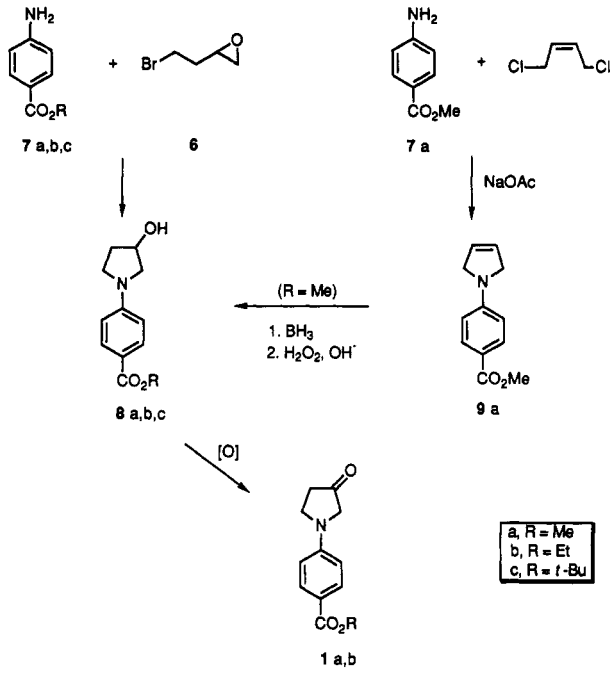
Scheme II



rt. The reaction was stirred at rt for 48.5 h and then quenched by addition of ethyl acetate (125 mL). Dicyclohexylurea was removed by filtration, and the filtrate was washed with water (3 × 250 mL) and brine (50 mL), dried over Na_2SO_4, filtered, and evaporated to afford an orange gum. Trituration with ether/hexanes afforded 1.22 g (61%) of a tan solid: mp 162–165 °C (lit.[8] mp 162–164 °C); ^1H NMR ($CDCl_3$) δ 2.72 (t, 2 H, CH_2CO, J = 7 Hz), 3.7–3.9 (superimposed t and s, 4 H, 2 CH_2N), 3.93 (s, 3 H, OCH_3), 6.22 and 7.94 (AB q, 4 H, ArH, J = 9 Hz).

***N*-[4′-(Ethoxycarbonyl)phenyl]-3-pyrrolidinone (1b). Method A.** The pyrrolidinol **8b** (100 mg, 0.42 mmol) and *N*-methylmorpholine *N*-oxide (148 g, 1.26 mmol) were dissolved in CH_2Cl_2 (5 mL) containing ca. 250 mg of powdered 4-Å molecular sieves and stirred for 10 min. Tetrapropylammonium perruthenate (TPAP, 7 mg, 0.02 mmol) was added, and the reaction mixture, which had turned black, was stirred for 4 h. The mixture was concentrated by rotary evaporation and applied directly to a silica gel column. Elution with CH_2Cl_2 followed by 1% MeOH in CH_2Cl_2 afforded recovered starting material (26 mg) and 53 mg (52%) of **1b** as colorless flakes: mp 143–144.5 °C; IR (Nujol) 1758, 1687, 1605 cm^{-1}; NMR ($CDCl_3$) δ 1.00 (t, J = 7 Hz, 3 H), 2.68 (t, J = 7.5 Hz, 2 H), 3.68 (t, J = 7.5, superimposed on a singlet at δ 3.68, 4 H), 4.22 (q, J = 7 Hz, 2 H), 6.43 and 7.78 (AB q, J = 9 Hz, 4 H). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.96; H, 6.52; N, 6.07.

Method B. The pyrrolidinol **8b** (500 mg, 2.12 mmol) and dicyclohexyl carbodiimide (1.43 g, 6.94 mmol) were dissolved in dry DMSO (13 mL). Crystalline phosphoric acid (99%, 100 mg, 1.06 mmol) was added, and the reaction mixture stirred for 22 h, diluted with ethyl acetate, chilled and made slightly basic by the addition of 1 N NaOH. Precipitated dicyclohexyl urea was removed by filtration, and the filtrate was dried ($MgSO_4$) and concentrated. Purification by the procedure described above in method A afforded 200 mg (40%) of **1b**, identical in all respects (NMR, IR, mp) with material prepared by method A.

Acknowledgment. We wish to thank Ms. Sandy Marousek for some technical assistance. This work was supported in part by grants from the National Institutes of Health (No. CA 028351, ECT) and from the Research Corporation (No. C-2642, RJK).

Registry No. **1a**, 90030-20-9; **1b**, 117098-11-0; **6**, 13287-42-8; **7a**, 619-45-4; **7b**, 94-09-7; **7c**, 18144-47-3; **8a**, 134031-02-0; **8b**, 134054-95-8; **8c**, 94930-28-6; **9a**, 134031-03-1; (*Z*)-1,4-dichloro-2-butene, 1476-11-5.

Highly Crowded Perchloropolyphenyl-*p*-xylylenes with Exceptional Thermal Stability

J. Castañer* and J. Riera

Departamento de Materiales Orgánicos Halogenados, Centro de Investigación y Desarrollo (C.S.I.C.), Jorge Girona 18-26, 08034 Barcelona, Spain

Received December 7, 1990 (Revised Manuscript Received April 29, 1991)

Introduction

As a continuation of our work on overcrowded aromatic chlorocarbons, we synthesized the perchloro-$\alpha,\alpha,\alpha',\alpha'$-tetraphenyl-*p*-xylylene (**5**; perchlorinated Thiele's hydrocarbon[1]) and studied its properties. Only four reports[2-5] dealing with this chlorocarbon have appeared to date. Ballester et al.[2-4] described products whose IR and UV spectra corresponded to mixtures of **5** and as much as 50 mol % of its αH, $\alpha' H$ precursor **3**. Veciana et al.[5] claimed that a synthesis of **5** was performed, but neither physical nor chemical properties of the product were given. Because the bulky chlorine substituents would force the twisting of the exocyclic carbon–carbon double bonds of the perchlorinated *p*-xylylenes, thus favoring the formation of a triplet state, perchloro-1,4-bis(9-fluorenylidene)cyclohexadiene (**6**) was also synthesized and its multiplicity ascertained.

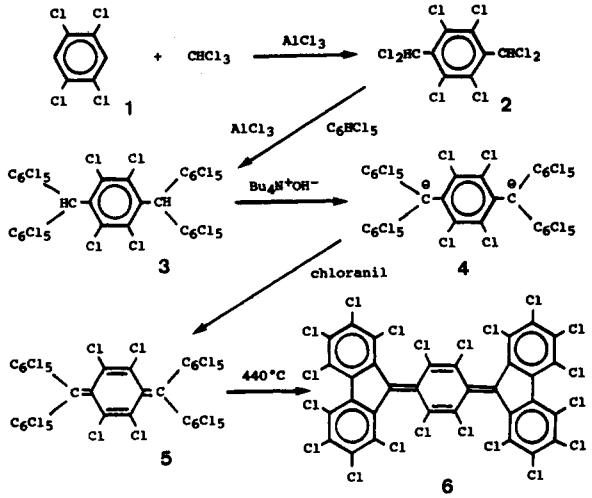
Results and Discussion

Perchloro-$\alpha,\alpha,\alpha',\alpha'$-tetraphenyl-*p*-xylylene (5). The $AlCl_3$-catalyzed Friedel–Crafts alkylation of pentachlorobenzene by $\alpha H,\alpha' H$-octachloro-*p*-xylene (**2**; prepared by Friedel–Crafts alkylation of 1,2,4,5-tetrachlorobenzene (**1**) by $CHCl_3$)[6] gave $\alpha H,\alpha' H$-tetraicosachloro-$\alpha,\alpha,\alpha',\alpha'$-tetraphenyl-*p*-xylene (**3**). Reaction of **3** with tetrabutylammonium hydroxide in THF DMSO afforded a dark reddish violet solution of the corresponding dianion **4**. This dianion was oxidized with chloranil to yield a virtually insoluble brick red compound, which was identified as chlorocarbon **5**. The UV–vis (λ 508 nm, ϵ 23 150) and IR spectra of **5** showed that the compounds reported by Ballester et al. (λ 502, ϵ 20 662)[2,4] and (λ 497 nm, ϵ 12 130)[3,4] were in fact mixtures of xylylene **5** and 11–50 mol % of its immediate precursor, the $\alpha H,\alpha' H$ derivative **3**. Upon crystallization, xylylene **5** incorporates 1 mol of $CHCl_3$. The chloroform is lost at 215 °C, and **5** decomposes at 395 °C. The compound's magnetic susceptibility (specific magnetic susceptibility = -0.510×10^{-6} emu) and the fact that a solution of **5** gives no ESR spectrum at room temperature clearly show that xylylene **5** is neither a triplet nor a double doublet, but a singlet. In contrast, it should be mentioned that the high degree of twisting about the

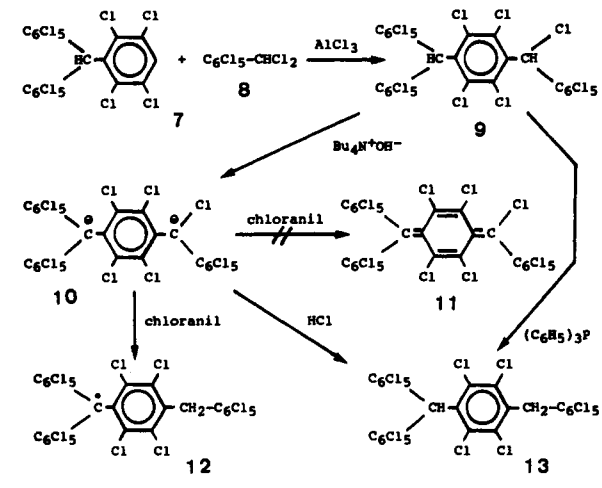
(1) Thiele, J.; Balhorn, H. *Chem. Ber.* **1904**, *37*, 1463.
(2) (a) Ballester, M.; Castañer, J.; Riera, J. Synthesis and Properties of Alkaromatic Chlorocarbons. A.D. Report **1968**, 672319. From *U.S. Govt. Res. Dev. Rep.* **1968**, *68*(18), 48; *Chem. Abstr.* **1969**, *70*, 46980t. (b) Monsó, J. M. Ph.D. Thesis, University of Barcelona, 1969.
(3) (a) Ballester, M.; Castañer, J.; Riera, J. Synthesis and Properties of Alkaromatic Chlorocarbons. Versatile Candidates for Thermostable, Inert Materials. A.D. Report **1973**, 763125. From *U.S. Govt. Rep. Announce.* **1973**, *73*(16), 43; *Chem. Abstr.* **1973**, *79*, 136646d. (b) Espinosa, J. M. Ph.D. Thesis, University of Barcelona, 1972.
(4) Ballester, M.; Olivella, S. *Polychloroaromatic Compounds*; Suschitzky, H., Ed.; Plenum Press: New York, 1974; p 154.
(5) Veciana, J.; Rovira, C.; Armet, A.; Domingo, V. M.; Crespo, M. I. *Mol. Cryst. Liq. Cryst.* **1989**, *176*, 77.
(6) Ballester, M.; Riera, J.; Castañer, J.; Rovira, C.; Armet, O. *Synthesis* **1986**, 64.

0022-3263/91/1956-5445$02.50/0

central biphenylic bond of the perchlorinated "Chichibabin hydrocarbon"[7] causes that compound to be a true double doublet that possesses a biphenyl structure, as its magnetic susceptibility and characteristic solution ESR spectrum show.[8]

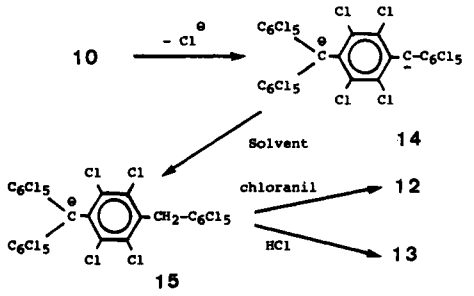


Perchloro-1,4-bis(9-fluorenylidene)cyclohexadiene (6). Heating xylylene **5** at 440 °C under argon gave a dark violet compound that was identified as chlorocarbon **6**. The compound's magnetic susceptibility (specific diamagnetic susceptibility = -0.531×10^{-6} emu) and the lack of a solution ESR spectrum at room temperature clearly showed that it is also a singlet. The cyclization of **5** to **6** was not unexpected because it was already known that the perchlorotriphenylmethyl (PTM) radical undergoes a similar cyclization at 300–10 °C to yield the perchloro-9-phenylfluorenyl (PPF) radical.[9,10] It should be pointed out that compound **6** is stable to at least 525 °C (differential scanning calorimetry, DSC; IR).



Attempted Synthesis of Perchloro-α,α,α'-triphenyl-*p*-xylylene (11). The $AlCl_3$-catalyzed Friedel–Crafts alkylation of αH,4*H*-tetradecachlorotriphenylmethane (**7**; prepared by Friedel–Crafts alkylation of 1,2,4,5-tetrachlorobenzene by αH-undecachlorodiphenylmethane)[6] by αH-heptachlorotoluene (**8**)[6,12] afforded $\alpha H,\alpha' H$-icosachloro-α,α,α'-triphenyl-*p*-xylene (**9**), the precursor of the desired xylylene **11**. However, all attempts to obtain xylylene **11** by means similar to those used to prepare **5**, i.e., by the reaction of **9** with tetrabutylammonium hydroxide followed by oxidation of the resulting dark violet solution with chloranil, failed. The only product isolated (in low yield; 13%) was a red compound identified as the $\alpha' H,\alpha' H$-nonadecachloro-4-benzyltriphenylmethyl radical (**12**) by elemental analysis and spectroscopic analysis (IR, UV–vis, and ESR). The ESR spectrum of **12** in solution consists of three lines (indicative of coupling with two hydrogens) with a hyperfine coupling constant of 1.6 G, which is of similar magnitude to those in the spectra of the tetradecachloro-4-methyltriphenylmethyl[12,13] (2.1 G) and tetradecachloro-4-(2,2-bis(ethoxycarbonyl)ethyl)triphenylmethyl[13] (1.15 G) radicals, and consequently is in accord with the postulated structure of **12**. Also the UV–vis spectrum of **12** displays the radical bands (around 380, 510, and 560 nm) characteristic of radicals of the PTM series.[8]

How radical **12** was formed can be explained by assuming that dianion **10** is unstable and eliminates chloride ion to yield a carbenoid intermediate like **14**. Species **14** may abstract hydrogen atoms from the solvent (THF is a good hydrogen atom donor) to give anion **15**. Finally, **15** could be oxidized by choranil to radical **12**. Such a mechanism is supported by the fact that acidification of the dark violet solution afforded $\alpha H,\alpha H,\alpha' H$-nonadecachloro-$\alpha,\alpha',\alpha'$-triphenyl-*p*-xylene (**13**), the protonated form of anion **15**. The structure of **13** was established by independent synthesis (i.e., dechlorination of **9** with triphenylphosphine).



Conclusions

It has been shown that, despite being highly crowded compounds, neither xylylene **5** nor bisfluorenylidene **6** possesses triplet or double doublet structures. In the case of **5**, this is consistent with the report of Montgomery et al.,[14] in which a singlet structure was claimed for the uncrowded Thiele's hydrocarbon. As far as bisfluorenylidene **6** is concerned, its singlet structure can be rationalized by taking into account the fact that it is already known that perchlorobis(9-fluorenylidene), a much more strained chlorocarbon (the degree of twisting about the exocyclic carbon–carbon double bond is 67°),[15] is also a singlet.[16] One important consequence of the singlet structures of **5** and **6** is the high thermal stability shown by both. It was found that **5** is stable up to 395 °C (DSC). At higher

(7) Chichibabin, A. E. *Chem. Ber.* **1907**, *40*, 1810.
(8) Ballester, M.; Riera, J.; Castañer, J.; Badía, C.; Monsó, J. M. *J. Am. Chem. Soc.* **1971**, *93*, 2215.
(9) Ballester, M.; Castañer, J.; Pujadas, J. *Tetrahedron Lett.* **1971**, 1699.
(10) Ballester, M.; Castañer, J.; Riera, J.; Pujadas, J. Armet, O.; Onrubia, C.; Río, J. A. *J. Org. Chem.* **1984**, *49*, 770.
(11) Ballester, M.; Molinet, C. *Anales Real Soc. Españ. Fis. Quim. Ser. B* **1958**, *54*, 151.
(12) Ballester, M.; Castañer, J.; Riera, J.; Ibañez. A.; Pujadas, J. *J. Org. Chem.* **1982**, *47*, 259.
(13) Ballester, M.; Veciana, J.; Riera, J.; Castañer, J.; Rovira, C.; Armet, O. *J. Org. Chem.* **1986**, *51*, 2472.
(14) Montgomery, L. K.; Huffman, J. C.; Jurczak, E. A.; Grendze, M. P. *J. Am. Chem. Soc.* **1986**, *108*, 6004.
(15) Ballester, M.; Castañer, J.; Riera, J.; de la Fuente, G.; Camps, M. *J. Org. Chem.* **1985**, *50*, 2287.
(16) Unfortunately, no crystals of **5** and **6** suitable for X-ray analysis could be isolated. Microcrystalline powders were always obtained.
(17) Armet, O.; Veciana, J.; Rovira, C.; Riera, J.; Castañer, J.; Molins, E.; Rius, J.; Miravitlles, C.; Olivella, S.; Brichfeus, J. *J. Phys. Chem.* **1987**, *91*, 5608.

temperatures it decomposes to bisfluorenylidene 6, a much more stable xylylene that can withstand temperatures as high as 525 °C without appreciable decomposition (DSC; IR). The high thermal stability of 5 and 6 can be attributed to the steric shielding brought about by the chlorine substituents. Similar shielding has been observed in polychlorinated triphenylmethyl radicals.[8,12-14]

Experimental Section

αH-Heptachlorotoluene (8). A mixture of pentachlorobenzene (100.0 g), anhydrous $AlCl_3$ (65.0 g), and $CHCl_3$ (750 mL) was refluxed for 20 h. The resulting dark mixture was treated with aqueous HCl, and the liquid was decanted. The two liquid layers were separated. The organic layer was washed with water, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexane) and then recrystallized (hexane) to give compound 8 (127.8 g; 96%): mp 121–2 °C (lit.[11] mp 119–21 °C); IR (KBr) 3035 (w), 1532 (m), 1378 (s), 1355 (s), 1280 (s), 1230 (m), 1210 (m), 1120 (m), 960 (s), 772 (s), 755 (s), 705 (s), 670 (s), 605 (s), 505 (s) cm^{-1}.

αH,α'H-Octachloro-p-xylene (2). A mixture of 1,2,4,5-tetrachlorobenzene (1; 15.06 g), anhydrous $AlCl_3$ (20.1 g), and $CHCl_3$ (200 mL) was refluxed for 22 h. The dark violet reaction mass was poured into a 1:1 mixture of ice and aqueous 2 N HCl. The mixture was diluted with $CHCl_3$ and decanted. The organic layer was washed with water, dried, and evaporated to dryness. The residue was purified by column chromatography on silica gel (hexane) and then recrystallized (hexane) to give compound 2 (26.3 g; 99%): mp 127–9 °C (lit.[18] mp 126–8 °C); IR (KBr) 3035 (w), 1388 (s), 1263 (s), 1222 (s), 1140 (s), 858 (s), 758 (s), 640 (s), 615 (s), 497 (s) cm^{-1}.

αH,α'H-Tetraicosachloro-α,α,α',α'-tetraphenyl-p-xylene (3). A mixture of xylene 2 (3.82 g; 10 mmol), pentachlorobenzene (12.53 g; 50 mmol), and anhydrous $AlCl_3$ (6.67 g; 50 mmol) was heated at 160 °C for 5 h. The resulting dark blue-violet solid mass was treated with $CHCl_3$ and aqueous 2 N HCl until the violet color disappeared. The resulting mixture was filtered. The liquid organic layer was decanted, dried, and evaporated to dryness. The resulting solid was purified by column chromatography on silica gel (hexane) to give pentachlorobenzene (2.26 g). The previously filtered solid was placed on the top of a silica gel layer in a Soxhlet extractor and was extracted for 8 d. A virtually insoluble white solid that accumulated in the extract was collected daily[19] and was characterized as compound 3 (7.15 g; 58%): mp > 450 °C; IR (KBr) 2920 (w), 1532 (w), 1360 (s), 1335 (s), 1320 (m), 1292 (s), 1236 (s), 1130 (m), 1115 (m), 850 (m), 800 (s), 715 (m), 686 (m), 670 (s), 650 (m), 640 (m), 620 (m), 532 (m), 505 (m) cm^{-1}; UV ($CHCl_3$), λ_{max} 260 (sh) nm, 283 (sh), 295, 305 (ε 30 800, 880, 1410, 1690). Anal. Calcd for $C_{32}H_2Cl_{24}$: C, 31.0; H, 0.2; Cl, 68.8. Found: C, 31.1; H, 0.2; Cl, 68.7.

αH,α'H-Icosachloro-α,α,α'-triphenyl-p-xylene (9). A mixture of αH,4H-tetradecachlorotriphenylmethane[6] (7; 8.88 g), αH-heptachlorotoluene (8; 20.32 g), and anhydrous $AlCl_3$ (2.15 g) was heated at 160 °C for 6 h. The resulting dark violet solid was treated with $CHCl_3$/aqueous HCl until the violet color disappeared. The mixture was filtered, and the collected solid was recrystallized ($CHCl_3$) to give 9 (8.21 g, 65%) as a colorless solid: mp > 350 °C; IR (KBr) 2970 (w), 1532 (w), 1365 (s), 1335 (s), 1292 (s), 1232 (m), 1131 (m), 918 (m), 805 (s), 780 (m), 668 (s), 500 (m) cm^{-1}. Anal. Calcd for $C_{26}H_2Cl_{20}$: C, 30.5; H, 0.2; Cl, 69.3. Found: C, 30.8; H, 0.2; Cl, 69.3.

Perchloro-α,α,α',α'-tetraphenyl-p-xylylene (5). A mixture of tetraphenyl-p-xylene (3; 1.000 g), 40% aqueous $Bu_4N^+OH^-$ (30 mL), THF (1500 mL), and DMSO (225 mL) was stirred for 30 h. Chloranil (8.0 g) was added to the dark reddish violet solution, and stirring was continued for 48 h. The solid that formed was collected by filtration and was purified in the manner described above for 3 to give a virtually insoluble red adduct of chlorocarbon 5 and $CHCl_3$ (0.766 g; 70%). The adduct decomposed at 215 °C (see below): IR (KBr) 1620 (w), 1452 (w), 1340 (s), 1330 (s), 1310 (m), 1262 (s), 1210 (m), 1110 (m), 988 (m), 810 (m), 746 (s), 710 (m), 665 (s), 640 (m), 605 (m), 540 (m), 502 (m) cm^{-1}; UV-vis ($CHCl_3$) λ_{max} 335, 508 nm (ε 7800, 23 150). Anal. Calcd for $C_{32}Cl_{24}\cdot CHCl_3$: C, 29.2; H, 0.1; Cl, 70.7. Found: C, 29.3; H, 0.1; Cl, 70.6.

The DSC curve of the adduct showed an endothermic peak at 215 °C. The thermogravimetric analysis (TGA) showed a weight loss corresponding to the elimination of 1 mol of $CHCl_3$ per mole of chlorocarbon. Heating the adduct at 250 °C in vacuo yielded 5 as a brick red powder that decomposed at 395 °C. Compound 5 displayed almost the same IR and UV-vis spectra as the adduct (however, a strong band at 746 cm^{-1} in the IR became a medium band at 750 cm^{-1}).[20] Anal. Calcd for $C_{32}Cl_{24}$: C, 31.3; Cl, 68.9. Found: C, 31.1; Cl, 69.0. Specific magnetic susceptibility: −0.518 × 10^{-6} emu.

Perchloro-1,4-bis(9-fluorenylidene)cyclohexadiene (6). Tetraphenyl-p-xylylene (5; 0.213 g) was heated at 440 °C under argon for 15 min. The dark violet solid obtained was purified by column chromatography on silica gel ($CHCl_3$). Recrystallization (hexane) gave a dark violet solid (0.168 g; 97%), mp > 525 °C (DSC), identified as chlorocarbon 6: IR (KBr) 1570 (w), 1545 (w), 1525 (w), 1375 (s), 1340 (s), 1288 (s), 1182 (m), 1137 (m), 850 (m), 790 (m), 730 (m), 680 (m), 628 (m), 530 (m) cm^{-1}; UV-vis (C_6H_{12}) λ_{max} 217, 322 (sh), 332, 530, 566 nm (ε 102 800, 66 200, 79 500, 26 350, 30 600). Anal. Calcd for $C_{32}Cl_{20}$: C, 35.1; Cl, 64.9. Found: C, 35.2; Cl, 65.0. Specific magnetic susceptibility: −0.531 × 10^{-6} emu.

α'H,α'H-Nonadecachloro-4-benzyltriphenylmethyl Radical (12). A solution of triphenyl-p-xylene (9, 0.602 g), 40% aqueous $Bu_4N^+OH^-$ (0.850 g), THF (400 mL), and DMSO (48 mL) was refluxed for 24 h. Upon mixing the reactants, the solution immediately became dark blue. With heating the solution slowly turned dark violet. The solution was then cooled, treated with p-chloranil (0.800 g; 10 min), diluted with water, and extracted with $CHCl_3$. The extract was washed with water, dried, and evaporated. The dark solid residue was purified by column chromatography on silica gel (CCl_4). Recrystallization (CCl_4/pentane) yielded a brick red solid (0.078 g, 13%), mp 295–300 °C identified as radical 12: IR (KBr) 2960 (w), 1515 (w), 1425 (w), 1360 (s), 1338 (s), 1300 (m), 1260 (m), 920 (m), 815 (m), 785 (m), 733 (m), 710 (m), 680 (m), 662 (m) cm^{-1}; UV-vis (CCl_4) λ_{max} 280, 336 (sh), 369 (sh), 385, 509, 562 nm (ε 6025, 5330, 16 630, 30 410, 1195, 1055); ESR g, 2.0029; no. of lines, 3 (1:2:1); a_H, 1.6 G; $a_{\alpha^{13}C}$, 30.4 G; $a_{ar^{13}C}$, 13.4, 10.7 G. Anal. Calcd for $C_{26}H_2Cl_{19}$: C, 31.6; H, 0.2; Cl, 68.2. Found: C, 31.9; H, 0.3.

Reaction of Triphenyl-p-xylene 9 with Tetrabutylammonium Hydroxide and Then with Aqueous HCl. A solution of triphenyl-p-xylene 9 (0.604 g), 40% aqueous $Bu_4N^+OH^-$ (1.00 g), THF (400 mL), and DMSO (48 mL) was refluxed for 24 h. The resulting dark violet solution was acidified with 2 N aqueous HCl, diluted with water, and extracted with $CHCl_3$. The extract was washed with water, dried, and evaporated to give a brown solid residue. Purification of the residue by column chromatography on silica gel (CCl_4) and recrystallization (CCl_4/hexane) yielded impure αH,αH,α'H-nonadecachloro-α,α',α'-triphenyl-p-xylene (13; 0.186 g; 32%) identified by IR and ^1H NMR spectroscopy (see the following text).

Reduction of Triphenyl-p-xylene 9. A solution of triphenyl-p-xylene 9 (0.320 g), Ph_3P (0.260 g), and benzene (100 mL) was refluxed for 48 h. The resulting solution was evaporated to dryness, and the residue was purified by column chromatography on silica gel (CCl_4) to yield αH,αH,α'H-nonadecachloro-α,α',α'-triphenyl-p-xylene (13; 0.304 g; 98%): mp 387 °C (DSC); IR (KBr) 2985 (w), 2925 (w), 1530 (w), 1420 (w), 1370 (s), 1360 (s), 1340 (s), 1300 (s), 1240 (m), 1135 (m), 1116 (m), 925 (m), 810 (s), 785 (m), 680 (s), 675 (s), 665 (s), 630 (m), 525 (m), 495 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.00 (s, 1 H), 4.86 (s, 2 H). Anal. Calcd for $C_{26}H_3Cl_{19}$: C, 31.6; H, 0.3; Cl, 68.1. Found: C, 31.5; H, 0.4; Cl, 67.9.

Acknowledgment. This investigation was supported by the DGICYT of MEC, Projects no. 0144-84 and PB87-0388.

(18) Harvey, P. G.; Smith, F.; Stacey, M.; Tatlow, J. C. *J. Appl. Chem.* **1954**, *4*, 319.

(19) The chloroform was replaced daily to eliminate soluble impurities that may have accumulated.

(20) The IR spectrum of $CHCl_3$ shows a very strong band in this region.

Registry No. 1, 95-94-3; 2, 2142-31-6; 3, 134757-85-0; 4, 134757-86-1; 5, 134757-87-2; 6, 134757-88-3; 7, 79839-44-4; 8, 2136-95-0; 9, 134757-89-4; 10, 608-93-5; 11, 134781-06-9; 12, 134757-90-7; 13, 134757-91-8.

A Stereospecific Route to 2-Deoxy-β-glycosides

Jacquelyn Gervay and Samuel Danishefsky*

Department of Chemistry, Yale University, New Haven, Connecticut 06511-8118

Received February 22, 1991

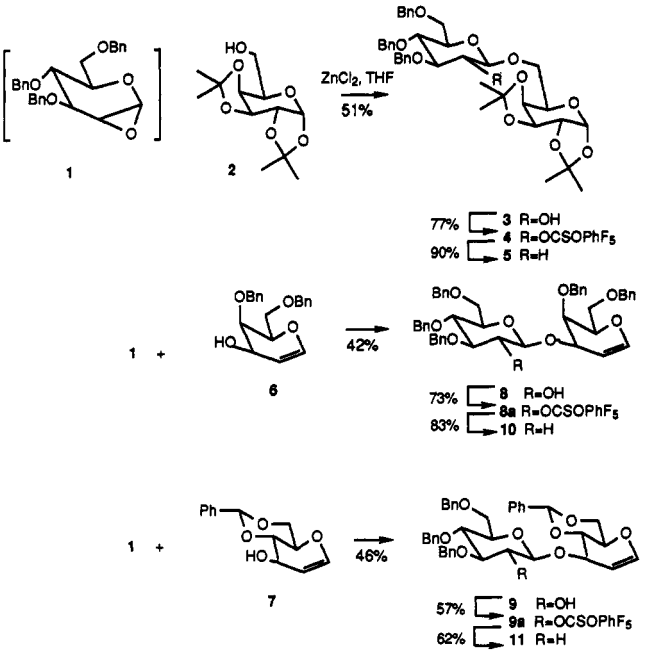
The 2-deoxy-β-glycoside unit is found in a variety of important antibiotics.[1-3] The stereospecific synthesis of such a linkage from various 2-deoxyglycosyl donors is complicated at several levels. First, the stereospecific installation of an anomeric activating group, with stereocontrol, in a system that lacks a directing influence at C_2 is beset with difficulties. Furthermore, lack of guidance from C_2 may erode the selectivity in the glycosylation reaction, if even a single C_1 anomer is available.

An ingenious solution to the problem was provided by Nicolaou, who used guidance from a C_2 α-phenylthio, C_1 β-fluoro arrangement (in turn generated by migration of a phenylthio group from $C_1 \rightarrow C_2$).[4] An alternative strategy involves activation of a glycal with an electrophile disposed to attack the double bond in an α sense. The α "onium" species, so generated, directs the glycosyl acceptor to the β-face of the C_1 of the donor. A particularly promising version of this method, utilizing thiosulfonium activation, was recently disclosed by Franck[5] with favorable stereoselectivity. In both the Nicolaou and Franck sequences, a C_2 phenylthio substituent is reductively cleaved to generate the 2-deoxy-β-glycoside system. The Franck method was applied to the synthesis of phenyl β-glycosides.

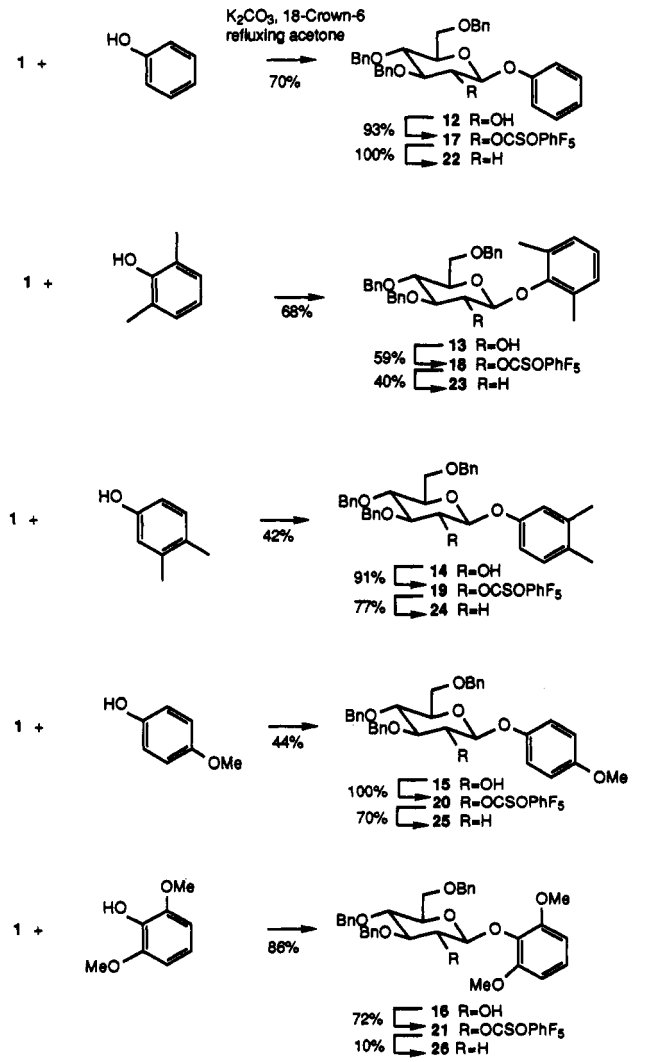
Recently the synthesis of 1α,2α oxiranes by direct epoxidation of D-glucal and D-galactal derivatives with 3,3-dimethyldioxirane was reported.[6] Under appropriate circumstances these epoxides function as stereospecific glycosyl donors, favoring β-face attack by the nucleophile by inversion at the anomeric carbon.[6,7] The deoxygenation of the C_2 hydroxyl group, generated from the glycosylation reaction, would be required to reach the title series. In this paper, we describe such deoxygenations. Applications to the synthesis of phenyl 2-deoxy-β-glycosides have been accomplished.

Reaction of tribenzyl-D-glucal with 3,3-dimethyldioxirane affords epoxide 1, which, on coupling with 1

Scheme I



Scheme II



(1) (a) Thiem, J.; Meyer, B. *J. Chem. Soc., Perkin Trans.* **1979**, *2*, 1331. (b) Thiem, J.; Meyer, B. *Tetrahedron* **1981**, *37*, 551.

(2) Koenuma, M.; Uchicha, N.; Yamaguchi, K.; Kawamura, Y. *J. Antibiot.* **1988**, *41*, 45.

(3) For a recent collection of natural products bearing this substructure, see ref 5.

(4) Nicolaou, K. C.; Ladduwahetty, T.; Randall, J. L.; Chucholowski, A. *J. Am. Chem. Soc.* **1986**, *108*, 2466.

(5) Franck, R. W.; Ramesh, S.; Kaila, N.; Grewal, G. *J. Org. Chem.* **1990**, *55*, 5.

(6) Danishefsky, S. J.; Halcolm, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 6661. For the first instance of epoxidation of a cyclic enol ether by the dioxirane method see: Baertschi, S. W.; Raney, K. D.; Stone, M. T.; Harris, T. M. *J. Am. Chem. Soc.* **1988**, *110*, 7929. For the preparation of the dioxirane reagent, see: Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847.

(7) Prior to our work,[6] there had been extensive studies of the use of 1,2-anhydro sugars (cf. Brigl's anhydride) as glycosylating agents. While inversion of C_1 had been observed with primary alcohols, related reactions with less reactive secondary alcohols, including saccharides, had afforded anomeric mixtures of glycosides in disappointing yield. The key to the success of the method lies in the use of nonparticipatory protecting groups. A thorough accounting of the prior art is provided in our previous paper[6] under citations 1–5 and 14.

0022-3263/91/1956-5448$02.50/0