Tetrahedron Letters,Vol.27,No.21,pp 2353-2356,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

Regiodirected Substitution of [2.2]Paracyclophanedienes and [2.2]Paracyclophanes through Tricarbonylchromium Complexation[1,2]

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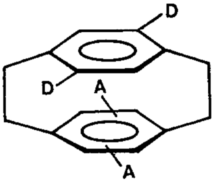
Abstract: *4,7-dialkoxy[2.2]paracyclophanes and the corresponding 1,9-dienes are shown to undergo selective complexation with $Cr(CO)_3L_3$-reagents on their less substituted benzene moiety. Lithiation/silylation of these complexes leads to arene- or bridge-substitution, respectively. An analogous behaviour is observed for the tricarbonylchromium[2.2]paracyclophane and its 1,9-diene.*

Arene tricarbonylchromium complexes are known to undergo direct metalation easily and regioselectively[3]. This and the possible subsequent electrophilic substitution of such complexes appeared to be a simple route to donor-acceptor-substituted [2.2]paracyclophane derivatives of type **1** from readily accessible 4,7-dialkoxy[2.2]paracyclophanedienes **2**[4] via their tricarbonylchromium complexes **4** and **6**.



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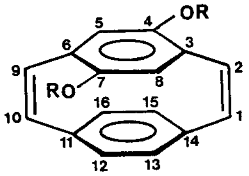
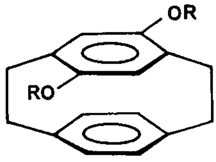


2

a) R = H
b) R = Me
c) R = Bu^n

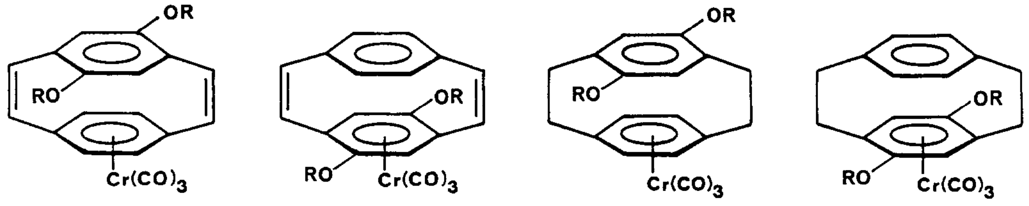


3

Hydroquinone **2a** was obtained by acid-catalyzed (acetic acid/methanol) enolization of the corresponding quinol[5] (94% yield, mp 231°C) and alkylated to its dimethyl- **2b** (87%)[6] and dibutyl ether **2c** (68%)[6] with dimethylsulfate and n-butylbromide, respectively. Catalytic hydrogenation of **2b** and **2c** (Pt, EtOH) afforded the saturated 4,7-dialkoxy[2.2]paracyclophanes **3b**[7] and **3c**[6] (80% and 92%), respectively.

The tricarbonylchromium complexes **4**/**5** and **6**/**7** were formed upon reacting **2** and **3** respectively with $(EtCN)_3Cr(CO)_3$ in dioxane[8] (method A) or $Cr(CO)_6$ in dibutylether/tetrahydrofuran (THF) 10:1 [9] (method B). It is noteworthy that all these complexations occurred regioselectively at the less substituted benzene ring[10] except for that of **6c** with $(EtCN)_3Cr(CO)_3$. Method A consistently gave better yields but with less regioselectivity (scheme 1).

Scheme 1. Product distribution (isol. yields after recrystallization) upon complexation of **2** and **3**.



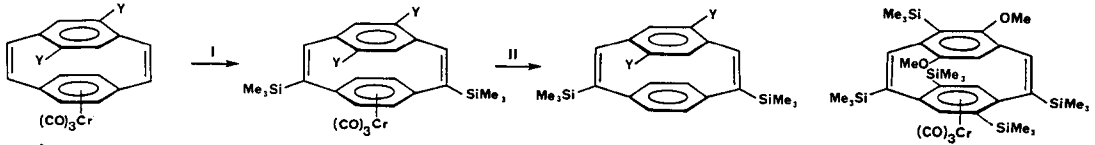
4 **5** **6** **7**

	4	5		6	7
b:	75%	5%	(A)	-	-
	37%	0%	(B)	54%	trace
c:	73%	5%	(A)	40%	39%

Lithiation of **4** with *n*-butyllithium/N,N,N',N'-tetramethylethylenediamine (*n*-BuLi/TMEDA)[3b] in THF and subsequent trapping with chlorotrimethylsilane (TMSCl) gave almost exclusively the 1,10-bistrimethylsilyl derivative **8** (**b**: 43%; **c**: 80% isolated)[6] along with minor amounts (**b**: 6%) of the 1,9-bistrimethylsilyl derivative. **4b** gave a substantial fraction (32% isolated) of the 1-monosilylated derivative upon treatment with 5 *n*-BuLi and TMSCl.

In contrast to this, the saturated complex **6c** was metalated at the tricarbonylchromium complexed benzene ring under identical conditions. Only a mono-lithiation/silylation was achieved (65% yield), however, even with a tenfold excess of *n*-BuLi after more than 40 hrs. Reacting the monosilylated complex **14c**[6] again with 10 *n*-BuLi/TMSCl gave the *para*-bissilylated complex *p*-**15c**[6]. The pseudo-*ortho*-configuration was assigned to **15c** on the basis of its ^{1}H-NMR-spectrum[11].

Scheme 2. Lithiation/silylation of [2.2]paracyclophane complexes.



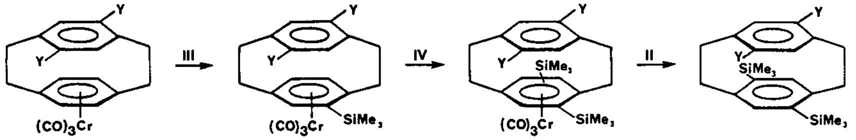
4 b/c (Y = OMe/OBu)
11 Y = H

8 b/c (Y = OMe/OBu)
12 Y = H

9 b/c (Y = OMe/OBu)
13 Y = H

10 b

I: 1) 5*n*-BuLi/TMEDA, THF, -78°C, 2h; 2) TMSCl. II: 1) CF_3CO_2H, O_2; 2) H_2O. III: Y≠H: 1) 10*n*-BuLi/ TMEDA, THF, -78°C, 40-50h; 2) TMSCl. Y=H: 1) 5*n*-BuLi/TMEDA, THF, -78°C, 41h; 2) TMSCl. IV: Y≠H: 10*n*-BuLi/TMEDA, THF, -78°C, 40-50h; 2) TMSCl. Y=H: 1) 10*n*-BuLi/TMEDA, THF, -78°C, 14h; 2) TMSCl.



6 Y = OBu
17 Y = H

14 Y = OBu
18 Y = H

15 Y = OBu
19 Y = H

16 Y = OBu
20 Y = H

The striking selectivity for bridge metalation in **4** and ring attack in **6** cannot be caused in any way by the alkoxy substituents as it is also observed for the parent complexes **11**[6] and **17**[12], which predominantly gave the 1,10-bissilylated **12** (41%)[6] and the p- and m-bissilylated complexes p/m-**19** (72%, p/m = 1.33)[6], respectively, the latter was obtained in two steps via the monosilyl derivative **18** (90%)[6].

Apparently in these compounds there is a delicate balance in the kinetic acidities of the various vinylic and arylic positions, which favors vinylic proton abstraction from the 1,10-positions in the diene complexes **4**, **11** and arylic deprotonation in their saturated analogues **6**, **17**. Once the vinylic 1,10-positions are protected as in **9b**, further stepwise metalation/silylation with 10 and 5 equivalents n-BuLi/TMEDA and TMSCl respectively surprisingly leads to the pentakistrimethylsilyl derivative **10b** (37% overall). As the ligands **9**, **13**, **16**, **20** can be liberated from the corresponding complexes by oxidation in trifluoroacetic acid, the three step sequence of complexation, lithiation and electrophilic substitution opens a new route to various compounds of type **1** with intramolecular charge transfer.

Table 1. Spectroscopical and physical data of selected new [2.2]paracyclophane chromium complexes.

Compound	mp., [°C] (N_2,sealed tube)	IR: (CH_2Cl_2): $\nu C\equiv O$ [cm^{-1}]	UV:(CH_2Cl_2, λ_{max}[nm] (lgε))	^{13}C-NMR($CDCl_3$): $\delta_{C\equiv O}$ [ppm]
4b	163(decomp.)	1960, 1880	338 (4.13)	234.75
4c	97-98	1959, 1879	337 (4.01)	234.93
5b	158-161(decomp.)	1953, 1872	334 (3.83), 410 (3.57)	235.26
5c	103-104	1953, 1869	335 (3.72), 4.06 (3.48)	235.60
6c	138	1954, 1874	336 (4.05)	235.22
7c	175-176	1947, 1861	339 (3.75)	236.17
8b	201	1954, 1876	339 (4.08)	235.16
8c	142-143	1954, 1876	338 (3.99)	235.30
p-15c	143-144	1947, 1871	340 (3.97)	235.40
11	190(decomp.)	1960, 1881	342 (3.97)	234.81
12	198-201	1952, 1875	345 (3.97)	235.18

^{1}H-NMR (270 Mhz, $CDCl_3$):

4c: δ= 0.96(t, $^3\underline{J}$ = 7.2, 6H, $C\underline{H}_3$), 1.45(m, 4H, $C\underline{H}_2CH_3$), 1.69(m, 4H, $C\underline{H}_2CH_2O$), 3.76(dt, $^2\underline{J}$ = 9.1, $^3\underline{J}$ = 6.6, 2H, $OC\underline{H}_2{}^a$), 3.85(dt, $^2\underline{J}$ = 9.1, $^3\underline{J}$ = 6.6, 2H, $OC\underline{H}_2{}^b$), 4.73 and 5.04(AA'BB' system, $^3\underline{J}$ = 7.0, $^4\underline{J}$ = 1.4, 12(13, 15,16)-H), 6.10(s, 5(8)-H), 6.72(d, $^3\underline{J}$ = 10.0, 1(10)-H), 7.11(d, $^3\underline{J}$ = 10.0, 2(9)-H).

6c: δ= 1.01(t, $^3\underline{J}$ = 7.3, 6H, $C\underline{H}_3$), 1.54(m, 4H, $C\underline{H}_2CH_3$), 1.77(m, 4H, $OCH_2C\underline{H}_2$), 2.53-2.82(m, 6H), 3.54(m, $^2\underline{J}$ = 12.2, $^3\underline{J}$ = 9.2, 2H), 3.75(dt, $^2\underline{J}$ = 9.2, $^3\underline{J}$ = 6.1, 2H, $OC\underline{H}_2{}^a$), 3.86(dt, $^2\underline{J}$ = 9.2, $^3\underline{J}$ = 6.1, 2H, $OC\underline{H}_2{}^b$), 4.55 and 4.85(AA'BB' system, $^3\underline{J}$ = 6.8, $^4\underline{J}$ = 1.9, 12(13,15,16)-H), 6.03(s, 5(8)-H).

7c: δ= 1.01(t, $^3\underline{J}$ = 7.3, 6H, $C\underline{H}_3$), 1.54(m, 4H, $C\underline{H}_2CH_3$), 1.75(m, 4H, $OCH_2C\underline{H}_2$), 2.29(m, 2H), 3.05-3.27(m, 6H), 3.59(dt, $^2\underline{J}$ = 8.5, $^3\underline{J}$ = 6.1, 2H, $OC\underline{H}_2{}^a$), 3.80(dt, $^2\underline{J}$ = 8.5, $^3\underline{J}$ = 6.1, 2H, $OC\underline{H}_2{}^b$), 4.40(s, 5(8)-H), 6.65 and 6.90(AA'BB' system, $^3\underline{J}$ = 8.0, $^4\underline{J}$ = 1.9, 12(13,15,16)-H).

8c: δ= 0.25(s, 18H, $SiC\underline{H}_3$), 0.97(t, $^3\underline{J}$ = 7.4, 6H, $C\underline{H}_3$), 1.48(m, 4H, $C\underline{H}_2CH_3$), 1.68(m, 4H, $OCH_2C\underline{H}_2$), 3.72(m, 2H, $OC\underline{H}_2{}^a$), 3.85(m, 2H, $OC\underline{H}_2{}^b$), 4.56 and 4.86(AA'BB' system, $^3\underline{J}$ = 7.1, $^4\underline{J}$ = 1.7, 12(13,15,16)-H), 6.01(s, 5(8)-H), 7.22(s, 2(9)-H).

p-15c: δ = 0.44(s, 18H, $SiC\underline{H}_3$), 0.99(t, $^3\underline{J}$ = 7.2, 6H, $C\underline{H}_3$), 1.52(m, 2H, $C\underline{H}_2CH_3$), 1.73(m, 2H, $C\underline{H}_2CH_2O$), 2.59(m, 2H, $C\underline{H}_2$), 2.78(m, 4H, $C\underline{H}_2$), 3.45(m, 2H, $C\underline{H}_2$), 3.73(dt, $^2\underline{J}$ = 9.1, $^3\underline{J}$ = 6.3, 2H, $OC\underline{H}_2{}^a$), 3.90(dt, $^2\underline{J}$ = 9.1, $^3\underline{J}$ = 6.3, 2H, $OC\underline{H}_2{}^b$), 4.94(s, 13(16)-H), 6.21(s, 5(8)-H).

References and footnotes.

[1] *Dedicated to Professor Heinz A. Staab on the occasion of his 60th birthday.*

[2] This work was supported by the Stiftung Volkswagenwerk, the Fonds der Chemischen Industrie as well as E. Merck AG, Darmstadt and CWH AG, Marl/Hüls.

[3] Cf. a) R.J. Card, W.S. Trahanovsky, J. Org. Chem. 45, 2555, 2560 (1980); b) M.F. Semmelhack, J. Bisaha, M. Czarny, J. Am. Chem. Soc. 101, 768 (1979); c) G. Jaonen, A. Meyer, G. Simmoneaux, J. Chem. Soc. Chem. Comm. 1975, 813.

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[6] All new compounds gave satisfactory elemental analysis data and were fully characterized by IR, ^{1}H-NMR (see table 1), (^{13}C-NMR in part), MS spectroscopy.

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[9] C.A. Mahaffy, P.L. Pauson, Inorg. Synth. 19, 154 (1979).

[10] This has its precedent in the regioselective complexation of 1,4-dimethoxynaphthalene. Cf. E.P. Kündig, V. Desobry, D.P. Simmons, J. Am. Chem. Soc. 105, 6962 (1983).

[11] This assignment rests on the observation in a series of such compounds that the resonance of a proton pseudo-geminal to an alkoxy group is shifted to lower and that of a pseudo-ortho positioned proton to higher field with respect to those in the unsubstituted compounds. Cf. a) H.J. Reich, D.J. Cram, J. Am. Chem. Soc. 91, 3534 (1969); b) T. Shinmyozu, T. Inazu, T. Yoshino, Chem. Lett. 1977, 1347.

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(Received in Germany 5 March 1986)