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THE CHLORINATION OF HEXAMETHYLBENZENE AND OCTAMETHYLNAPHTHALENE WITH SULFURYL CHLORIDE-SILICA GEL (SC/SG)

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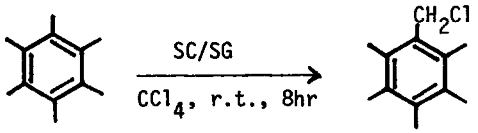
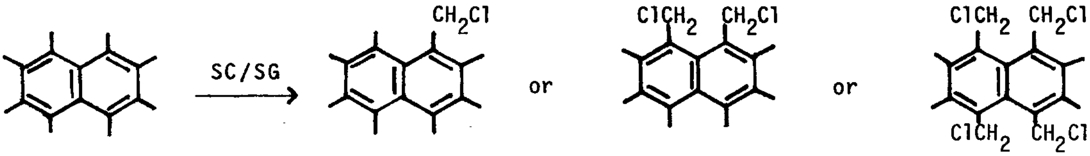
A catalytic effect by silica gel on electrophilic aromatic chlorinations by sulfuryl chloride was recently described.[1] We wish to report that this technique is synthetically useful for side-chain electrophilic chlorination of highly substituted aromatic compounds. Our results also bear on the recent controversy over whether such reactions occur by an electron-transfer[2] or electrophilic[3] mechanism.

A solution of hexamethylbenzene (1, 1.62 g, 10 mmol) in CCl_4 (25 ml) to which was added 0.35 g of silica gel[4] and 1.35 g (10 mmol) of sulfuryl chloride was stirred at room temperature for 8 hr. Work-up by washing with saturated $NaHCO_3$ solution, drying (Na_2SO_4) and removing the solvent gave 1.9 g (96%) of pentamethylbenzyl chloride 2, mp 79-81° (hexanes).[5] Under similar conditions, but with the silica gel omitted, no chlorination occurred (<1% in 72 hr). In view of the demonstration that SC/SG acts by an electrophilic mechanism,[1a,6] our results support the conclusions of Baciocchi and Illuminati[3] that polar α-chlorination of 1 occurs by an ionic rather than electron-transfer mechanism.



1 2 (96%)

Chlorination of octamethylnaphthalene (3)[7] by SC/SG can be controlled to give excellent yields of mono-, di- or tetrachloro derivatives, depending on the reagent/substrate mol ratio. The reactions were run at room temperature using procedures similar to those described for the conversion of 1 to 2.



3

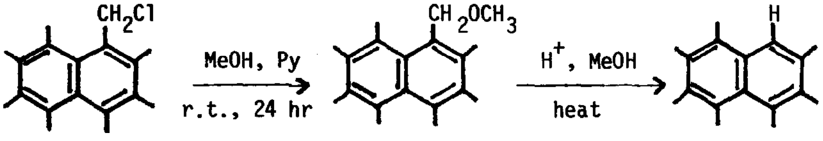
4 (96%)
(1:1 mol ratio, 4 hr)
mp 126-130°

5 (87%)
(2:1 mol ratio, 8 hr)
mp 184-185.5°

6 (91%)
(4:1 mol ratio, 8 hr)
mp 232-234°

The same chlorination products were obtained from 3 and sulfuryl chloride alone, but the reaction mixtures had to be refluxed (4, 7 hr; 5, 17 hr; 6, 36 hr), the yields were lower, and the products were less clean and difficult to purify. Thus the catalytic effect of the silica gel is marked.

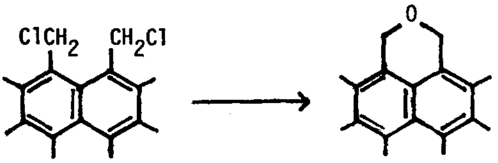
Compound 4 (mp 126-130°)[8] was shown to have the chloromethyl group in the 1-position by the following reaction sequence:



4 7 (60%) 8 (97%)

Treatment of 4 (1.0 g, 3.64 mmol) with methanol (25 ml) and pyridine (5 ml) in ether solution (250 ml) at room temperature for 24 hr gave the methyl ether 7 (0.59 g, 60%),[9,10] mp 90.5-92°. When 7 (0.1 g) was warmed for 10 min with methanol (10 ml) containing 1 drop of 37% HCl, the known[11] heptamethylnaphthalene 8 was obtained in nearly quantitative yield. Compound 4 was converted directly to 8 by refluxing methanol.[12]

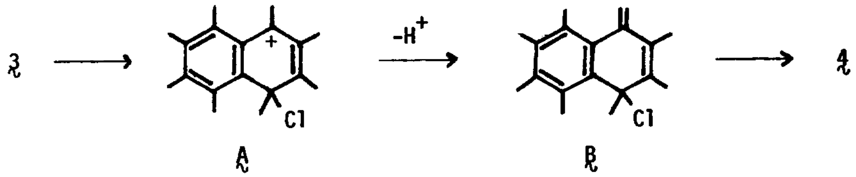
The room temperature nmr spectrum of 5[9,13] consisted of four singlets at δ2.30 (6H), 2.42 (6H), 2.65 (6H) and 4.72 (4H), indicating a symmetric structure. Since 5 could be prepared by further chlorination of 4 with SC/SG (93%, 6 hr), the chloromethyl groups in 5 must be in either the 1-4, 1-5 or 1-8 positions. That the latter was the case was shown by the hydrolysis of 5 (by chromatography on silica gel) to the cyclic ether 9,[9,14] mp 194-198°.



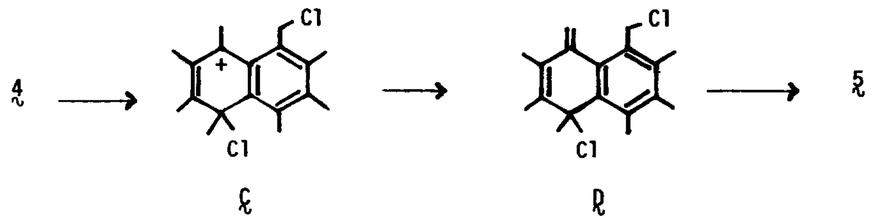
5 9

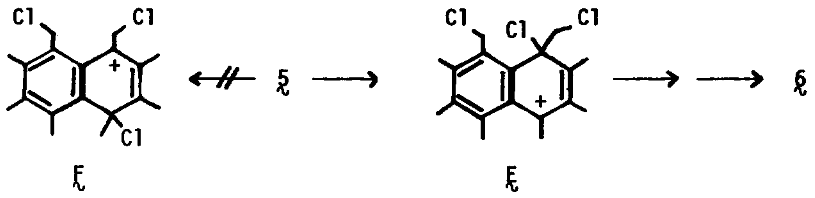
The nmr spectrum of 6[9,13] at 75° consisted of two sharp singlets at δ2.50 (12H) and 4.94 (8H). This spectrum indicated a symmetric structure, with the chloromethyl groups in either the 1,4,5,8 or 2,3,6,7 positions. That the former is correct was shown by the synthesis of 6 through further chlorination of 5 with SC/SG (93%, 8 hr).

The regiospecificity of these chlorinations of octamethylnaphthalene is striking. The most likely position for initial electrophilic attack is at C1,[7,15] not only for electronic reasons but also because attack at this position relieves a 1,8-peri interaction (in the intermediate A).



Explanations for the orientation on further chlorination can at this time only be speculative. If the second substitution occurs by the same mechanism as the first, we muct conclude that electrophilic attack occurs as shown in **C**. Because of the deactivating effect of the chloromethyl group in **4**, it is not surprising that the second chlorination occurs in the other ring, but the preferred 1,8 (rather than 1,5) orientation might not have been predicted. The formation of **6** from **5** requires attack at ring carbons which bear the chloromethyl groups. This is reasonable not only because strain due to peri-chloromethyl groups is relieved, but also because the positive charge is stabilized by methyl (**E**) rather than chloromethyl (**F**) groups.





The synthetic utility of SC/SG as a chlorinating agent, and the mechanism of silica gel catalysis[16] are being further explored.

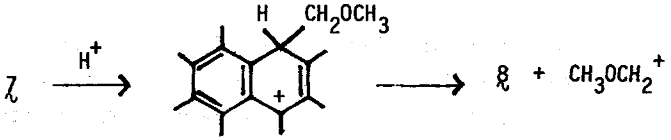
Acknowledgement: We are indebted to the National Institutes of Health (GM 15997) and to the National Science Foundation (GP 43659-X) for partial support of this research.

REFERENCES AND NOTES

1. (a) M. Hojo and R. Masuda, Synthetic Comm., **5**, 169 (1975). (b) Catalysis by more conven-

tional Lewis acids is also known; see W. D. Watson, Tetrahedron Lett., 2591 (1976) for an example and leading references.

2. J. K. Kochi, Tetrahedron Lett., 4305 (1974).
3. E. Baciocchi and G. Illuminati, Tetrahedron Lett., 2265 (1975); E. Bacciochi, L. Mandolini and A. Patara, Tetrahedron Lett., 2268 (1975). For a review, see S. R. Hartshorn, Chem. Soc. Reviews, **3**, 167 (1974).
4. Woelm silica gel, <0.063 mm, was used; activation was not essential.
5. W. J. Humphlett and C. R. Hauser, J. Am. Chem. Soc., **72**, 3289 (1950).
6. For example, toluene gave o- and p-chlorotoluene rather than benzyl chloride.[1a]
7. H. Hart and A. Oku, J. Org. Chem., **37**, 4269 (1972).
8. Nmr ($CDCl_3$): singlets at δ2.28 (9H), 2.43 (9H), 2.67 (3H), 4.80 (2H).
9. A satisfactory elemental analysis was obtained.
10. Nmr ($CDCl_3$): singlets at δ2.30 (9H), 2.38 (3H), 2.45 (6H), 2.60 (3H), 3.45 (3H), 4.40 (2H).
11. A. Oku and Y. Yuzen, J. Org. Chem., **40**, 3850 (1975).
12. The facile conversion of **7** to **8** must be due to the relief of strain and the stability of $CH_3OCH_2^+$ as a leaving group.



13. The restricted rotation of the chloromethyl groups in **4**, **5** and **6**, as studied by variable temperature nmr, will be the subject of a separate communication.
14. Previously synthesized by J. B-C. Jiang, Ph.D. thesis, Michigan State University, 1975.
15. B. J. Abidir, J. W. Cook and D. T. Gibson, J. Chem. Soc., 8 (1953); see also ref. 11.
16. One possibility is a ClO_2S-O-Si- intermediate formed by reaction between sulfuryl chloride and hydroxyl groups on the surface of the silica gel.