Ionization Shifts of ^{13}C NMR Resonances (THF-d_8, −55 °C, 100 MHz; ΔI = δ(4) − δ(3))



3 **4**

	3	**4**	ΔI
α^a	42.5	72.7	+30.2
$C_1(OCH_3)$	55.4	55.1	−0.3
γ^a	85.8	92.1	+6.3
β^a	88.7	101.9	+13.2
ortho (compl.)	93.0	74.0	−19.0
meta (compl.)	93.6	99.8	+6.2
para (compl.)	94.7	80.5	−14.2
meta (compl.)	94.7	100.8	+6.1
ortho (compl.)	94.8	75.9	−18.9
C_3 (anisyl)	114.7	113.3	−1.4
ipso (compl.)	115.9	135.7	+19.8
C_5 (anisyl)	123.9	129.1	+5.2
C_4 (anisyl)	129.2	129.3	+0.1
C_8 (phenyl)	129.2	128.6	−0.6
C_7 (phenyl)	129.4	128.5	−0.9
C_9 (phenyl)	132.5	123.1	−9.4
C_6 (phenyl)	133.9	137.5	+3.6
C_2 (anisyl)	160.0	155.6	−4.4
CO	234.5	239.4	+4.9

[a] Assignment based on the propargyl resonances of the free ligands[12] (C_α, δ 43.6 and 70.6; C_β, δ 91.1 and 112.7; C_γ, δ 85.0 and 94.3).

In conclusion we have shown that both propargylic cations *and* anions can be efficiently stabilized by chromium carbonyl arene substituents, and regioselective trapping reactions of the anionic species have set the stage for novel extended side-chain functionalizations.

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(14) **5**: 75 mg (70%). Mp: 158−159 °C. ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 1.99 (s, 3H), 3.72 (s, 3H), 5.61 (m, J = 6.7 Hz, 2H), 5.76 (t, J = 6.1 Hz, 1H), 5.85 (d, J = 6.9 Hz, 1 H), 6.19 (d, J = 6.8 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 7.39−7.41 (m, 3H), 7.53−7.56 (m, 4H). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 29.38 (CH_3), 43.65 ($C_{quat.}$), 55.29 (CH_3), 84.82 ($C_{quat.}$), 92.68 (CH, 2 signals overlap), 93.05 ($C_{quat.}$), 93.20 (CH), 94.26 (CH), 95.73 (CH), 114.00 (CH), 119.60 ($C_{quat.}$), 122.50 ($C_{quat.}$), 127.59 (CH), 128.73 (CH, 2 signals overlap), 131.58 (CH), 136.41 ($C_{quat.}$), 158.46 ($C_{quat.}$), 233.95 ($C_{quat.}$, CO). MS (70 eV), m/z (%): 448 (M^+, 7), 392 (M^+ − 2 CO, 2), 364 (M^+ − 3 CO, 100), 312 (M^+ − $Cr(CO)_3$, 5). IR (KBr): $\tilde{\nu}$ = 1964 cm^{-1}, 1894, 1874. UV/vis (DMSO): λ_{max} (ϵ) = 317 nm (9950). Anal. Calcd for $C_{26}H_{20}CrO_4$ (448.44): C, 69.64; H, 4.50. Found: C, 69.13; H, 4.51.

(15) Deprotonation with *n*-butyllithium between −52 and −40 °C and subsequent trapping with methyl iodide furnished the expected alkyne **5** in only 20% yield.

(16) **6**: 93 mg (76%). Mp: 142−150 °C (dec). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 0.01 (s, 6H) and 0.05 (s, 3H) (presumably due to hindered rotation), 3.77 (s, 3H), 5.62 (d, J = 6.0 Hz, 1H), 5.64 (d, J = 6.0 Hz, 1H), 5.72−5.78 (m, J = 5.8 Hz, 3H), 7.01−7.03 (m, 4H), 7.24−7.46 (m, 9H). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 1.96 and 2.15 (CH_3, ratio: 2:1, presumably due to hindered rotation), 55.39 (CH_3), 93.97 (CH), 94.21 (CH), 94.39 (CH), 94.81 (CH), 94.85 ($C_{quat.}$), 98.85 (CH), 106.94 ($C_{quat.}$), 109.07 ($C_{quat.}$), 114.53 (CH), 125.52 ($C_{quat.}$), 127.23 (CH), 128.10 (CH), 129.09 (CH), 129.82 (CH), 132.63 ($C_{quat.}$), 159.48 ($C_{quat.}$), 206.78 ($C_{quat.}$), 233.89 ($C_{quat.}$, CO). MS (70 eV), m/z (%): 506 (M^+, 8), 423 (M^+ − C_5H_7O, 34), 422 (M^+ − 3 CO, 80), 370 (M^+ − $Cr(CO)_3$, 9), 356 (32), 355 (M^+ − $Cr(CO)_3$, − CH_3, 100), 297 (M^+ − $Cr(CO)_3$ − $(CH_3)_3$-Si, 32), 84 ($C_5H_8O^+$, 22), 82 ($C_5H_6O^+$, 40), 73 ($(CH_3)_3Si^+$, 55), 52 (Cr^+, 13). IR (KBr): $\tilde{\nu}$ = 1960 cm^{-1}, 1883, 1869. UV/vis (DMSO): λ_{max} (ϵ) = 322 nm (10500). Anal. Calcd for $C_{28}H_{26}CrO_4Si$ (506.59): C, 66.39; H, 5.17. Found: C, 66.27; H, 5.33.

(17) **Isomerization of 3 to 7**: To a cooled suspension (−10 °C) of 30 mg (0.27 mmol) of KO^{t}Bu in 7 mL of THF was added dropwise a solution of 200 mg (0.46 mmol) the propargyl compound **3** in 4 mL of THF. After a few drops the color instantaneously changed from orange to red. After stirring for 10 min the reaction mixture was filtered over silica gel and eluted with diethyl ether. After removing the solvents in vacuo 190 mg (95%) of an orange-red oil is obtained that slowly crystallizes from diethyl ether/pentane to give 136 mg (68%) of orange platelets. Mp: 115−118 °C. ^{1}H NMR ([D$_6$]DMSO, 400 MHz): δ = 3.77 (s, 3H), 5.61 (d, J = 6.0 Hz, 1H), 5.66 (d, J = 6.9 Hz, 1H), 5.72 (t, J = 6.1 Hz, 1H), 5.78 (t, J = 6.4 Hz, 2H), 7.02 (s, 1H), 7.01−7.03 (d, J = 8.6 Hz, 2H), 7.27 (t, J = 7.2 Hz, 1H), 7.35 (d, J = 7.6 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 7.3 Hz, 2H). ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 55.40 (CH_3), 94.01 (CH), 94.25 (CH), 94.42 (CH), 94.80 (CH), 94.85 (CH), 98.85 (CH), 106.96 ($C_{quat.}$), 109.07 ($C_{quat.}$), 114.55 (CH), 125.55 ($C_{quat.}$), 127.24 (CH), 128.10 (CH), 129.10 (CH), 129.82 (CH), 132.64 ($C_{quat.}$), 159.49 ($C_{quat.}$), 206.79 ($C_{quat.}$), 233.91 ($C_{quat.}$, CO). MS (70 eV), m/z (%): 434 (M^+, 10), 378 (M^+ − 2 CO, 1), 352 (M^+ − C_5H_6O, 10), 351 (M^+ − C_5H_7O, 29), 350 (M^+ − 3 CO, 100), 298 (M^+ − $Cr(CO)_3$, 19). IR (KBr): $\tilde{\nu}$ = 1962 cm^{-1}, 1882. UV/vis (DMSO): λ_{max} (ϵ) = 320 nm (10100). Anal. Calcd for $C_{25}H_{18}CrO_4$ (434.41): C, 69.12; H, 4.18. Found: C, 69.35; H, 4.35.