Tetrahedron Vol. 41, No. 24, pp. 5797 to 5802, 1985.
Printed in Great Britain.

0040-4020/85 $3.00 + .00

CARBENE LIGANDS AS ANTHRACYCLINONE-SYNTHONS—II†

CHROMIUM MEDIATED CYCLOADDITION OF ALKYNES, CARBENES AND CARBON MONOXIDE: APPLICATION TO RING B SYNTHESIS IN ANTHRACYCLINONES

KARL HEINZ DÖTZ* and MICHAEL POPALL
Anorganisch-chemisches Institut der Technischen Universität München, Lichtenbergstrasse 4, 8046 Garching, West Germany

(*Received in USA* 14 *May* 1984)

Abstract—The cycloaddition of Cr-co-ordinated alkyne, carbene and carbonyl ligands provides a variable route to the anthracyclinone skeleton. The key step of a formal total synthesis of 4-demethoxydaunomycinone (1) is based on the reaction of carbonyl–carbene complex 15—used as a CD ring synthon—and alkyne 9 leading to the formation of ring B.

The use of transition metals in organic synthesis represents a powerful method to improve the regio-, stereo- and enantioselectivity[2] which play an important role in the formation of C—C bonds related to natural product synthesis. Some years ago we described the reaction of chromium–carbene complexes with alkynes which is characterized by the coupling of alkyne, carbene and carbonyl ligands.[3,4] Depending on the nature of the reagents and the reaction conditions, aromatic co-cyclization[4–6] and carbene annulation products[7–9] as well as, in some cases, furans[7,10] or cyclobutenones[11] are obtained. Until now the formation of hydroquinones, originating from the cycloaddition of Cr-co-ordinated alkynes, aryl or vinyl carbenes and carbon monoxide, has received the widest attention[12] (Scheme 1). The hydroquinone can be released from the metal either by ligand substitution by, e.g. carbon monoxide, or by oxidation to the quinone system.

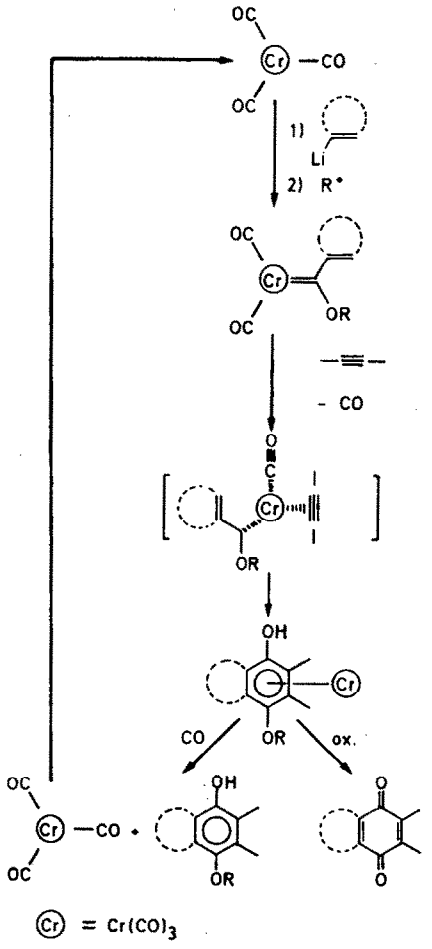
The reaction is compatible with various functional groups in the alkyne (excluding nucleophilic alkynes such as ynamines) and proceeds, in general, with a 70–90% isolated yield. The alkyne incorporation occurs regioselectively[13,14] and is governed by steric factors; e.g. using 1-alkynes, the alkyl chain ends up exclusively nearer the phenolic group. The reaction has been investigated by a kinetic study[15] and has been shown to involve vinyl ketene intermediates.[16,17] The scope of the annulation of aryl and vinyl carbene ligands has already been exemplified by the synthesis of vitamins K and E[18–20] and naphthoquinoid antibiotics.[21] Since the carbene complexes are accessible from commercially available hexacarbonyl chromium in good to excellent yields,[22] we have extended our work to synthetic studies in the anthracyclinone series which form the aglycon of the potent anti-cancer reagents of the anthracycline group.[23]

RESULTS AND DISCUSSION

Carbene complex approach to anthracyclinones

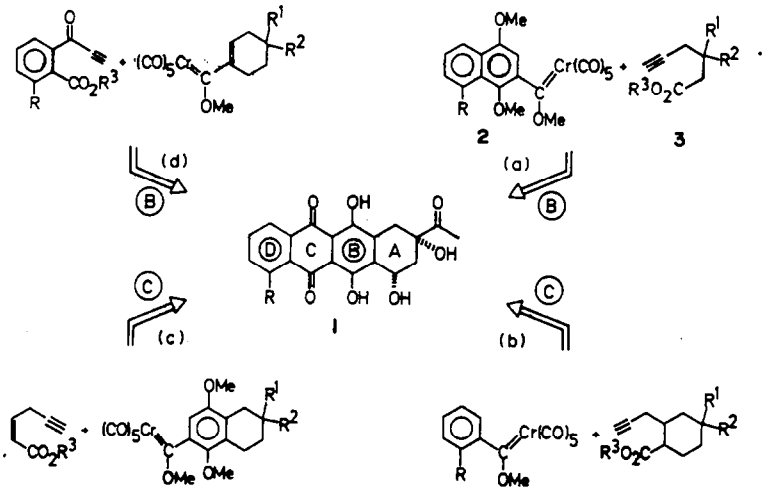
As a target in the anthracyclinone series we have chosen the daunomycinone derivatives 1. The tetracyclic skeleton contains a hydroquinoid ring B and a quinone ring C both of which should be accessible from suitable carbene complexes and alkynes. Four possible strategies (a–d) are symbolized in Scheme 2.

We have focused on approaches starting from *o*-methoxyaryl–carbene complexes and report here on



Scheme 1. Chromium-mediated cycloaddition of alkynes, carbenes and carbon monoxide.

† For Part I in the series see: Dötz *et al.*[1]

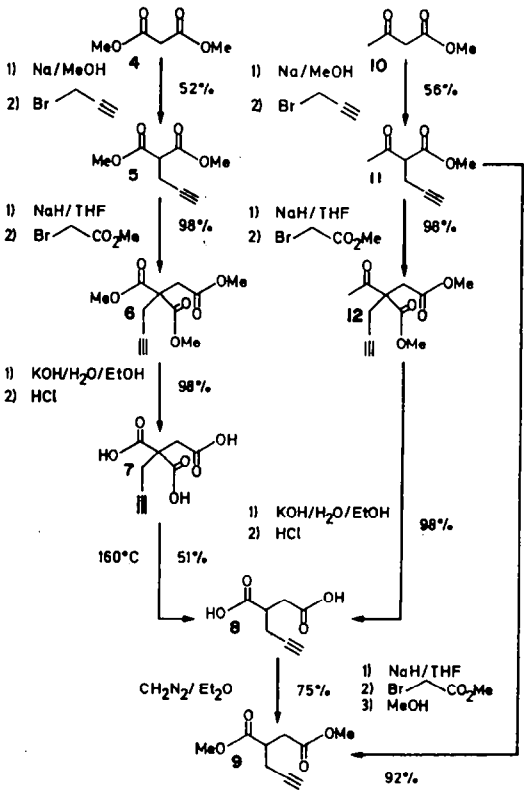


Scheme 2. Carbene complex based strategies directed towards daunomycinones 1.

route a which combines the CD ring synthon 2 with alkyne 3. The cycloaddition aims at the formation of the hydroquinoid ring B. Another approach similar to route d has been reported recently.[24]

Alkyne components

The alkyne component can be synthesized following two pathways as outlined in Scheme 3. Both routes start with readily available reagents, dimethylmalonate (4) resp. methylacetylacetate (10). Alkynilation leads to propargyl esters 5 and 11. Bisalkynilation by-products, formed in amounts varying with the reaction conditions, can be separated by distillation. The following steps, alkylation with methyl bromoacetate and subsequent alkaline hydrolysis, proceed nearly quantitatively. Decarboxylation of the triscarboxylic acid 7 requires rather drastic conditions concomitant with only moderate yields. However, these problems can be overcome by alkaline cleavage of the β-ketoester 12. Subsequent esterification yields the diester 9. Ester cleavage of 12 *without* hydrolysis is effected by sodium hydride. Using this method a direct route is provided from 11 to the alkynyl diester 9 which, thus, can be obtained from methylacetylacetate in a two-step sequence with reasonable yield.

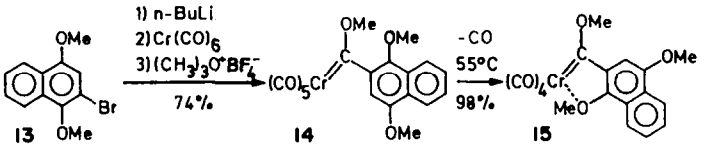


Scheme 3. Synthesis of propargyl diester (9).

Carbonyl carbene complexes

The synthesis of the carbene complexes (Scheme 4) starts with 2-bromo-1,4-dimethoxynaphthalene (13) which is accessible from naphthohydroquinone in 75% yield.[25] Metalation with *n*-butyllithium and subsequent addition to a suspension of hexacarbonyl chromium in ether leads to the acyl metalate which can be stored at −78° in an inert gas atmosphere. The methylation is best effected by either methyl fluorosulphonate in dichloromethane or trimethyloxonium tetrafluoroborate using a two-phase system (water–pentane). The pentacarbonyl–carbene complex, 14, can be isolated by crystallization or flash chromatography giving analytically pure samples which can be shortly handled in air. Warming above 50° induces the elimination of a *cis*-CO ligand.[1] The co-ordination of the *o*-methoxy group leads to the tetracarbonyl–carbene complex 15. Using a donor solvent the decarbonylation proceeds smoothly and nearly quantitatively. Thus, 15 is obtained from the bromonaphthalene in 73% isolated yield.

The metalacycle 15 undergoes ring opening via cleavage of the Cr—O bond under mild conditions. Thus, it represents a stabilized form of a tetracarbonyl–carbene complex, the formation of which has been shown to precede the cycloaddition of alkyne, carbene and carbonyl ligands.[15] The co-ordination of the methoxy group is clearly shown by NMR spectroscopy. In comparison with the pentacarbonyl complex 14 a

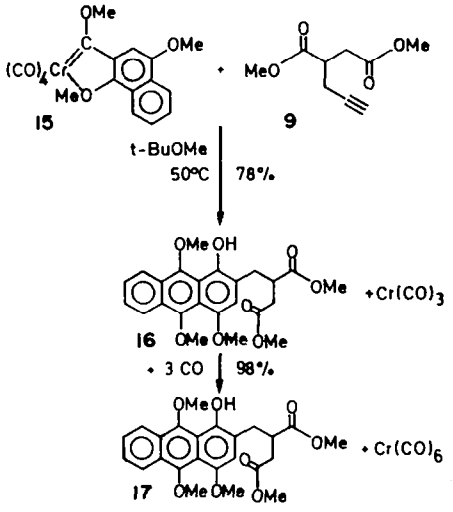


Scheme 4. Synthesis of carbene complexes **14** and **15**.

significant downfield shift is observed both for the 1-methoxy protons (*ca* δ 1) and the 1-methoxy carbon atom (*ca* δ 13) (see Experimental). On the other hand, the carbene resonance signal is shifted upfield (*ca* δ 17) indicating an increased electron density on the metalacyclic carbene carbon atom. The synthesis and properties of chelated carbene complexes are discussed separately.[1]

Cycloadditon and decomplexation

Whereas the carbene complexes **14** and **15** can be handled in air for some time, their reaction with alkynes requires an inert gas atmosphere. Donor solvents, such as cyclic or acyclic ethers, have been proved as solvents of choice. Using alkyne **9** the cycloaddition leading to anthracene derivative **16** is complete within several minutes at 50° (Scheme 5). The reaction can be easily monitored by IR spectroscopy due to different ν^{CO} absorptions characteristic for tetracarbonyl and tricarbonyl complexes. Since **16** is *very* air-sensitive in solution, it is convenient to isolate the product by crystallization which avoids a tedious work-up by chromatography. The metal carbonyl fragment is readily removed by warming in a CO atmosphere. This method affords the metal-free anthracene **17** in a clean reaction. Moreover, the chromium can be recycled to give the hexacarbonyl complex which serves as the starting material in the carbene complex synthesis. Alternatively, the metal ring cleavage is effected by oxidation. However, in general, this procedure gives lower yields, the metal is oxidized irreversibly to Cr(III) species and the products have to be isolated by chromatography.



Scheme 5. Carbene complex-mediated formation of ring B in anthracyclinone synthesis.

The anthracene derivative **17** is a suitable intermediate in the synthesis of 4-demethoxydaunomycinone (**1**). Well-established procedures for the cyclization and the functionalization of ring A as well as for the oxidation of ring C have been developed by other groups[26–29] as outlined in Scheme 6. Current studies are underway to demonstrate the scope of the Cr-mediated cycloaddition in the synthesis of anthracyclinones.

EXPERIMENTAL

General technique

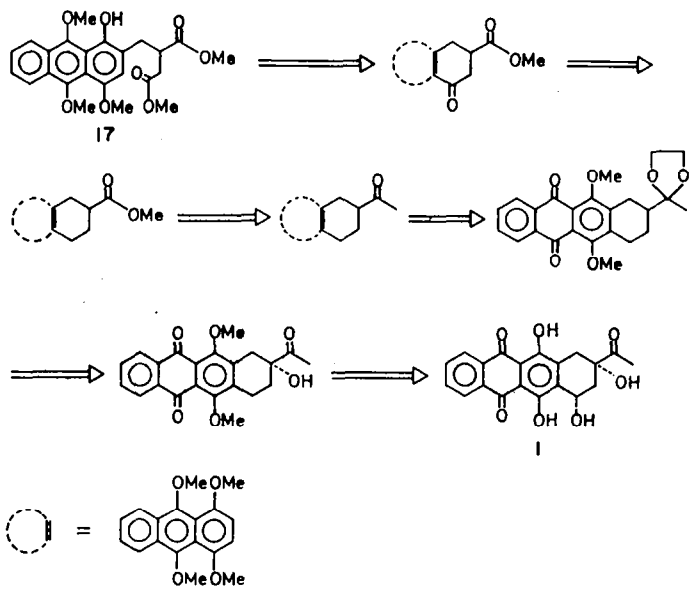
As far as necessary, all reactions and preparative work were carried out under an atmosphere of dried N_2 or Ar. Solvents used for reactions involving organometallics were dried using standard methods, distilled, N_2-saturated and stored under N_2. The silica gel used for column chromatography, silica gel 60 (E. Merck, Darmstadt, 0.06–0.20 mm), was dried at high vacuum and kept under N_2. For preparative TLC we used TLC plates purchased from E. Merck, Darmstadt. M.ps were ascertained under Ar in closed capillary tubes and are uncorrected. The following instruments served for spectroscopic characterization. IR spectrometer: Perkin–Elmer models 283 B and 577; ^{1}H-NMR spectrometer: Jeol PMX 60; ^{13}C-NMR spectrometer: Jeol FX 60; mass spectrometer: Varian MAT 311 A (EI).

The NMR data are reported in ppm using TMS as internal standard (on a δ scale) and are listed in the following order: chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad) and coupling constant (Hz).

Alkynes

2-Carbomethoxy-4-pentynoic acid methylester (**5**).[30] In 400 ml of dried MeOH 11.95 g (0.52 mol) Na was dissolved under reflux. The soln was cooled to 0° and slowly dropped into 66.06 g (0.50 mol) **4** stirring well and cooling with ice-water. After 30 min 64.24 g (0.54 mol) propargylbromide was added carefully dropwise. During this procedure the initially colourless soln turned yellow–orange and a white ppt, NaBr, appeared. Then the mixture was slowly warmed to room temp. The reaction was completed by refluxing overnight. After cooling the solvent was removed at reduced pressure, the residue was extracted with Et_2O (6 × 100 ml), the extracts were washed with H_2O and brine (3 × 100 ml) and dried over Na_2SO_4. After removal of the solvent at reduced pressure a yellow oil was obtained, which was separated by fractionated high vacuum distillation, to give **5** as a colourless oil; 44.24 g (52%). B.p. 70–72°/oil pump vacuum. IR $\nu_{max}^{film,NaCl}$ cm^{-1}: 3295, 3000, 2947, 2840, 2120, 1755, 1740, 1440, 1348, 1282, 1245, 1210, 1162, 1075, 1035, 974, 952, 852. ^{1}H-NMR (CCl_4): δ 1.87 (t, $^4J_{H,H}$ = 2.4 Hz, 1H, —C≡C—H), 2.60 (dd, $^4J_{H,H}$ = 2.4 Hz, $^3J_{H,H}$ = 7.5 Hz, 2H, —CH_2—C≡C—), 3.41 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, R_3C—H), 3.64 (s, 6H, 2OMe).

3,3-Dicarbomethoxy-5-hexynoic acid methylester (**6**).[31] In 500 ml of dry THF 42.54 g (0.25 mol) **5** were dissolved and with intensive stirring at room temp a suspension of 7.44 g (0.31 mol) NaH in 50 ml THF was added dropwise within 30 min. After 1 hr 42.83 g (0.28 mol) bromoacetic acid methylester were added in one portion. Immediately a milky yellow suspension was formed, which was heated under reflux for 2 hr to complete the reaction. After cooling it was filtered through 5 cm of silica



Scheme 6. Final route to 4-demethoxydaunomycinone (1).[26–29]

gel. The solvent and excess bromoacetic acid methylester are removed at reduced pressure. The residue, a slightly yellow oil, was pure **6** as shown by ^{1}H-NMR spectroscopy; 59.35 g (98%). IR $\nu_{max}^{film,NaCl}$ cm^{-1}: 3280, 3000, 2952, 2890, 2840, 1740, 1440, 1410, 1364, 1322, 1295, 1260, 1202, 1176, 1078, 1052, 1004, 988, 905, 890, 860. ^{1}H-NMR (CCl_4): δ 1.94 (t, $^4J_{H,H}$ = 2.5 Hz, 1H, —C≡C—H); 2.87 (d, $^4J_{H,H}$ = 2.5 Hz, 2H, —CH_2—C≡C—), 3.03 (s, 2H, —CH_2—CO—), 3.60 (s, 3H, —OMe), 3.66 (s, 6H, 2OMe).

3,3-Dicarboxylic-5-hexynoic acid (**7**). Compound **6** (58.13 g, 0.24 mol) was dissolved in 134 ml EtOH. With vigorous stirring 68 g (1.21 mol) KOH, dissolved in 66 ml H_2O, was added and the mixture was heated under reflux for 5 hr. After cooling to 0° conc HCl was added to pH 1. After the removal of EtOH at reduced pressure the remaining paste was extracted with CH_2Cl_2 (5 × 200 ml) and the organic layer with brine (2 × 200 ml) and dried over Na_2SO_4. Removal of the solvent gave a white solid, **7**, which was not further purified; 47.07 g (98%). IR ν_{max}^{KBr} cm^{-1}: 3420, 3300, 3262, 3200–2500, 2120, 1730, 1440, 1415, 1352, 1295, 1281, 1216, 1190, 1140, 1080, 1045, 960, 932, 915, 872, 860, 820, 796, 745, 722, 702, 692, 668, 638. ^{1}H-NMR (d_6-Me_2CO): δ 2.44 (t, $^4J_{H,H}$ = 2.6 Hz, 1H, —C≡C—H), 3.01 (d, $^4J_{H,H}$ = 2.6 Hz, 2H, —CH_2—C≡C—), 3.13 (s, 2H, —CH_2—CO—).

2-Acetyl-4-pentynoic acid methylester (**11**).[30] In 250 ml of dried MeOH 11.95 g (0.52 mol) Na was dissolved under reflux. The soln was cooled to 0° and added dropwise to 58.06 g (0.50 mol) **10** under stirring and cooling with ice water. After 20 min, 64.24 g (0.54 mol) propargylbromide was added in a few portions and the mixture was refluxed for 15 hr. Soon the initial colourless soln became orange and a white ppt, NaBr, appeared. After cooling the solvent was removed at reduced pressure, the residue was extracted with Et_2O (5 × 100 ml), the extracts were washed with H_2O and brine (3 × 100 ml) and dried over Na_2SO_4. Removal of the solvent at reduced pressure gave a yellow oil, which was separated by fractionated high vacuum distillation, to give **21** as a colourless oil; 43.5 g (56%). B.p. 65–67°/oil pump vacuum. IR $\nu_{max}^{film,NaCl}$ cm^{-1}: 3285, 3000, 2952, 2840, 2120, 1742, 1720, 1436, 1360, 1320, 1270, 1230, 1192, 1175, 1152, 1074, 1035, 1010, 980, 928, 875, 838. ^{1}H-NMR (CCl_4): δ 1.87 (t, $^4J_{H,H}$ = 2.5 Hz, 1H, —C≡C—H), 2.22 (s, 3H, —CO—Me), 2.57 (dd, $^4J_{H,H}$ = 2.5 Hz, $^3J_{H,H}$ = 7.5 Hz, 2H, —CH_2—C≡C—), 3.56 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, R_3C—H), 3.67 (s, 3H, —CO_2Me).

3-Acetyl-3-carbomethoxy-5-hexynoic acid methylester (**12**).[31] Compound **11** (40.26 g, 0.26 mol) was dissolved in 400 ml of dry THF and at room temp 8.00 g (0.33 mol) NaH (as a suspension in 60 ml THF) was added dropwise. After 1 hr, 44.33 g (0.29 mol) bromoacetic acid methylester was added in one portion. Immediately a milky yellow suspension was obtained which was heated under reflux for 1.5 hr to complete the reaction. After cooling and filtration through 6 cm of silica gel the solvent and excess bromoacetic acid methylester were removed at reduced pressure. The residue, a slightly yellow oil, was pure **12** as shown by ^{1}H-NMR spectroscopy; 57.91 g (98%). IR $\nu_{max}^{film,NaCl}$ cm^{-1}: 3280, 3000, 2952, 2840, 1730, 1440, 1364, 1345, 1320, 1282, 1245, 1185, 1175, 1076, 1048, 1002, 980, 880, 840. ^{1}H-NMR (CCl_4): δ 1.92 (t, $^4J_{H,H}$ = 2.5 Hz, 1H, —C≡C—H), 2.07 (s, 3H, —COMe), 2.79 (d, $^4J_{H,H}$ = 2.5 Hz, 2H, —CH_2—C≡C—), 2.90 (s, 2H, —CH_2—CO—), 3.51 (s, 3H, —CO_2Me), 3.60 (s, 3H, —CO_2Me).

3-Carboxylic-5-hexynoic acid (**8**). (a) Compound **7** (46.03 g, 0.23 mol) was heated for *ca* 5 hr at 160° (as long as CO_2 was evolved). Extraction of the yellow–brown viscous oil with Et_2O (5 × 200 ml) gave a yellow–brown half-solid crude product **8**; 18.32 g (51%). (b) Under vigorous stirring a soln of 70.13 g (1.25 mol) KOH in 80 ml H_2O was added to 56.56 g (0.25 mol) **12**, dissolved in 160 ml EtOH and the mixture was refluxed for 5 hr. After cooling to 0° and acidification with conc HCl to pH 1 the solvent and the formed HOAc were removed at high vacuum. The residue, a brownish product was extracted with Et_2O (5 × 150 ml) and the organic phase was washed with brine (2 × 75 ml) and dried over Na_2SO_4. Removal of the solvent gave crude **8**, a yellowish solid; 38.25 g (98%). IR ν_{max}^{KBr} cm^{-1}: 3290, 3200–2500, 1740, 1700, 1440, 1410, 1318, 1210, 1178, 1038, 950, 914, 878, 812, 775, 684, 665, 630. ^{1}H-NMR (d_6-Me_2CO): δ 2.39 (t, $^4J_{H,H}$ = 2.2 Hz, 1H, —C≡C—H), 2.59 (dd, $^4J_{H,H}$ = 2.2 Hz, $^3J_{H,H}$ = 6.1 Hz, 2H, —CH_2—C≡C—), 2.73 (d, $^3J_{H,H}$ = 6.1 Hz, 2H, —CH_2—CO—), 3.00 (m, 1H, R_3C—H).

3-Carbomethoxy-5-hexynoic acid methylester (**9**). (a) Crude **8** (37.47 g, 0.24 mol) was dissolved in 300 ml Et_2O. With slight stirring, 700 ml of a 1 M soln of diazomethane in Et_2O (−15°) were added dropwise. The excess diazomethane was removed at reduced pressure. A yellowish oil was obtained which gave a colourless oil after fractionated high vacuum distillation; 33.15 g (75%). (b) At room temp 0.62 g (26 mmol) NaH were added in a few portions to a soln of 2.00 g (13 mmol) **11** in 40 ml THF [for larger amounts see details for **12** (above)]. After 20

min 2.29 g (15 mmol) bromoacetic acid methylester was added in one portion and the mixture was refluxed for 5 hr. Sometimes it was advantageous to use a few drops of MeOH before heating. After cooling the solvent was separated from a brown solid, which was then extracted twice with 60 ml THF. The THF soln was filtered through 3 cm of silica gel. The solvent and excess bromoacetic acid methylester were removed at reduced pressure. The crude product, a yellowish oil, was fractionated by high vacuum distillation and gave a colourless oil; 2.20 g (92%). B.p. 80–82°/oil pump vacuum. IR $\nu_{max}^{film, NaBr}$ cm^{-1}: 3280, 3000, 2950, 2840, 1740, 1440, 1415, 1375, 1360, 1310, 1280, 1240, 1210, 1170, 1100, 1050, 1010, 892, 870, 835. ^{1}H-NMR (CCl_4): δ 1.90 (t, $^4J_{H,H}$ = 2.4 Hz, 1H, —C≡C—H), 2.46 (dd, $^4J_{H,H}$ = 2.4 Hz, $^3J_{H,H}$ = 5.6 Hz, 2H, —CH_2—C≡C—), 2.62 (d, $^3J_{H,H}$ = 5.6 Hz, 2H, —CH_2—CO—), 2.90 (m, 1H, R_3C—H), 3.59 (s, 3H, —OMe), 3.62 (s, 3H, —OMe). MS *m/z* (%): 184 $[M]^+$ (0.1), 169 (1), 153 (74), 152 (74), 125 (44), 124 (100), 93 (20), 83 (29), 82 (66), 79 (28), 74 (8), 65 (54), 59 (78). (Found: C, 58.95; H, 6.62%; $C_9H_{12}O_4$ 184.2. Requires: C, 58.69; H, 6.57%.)

Carbene complexes

Pentacarbonyl[methoxy(1,4 - dimethoxy - 2 - naphthyl) - carbene]chromium(0) (**14**).[1] To a soln of 4.01 g (15 mmol) **13**[25] in 40 ml Et_2O was added at room temp 9.36 ml (15 mmol) of a 1.6 M soln of *n*-BuLi in hexane within 45 min and the mixture changed from yellow to orange. To complete the reaction it was stirred for 2 hr after which the lithionaphthalene was added dropwise over 30 min to a suspension of 3.30 g (15 mmol) hexacarbonyl chromium in 75 ml Et_2O. The suspension first turned lemon yellow and then gradually to reddish brown. After stirring for 2 hr the Et_2O was removed at reduced pressure. The dusty-dry ocher–yellow lithium acylmetalate was dissolved in 100 ml H_2O. Pentane (100 ml) and 3.34 g (22.5 mmol) trimethyloxonium tetrafluoroborate were added and the mixture was stirred vigorously. Extraction with pentane (5 × 100 ml) gave a deep red soln which was dried over Na_2SO_4. [Alternatively, the lithium acylmetalate, dissolved in 100 ml CH_2Cl_2, could be alkylated by 1.7 g (15 mmol) methyl fluorosulphonate. Sometimes a few ml MeOH was needed for starting the methylation. On warming to room temp the mixture turned deep red. After 1 hr a few ml MeOH was added to destroy excess methyl fluorosulphonate. After 30 min the mixture was filtered through silica gel.] Removal of the solvent gave a deep red oil which was chromatographed over silica gel in pentane–CH_2Cl_2 at −25°. Hard red crystals were obtained from pentane–Et_2O at −78°; 4.7 g (74%), m.p. 93°. IR ν_{max}^{hexane} (CO) cm^{-1}: 2062 (s), 1988 (m), 1962 (vs), 1949 (vs). ^{1}H-NMR (d_6-C_6H_6): δ 3.53 (s, 3H, naphthyl-OMe), 3.58 (s, 3H, $C_{carbene}$—OMe), 3.63 (s, 3H, naphthyl-OMe), 6.35 (s, 1H, H-3), 7.23 (m, 2H, H-6, H-7), 7.91 (m, 1H, H-5 or H-8), 8.34 (m, 1H, H-5 or H-8). ^{13}C-NMR (d_6-C_6H_6): δ 353.19 ($C_{carbene}$), 224.93 (CO_{trans}), 216.95 (CO_{cis}), 152.51 (C-1, C-4), 140.14 (C-2), 127.64, 126.62, 123.05 (C-5–C-10), 98.14 (C-3), 65.75 ($C_{carbene}$—OMe), 61.85 (OMe-1), 55.01 (OMe-4). MS *m/z* (%): 422 $[M]^+$ (14), 394 (7), 366 (11), 338 (14), 310 (32), 282 (93), 267 (19), 252 (26), 237 (21), 224 (24), 222 (25), 209 (32), 153 (12), 134 (13), 52 (100). (Found: C, 54.10; H, 3.49; Cr, 12.26%; $C_{19}H_{14}CrO_8$ 422.3. Requires: C, 54.04; H, 3.34; Cr, 12.31%.)

Tetracarbonyl[methoxy(1,4 - dimethoxy - 2 - naphthyl) - carbene]chromium(0) (**15**).[1] A soln of 4.22 g (10 mmol) **14** in 25 ml *t*-butyl methylether was warmed at 55° under reflux for 8 hr while a slight stream of N_2 was bubbled through. Removal of the solvent at reduced pressure and crystallization in pentane–Et_2O at −78° gave hard reddish brown crystals; 3.86 g (98%), m.p. 147°. IR ν_{max}^{hexane} (CO) cm^{-1}: 2016 (s), 1950 (s), 1930 (vs), 1871 (s). ^{1}H-NMR (d_6-C_6H_6): δ 3.41 (s, 3H, OMe-4), 3.53 (s, 3H, $C_{carbene}$—OMe), 4.65 (s, 3H, OMe-1), 6.70 (s, 1H, H-3), 7.19 (m, 2H, H-6, H-7), 8.30 (m, 2H, H-5, H-8). ^{13}C-NMR (d_6-C_6H_6): δ 336.09 ($C_{carbene}$), 232.75 (CO_{trans}), 215.98 (CO_{cis}), 153.32 (C-1), 132.00 (C-4), 129.08 (C-2), 127.44, 123.70, 122.88 (C-5–C-10), 91.63 (C-3), 74.87 (OMe-1), 67.71 (carbene—OMe), 55.01 (OMe-4). MS *m/z* (%): 394 $[M]^+$ (3), 366 (3), 338 (3), 310 (8), 282 (22), 252 (6), 220 (25), 209 (9), 188 (98), 173 (100), 145 (24), 130 (13), 108 (29), 102 (13), 80 (49), 52 (98). (Found: C, 54.57; H, 3.51; Cr, 13.16%; $C_{18}H_{14}CrO_7$ 394.3. Requires: C, 54.83; H, 3.58; Cr, 13.19%.)

Cycloaddition and decomplexation

Tricarbonyl[3 - carbomethoxy - 4 - (1' - hydroxy - 4',9',10' - trimethoxy - 2' - anthracenyl)butanoic acid methylester] - chromium(0) (**16**). Compound **15** (1.97 g, 5 mmol) was dissolved under Ar in 25 *t*-butyl methylether and warmed at 50° after which 1.01 g (5.5 mmol) of **9** were added dropwise. The initial red–brown soln immediately turned deep black and a ppt of the tricarbonyl complex was obtained. After a few minutes the suspension was cooled to −40°, the solvent was decanted and the black solid was dissolved in CH_2Cl_2 and precipitated with pentane at −50°. Removal of the solvent and drying at high vacuum gave a black–brown solid **16**; 2.26 g (78%). IR ν_{max}^{KBr} cm^{-1}: 3440, 3000, 2942, 2920, 2840, 2820, 1935, 1855, 1735, 1625, 1600, 1560, 1500, 1440, 1410, 1330, 1318, 1266, 1208, 1162, 1110, 1060, 1030, 1000, 965, 930, 890, 845, 808, 773, 680, 630.

3 - Carbomethoxy - 4 - (1' - hydroxy - 4',9'10' - trimethoxy - 2' - anthracenyl)butanoic acid methylester (**17**). Compound **16** (1.16 g, 2 mmol) was dissolved in 200 ml Et_2O and stirred in an autoclave at 70° under a CO pressure of 75 bar for 72 hr. Cooling to −50° and filtration through 2 cm silica gel gave a separation of hexacarbonyl chromium. Removal of the solvent at reduced pressure gave **17** as a yellow–orange waxy solid, which could be further purified by preparative TLC; 0.86 g (98%). IR ν_{max}^{KBr} cm^{-1}: 3440, 3070, 3000, 2950, 2920, 2842, 1740, 1629, 1590, 1530, 1510, 1460, 1440, 1425, 1395, 1368, 1310, 1250, 1215, 1165, 1140, 1100, 1032, 995, 935, 850, 775, 740, 638. ^{1}H-NMR ($CDCl_3$): δ 3.30–2.77 (m, 4H, alkyl-H), 3.73–3.30 (m, 1H, R_3C—H), 3.71 (s, 6H, 2 CO_2Me), 3.83 (s, 3H, —OMe), 3.92 (s, 3H, —OMe), 3.98 (s, 3H, —OMe), 6.48 (s, 1H, H-3), 7.72–7.37 (m, 2H, H-6, H-7), 8.43–8.09 (m, 2H, H-5, H-8). MS *m/z* (%): 442 $[M]^+$ (38), 411 (27), 380 (100), 319 (77), 284 (90), 267 (43), 249 (29), 223 (26), 153 (22), 152 (17), 59 (32). (Found: C, 66.42; H, 5.96%; $C_{24}H_{26}O_8$ 442.5. Requires: C, 65.15; H, 5.92%.)

REFERENCES

[1] K. H. Dötz, W. Sturm, M. Popall and J. Riede, *J. Organomet. Chem.* **277**, 267 (1985).

[2] For a recent review covering selected topics see: *Modern Synthetic Methods* (Edited by R. Scheffold), Vol. 3, pp. 61–353. Salle and Sauerländer, Frankfurt (1983).

[3] K. H. Dötz, *Angew. Chem.* **87**, 672 (1975); *Ibid. Int. Ed. Engl.* **14**, 644 (1975).

[4] K. H. Dötz and R. Dietz, *Chem. Ber.* **111**, 2517 (1978).

[5] K. H. Dötz and R. Dietz, *Ibid.* **110**, 1555 (1977).

[6] K. H. Dötz and W. Kuhn, *J. Organomet. Chem.* **252**, C78 (1983).

[7] K. H. Dötz, *Ibid.* **140**, 177 (1977).

[8] K. H. Dötz and D. Neugebauer, *Angew. Chem.* **90**, 898 (1978); *Ibid. Int. Ed. Engl.* **17**, 851 (1978).

[9] K. H. Dötz, R. Dietz, C. Kappenstein, D. Neugebauer and U. Schubert, *Chem. Ber.* **112**, 3682 (1979).

[10] K. H. Dötz, R. Dietz and D. Neugebauer, *Ibid.* **112**, 1486 (1979).

[11] K. H. Dötz and R. Dietz, *J. Organomet. Chem.* **157**, C55 (1978).

[12] For a recent review, see: K. H. Dötz, *Pure Appl. Chem.* **55**, 1689 (1983); *Angew. Chem.* **96**, 573 (1984); *Ibid. Int. Ed. Engl.* **23**, 587 (1984).

[13] K. H. Dötz, J. Mühlemeier, U. Schubert and O. Orama, *J. Organomet. Chem.* **247**, 187 (1983).

[14] W. D. Wulff, P. C. Tang and J. St. McCallum, *J. Am. Chem. Soc.* **103**, 7677 (1981).

[15] H. Fischer, J. Mühlemeier, R. Märkl and K. H. Dötz, *Chem. Ber.* **115**, 1355 (1982).

[16] K. H. Dötz and W. Sturm, *J. Organomet. Chem.* **285**, 205 (1985).

Preliminary results have been reported: *Second International Conference on Organometallic Chemistry Directed Toward Organic Synthesis*, Dijon (1983).
[17] K. H. Dötz and B. Fügen-Köster, *Chem. Ber.* **113**, 1449 (1980).
[18] K. H. Dötz and I. Pruskil, *J. Organomet. Chem.* **209**, C4 (1981).
[19] K. H. Dötz, I. Pruskil and J. Mühlemeier, *Chem. Ber.* **115**, 1278 (1982).
[20] K. H. Dötz and W. Kuhn, *Angew Chem.* **95**, 750 (1983); *Ibid. Int. Ed. Engl.* **22**, 732 (1983); *Angew. Chem. Suppl.* 1045 (1983).
[21] M. F. Semmelhack, J. J. Bozell, T. Sato, W. Wulff, E. Spiess and A. Zask, *J. Am. Chem. Soc.* **104**, 5850 (1982).
[22] *Inorg. Synth.* (Edited by D. F. Shriver), Vol. XIX, p. 164 (1979).
[23] For recent reviews see: *Anthracycline Antibiotics* (Edited by H. S. El Khadem). Academic Press, New York (1982); F. Arcamone, *Doxorubicin Anticancer Antibiotics*. Academic Press, New York (1981).
[24] W. D. Wulff and P.-C. Tang, *J. Am. Chem. Soc.* **106**, 434 (1984).
[25] J. B. Data and R. D. Bennett, *J. Med. Pharm. Chem.* **4**, 327 (1961).
[26] C. M. Wong, R. Schwenk, D. Popien and T.-L. Ho, *Can. J. Chem.* **51**, 466 (1973).
[27] F. M. Hauser and S. Prasanna, *J. Am. Chem. Soc.* **107**, 6378 (1981).
[28] C. M. Wong, D. Popien, R. Schwenk and J. T. Raa, *Can. J. Chem.* **49**, 2712 (1971).
[29] S. D. Kimball, D. R. Walt and F. Johnson, *J. Am. Chem. Soc.* **103**, 1561 (1981).
[30] R. A. Cormier, W. L. Schreiber and W. C. Agosta, *J. Am. Chem. Soc.* **95**, 4873 (1973).
[31] J. S. Swenton and P. W. Raynolds, *J. Am. Chem. Soc.* **100**, 6188 (1978).