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REACTIONS OF ARYL CHROMIUM CARBENE COMPLEXES WITH ALKOXALKYNE: O-QUINONEMETHIDE FORMATION AND UNUSUAL DIELS-ALDER DIMERIZATION

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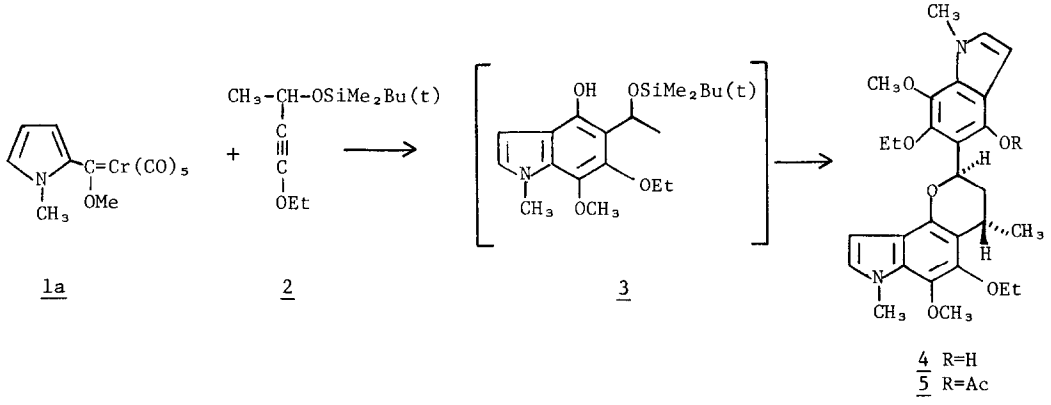
ABSTRACT; Reactions of a pyrrole- and a phenyl-carbene chromium complexes with 3-alkoxy-1-ethoxy-1-butyne produced dimers through o-quinone-methide formation from the alkyne-carbene cycloaddition products and subsequent Diels-Alder dimerization.

Hydroindoloquinone is an important structural type which may be directly accessible by reaction of an alkyne, CO, and a pyrrole carbene-chromium complex (1a). The basic alkyne cycloaddition process has been studied extensively[1], usually with aryl- and vinyl-carbene complexes, and has begun to be applied in natural product synthesis.[2] We reported the first use of a pyrrole-carbene complex, and observed interception of a key intermediate when ethyl propiolate is the alkyne.[3] In this paper, we report the reaction of the electron-rich alkyne (2) with the same complex (1a), which leads to a remarkable structure (4), a dimer of the expected indole product (3). The dimer is understood in terms of a highly regioselective formation of 3, followed by an unexpected elimination and subsequent Diels-Alder dimerization. A parallel process is observed with the phenyl-carbene complex (1b). This is the first example of an alkoxyalkyne participating in the alkyne-carbene cycloaddition reaction.



1a 2 3

4 R=H
5 R=Ac

Reaction of ethoxyacetylene with n-BuLi (THF, 1.0 mol.eq.,-78°C, argon), followed by quenching with acetaldehyde (-78°C) gave an alcohol which was directly treated with t-butyldimethylsilyl chloride (imidazole, DMF, 23°C) to give the desired alkyne (2, 76% yield overall). The carbene complex (1a) was prepared as before[3] from 2-lithio-N-methyl pyrrole and chromium hexacarbonyl, followed by methylation with trimethyloxonium tetrafluoroborate (64% yield, orange-yellow crystalline). A solution of 1a (9.5 mmole) and alkyne (2, 15 mmole) in THF (350mL) was heated under argon at 65°C (bath temperature) for 5 hrs. TLC analysis indicated complete reaction after 4-6 hrs. The mixture was cooled, concentrated by rotary evaporation, and the major product (4) was isolated as an oil by silica gel flash column chromatography (68% yield).[4] Acetylation (acetic anhydride, dry pyridine, 23°C) gave a crystalline monoacetate, mp 119-120°C, which was subjected to X-ray crystallographic analysis to reveal structure 5. Similarly, reaction of 1b with 2 under identical conditions gave a dimeric product with parallel spectral data [4], and is assigned structure 7.

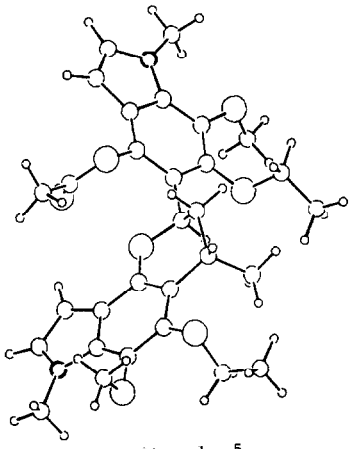
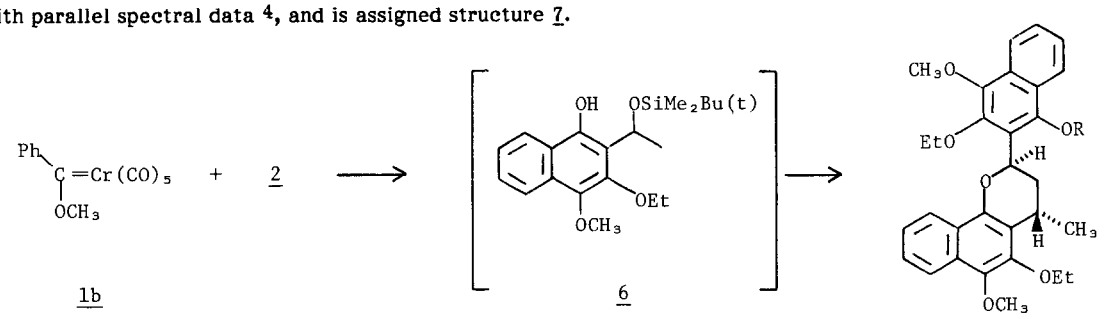


Fig. 1, 5



1b 6

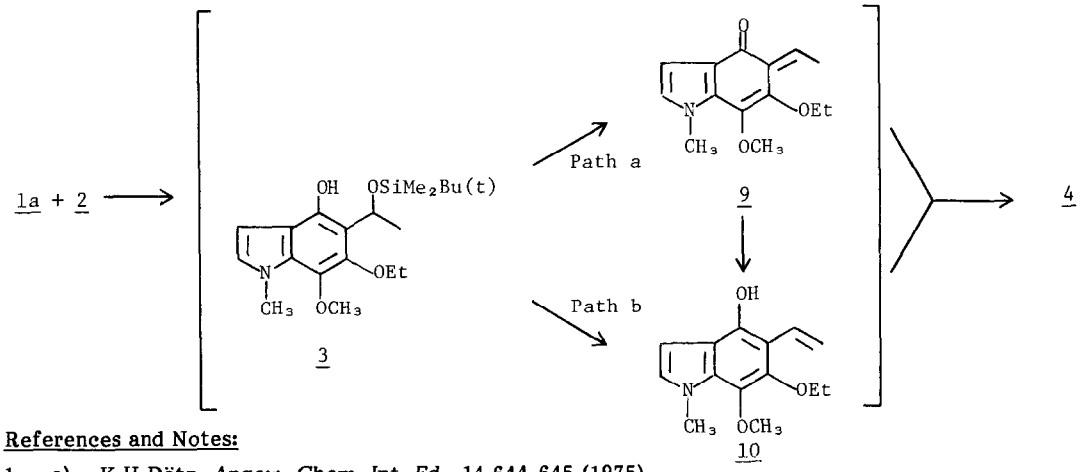
7 R=H

8 R=Ac

A plausible pathway for formation of 4 and 7 is shown for 4 in scheme-1. The well established cycloaddition pathway produces the indolohydroquinone (3) (perhaps partly or largely present with $Cr(CO)_3$ coordinated to the arene ring[5]). Then elimination of the side chain oxygen unit is assisted by the phenyl group (path a) to give a transient o-quinonemethide (9). Isomerization by a proton shift would provide the styryl derivative (10), and Diels-Alder cycloaddition between 9 and 10 would lead to the observed product (4). Alternately, direct elimination of a trialkylsilanol from 3 (path b) could provide the styryl derivative, 10. The elimination process to give 9 is unexpectedly facile, but has close parallels in a proposed general mechanism of action of quinone antibiotics (bioreductive alkylation).[6] The structure of 3 requires that the carbene carbon of 1a attach to the ethoxy-bearing carbon of alkyne (2) with 100% regioselectively. This high regioselectivity is consistent with earlier observations with unsymmetrical alkynes[1b,1c] and is rationalized in terms of a dominating steric

effect. This result extends the general trend that electronic effects of substituents on the alkyne are relatively unimportant in determining the selectivity in the cycloaddition process.

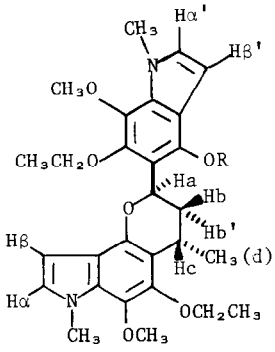
Scheme - 1



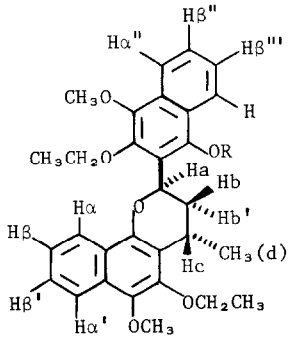
References and Notes:

1. a) K.H.Dötz, *Angew. Chem. Int. Ed.*, 14 644-645 (1975).
   b) K.H.Dötz, B. Fügen-Köster, *Chem. Ber.*, 113 1449-1457 (1980).
   c) W.D.Wulff, P.C.Tang and J.S.McCallum, *J. Amer. Chem. Soc.*, 103, 7677-7678 (1981).
   d) W.D.Wulff, K.S.Chan, P.C.Tang, *J. Org. Chem.*, 49, 2293-2295 (1984).
2. a) M.F.Semmelhack, J.J.Bozell, *Tet. Lett.*, 23, 2931-2934 (1982).
   b) M.F.Semmelhack, J.J.Bozell, T.Sato, W.D.Wulff, E. Spiess, A. Zask, *J. Amer. Chem. Soc.*, 104, 5850-5852 (1982).
   c) K.H.Dötz, I.Pruskil, *J. Organometallic Chem.*, 209, C_4-C_6, (1981).
   d) M.A.McGuire, L.S.Hegedus, *J. Amer. Chem. Soc.*, 104, 5538-5540 (1982).
   e) L.S.Hegedus, M.A.McGuire, L.M.Schultz, C. Yijun, O.P.Anderson, *J. Amer. Chem. Soc.*, 106, 2680-2687 (1984).
   f) W.D.Wulff, P.C.Tan, *J. Amer. Chem. Soc.*, 106, 434-436 (1984).
3. A. Yamashita, T.A.Scahill, *Tet. Lett.*, 23, 3765-3768 (1982).
4. Spectral data. For 4: MS (FBA); 494. IR (neat); 3406, 1634, 1493, 1462, 1321, 1060. ^{1}H NMR ($CDCl_3$); δ8.02 (s, 1H, ArOH), 6.85-6.75 (m, Jαβ=3.1Hz, 2H, Hα, Hα'), 6.53-6.45 (d, d, Jαβ=3.1Hz, 2H, Hβ, Hβ'), 5.75 (dd, Jab=11.3Hz, Jab'=1.9Hz, 1H, Ha), 4.25-4.00 (m, 4H, two of $ArOCH_2CH_3$), 3.96, 3.93, 3.91, 3.77 (4s, 4x3H, two of $ArOCH_3$ and two of NCH_3), 3.40-3.00 (m, 1H, H_c), 2.4-2.1 (m, Jbb'=13Hz, Jab=12.0Hz, Jbc=6.0Hz, 1H, Hb), 2.05-1.75 (m, Jab'=2.0Hz, Jb,c~OHz, 1H, Hb'), 1.50 [d, J=6.8Hz, 3H, CH_3(d)], 1.40 (t, J=7.0Hz, 6H, two of $ArOCH_2CH_3$). For 5: High resolution MS mole wt; 536-2523. Calcd; 536-2522. IR(Nugol); 1766, 1624, 1490, 1464. ^{1}H NMR ($CDCl_3$); δ6.86 (d, Jαβ=3.1Hz, 1H, Hα), 6.71 (d, Jα'β'=3.1Hz, 1H, Hα'), 6.41 (d, 1H, Hβ), 6.22 (d, 1H, Hβ'), 5.70 (dd, Jab=12.0Hz, Jab'=2.0Hz, 1H, Ha), 4.25-4.00 (two overlapped q, two of $ArOCH_2CH_3$),

3.97, 3.95, 3.93, 3.(4s, 4x3H, two of ArO$\underline{CH_3}$, two of N$\underline{CH_3}$), 3.3-3.2 (m, 1H, Hc), 2.74-2.6 (m, Jbb'=13.3Hz, Jbc=5.4Hz, 1H, Hb), 2.01 (s, 3H, CO$\underline{CH_3}$), 1.83-1.75 (dd, Jb'c=1.0Hz, 1H, Hb'), 1.47 [d, J=7.0Hz, 3H, CH_3(d)], 1.42 (t, J=6.9Hz, 3H, ArOCH$_2\underline{CH_3}$), 1.35 (t, J-7.0Yz, 3H, ArOCH$_2\underline{CH_3}$). Anal; C,H,N. For $\underline{7}$: MS; 488. IR (neat); 3411, 1631, 1596, 1454, 1370, 1277, 1059. ^{1}H NMR ($CDCl_3$); δ8.35 (s, 1H, ArOH), 8.30-7.95 (m, 4H, Hα, Hα', Hα", Hα'"), 7.60-7.31 (m, 4H, Hβ, Hβ', Hβ", Hβ'"), 5.93 (dd, Jab=11.8 Hz, Jab'=2.0Hz, 1H, Ha), 4.50-4.10 (m, 4H, two of ArO$\underline{CH_2}$CH$_3$), 3.95 (s, 6H, two of ArO$\underline{CH_3}$), 3.5-3.1 (m, 1H, Hc), 2.75-1.90 (m, 2H, Hb, Hb'), 1.56 [d, J-6.6Hz, 3H, CH_3(d)], 1.47 (t, J=7.0Hz, 3H, ArOCH$_3$), 1.44 (t, J-7.1Hz, 3H, ArOCH$_3$). For $\underline{8}$: High resolution MS mol. wt; 530.1200. Calcd; 530.2304. IR (neat); 1770, 1626, 1595, 1455, 1373, 1196, 1059. ^{1}H NMR ($CDCl_3$); δ8.25-7.90 (m, 4H, Hα, Hα', Hα", Hα'"), 7.76-7.20 (m, 4H, Hβ, Hβ', Hβ", Hβ'"), 5.82 (dd, Jab=11.8Hz, Jab'=2.0Hz, 1H, Ha), 4.45-4.10 (two overlapped q, two of ArO$\underline{CH_2}$CH$_3$), 4.02, 3.94 (2s, 2x3H, two of ArO$\underline{CH_3}$), 3.00-2.60 (m, 1H, Hc), 2.50-2.00 (m, 2H, Hb, Hb'), 2.03 (s, 3H, CO$\underline{CH_3}$), 1.51 [d, J=6.1Hz, 3H, CH_3(d)], 1.47 (t, J=6.9Hz, 3H, ArOCH$_2\underline{CH_3}$), 1.34 (t, J=7.0Hz, 3H, ArOCH$_2\underline{CH_3}$), 1.34 (t, J=7.0Hz, 3H, ArOCH$_2\underline{CH_3}$). Anal; C, H. The stereochemistry of the pyran ring in compounds $\underline{4}$, $\underline{5}$, $\underline{7}$, and $\underline{8}$ is proven by the magnitudes of the J-couplings of Ha, Hb, Hb', and Hc. Proton Ha is coupled to Hb with a large axial coupling of 11.8Hz, to Hb' with a typical Jaxial-equatorial value of 2.0Hz. The protons Hb and Hb' have a geminal coupling of 13.0Hz. They are coupled to Hc with J_{Hb-Hc} = 5.6Hz, $J_{Hb'-Hc}$ = 0~1Hz: typical equatorial-axial and equatorial-equatorial coupling constants. The proton Hc is also coupled to the axial methyl with a coupling of 6.7Hz.



$\underline{4}$ R=H
$\underline{5}$ R=Ac



$\underline{7}$ R=H
$\underline{8}$ R=Ac

5. Normally the reaction first forms the Cr(CO)3 attached naphthol ring. However, the highly substituted naphthol chromium tricarbonyl complexes easily release Cr(CO)3, then partially or fully release during isolation procedure. See ref. 1a), 1b), and 2c).

6. a) H. W. Moore and R. Czerniak, *Med. Res. Rev.*, $\underline{1}$, 249(1981).
b) A. T. Lin, L. A. Crosby, C. W. Shansky, A. C. Sartorelli, *J. Med. Chem.*, $\underline{15}$, 1247(1972).

7. The crystallographic data has been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.

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