113. Highly Regioselective Nitration of Hexamethylbenzene and Its Derivatives to Dinitroprehnitene with Excess Nitronium Tetrafluoroborate[1])

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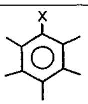
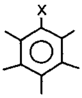
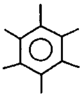
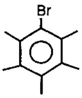
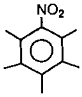
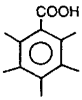
Hexamethylbenzene and its derivatives undergo very clean regioselective dinitration to dinitroprehnitene (1,2,3,4-tetramethyl-5,6-dinitrobenzene) with excess of nitronium tetrafluoroborate in dry CH_2Cl_2 solution. The mechanism of this unexpected new nitration is also discussed.

1. Introduction. – Nitration of hexamethylbenzene with fuming HNO_3 was investigated by *Suzuki* [2]. The reaction was found to be complex resulting in a mixture of products. The products identified in the mixture included 2,3,4,5,6-pentamethylbenzyl nitrate, 5,6-bis(nitroxymethyl)-1,2,3,4-tetramethylphenyl nitrate, 2,3,4,5,6-pentamethylphenylnitromethane, bis(2,3,4,5,6-pentamethylbenzyl) ether, pentamethylbenzaldehyde along with other unidentified compounds. On the basis of the products isolated, *Suzuki*

Table. *Preparation of Dinitroprehnitene from Hexamethylbenzene and Its Derivatives Using $NO_2^+BF_4^-$*

	 $NO_2^+BF_4^-$	Yield[a]) [%] of dinitroprehnitene
	1:65	95
	1:5	90
	1:4	96
	1:5	92

[a]) Isolated yield, product characterized by spectroscopic means.

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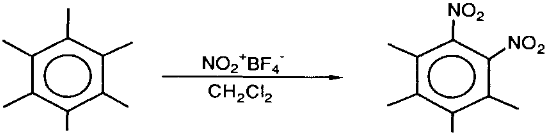
[1]) Aromatic substitutions, Part 61. Part 60: [1].

[2] suggested a possible path by which hexamethylbenzene can be converted into dinitroprehnitene (= 1,2,3,4-tetramethyl-5,6-dinitrobenzene). However, the method [2] was of little preparative value, and no significant amount of dinitroprehnitene was formed under the used conditions [3]. One of us [4] has reported the preparation of the long-lived hexamethylbenzenium nitrite by treating hexamethylbenzene in SO_2 with $NO_2^+BF_4^-$ dissolved in FSO_3H/SO_2 at −70°. The ion was characterized by ^{1}H-NMR spectrometry. The ion was also investigated by *Koptyug* and coworkers [5] who have, however, not identified products of the ion at the relatively elevated temperature ($> -8°$) of their studies.

In continuation of our interest in the nitration of organic compounds [6], we wish to report the unexpected finding that excess $NO_2^+BF_4^-$ in CH_2Cl_2 solution reacts cleanly with hexamethylbenzene and its derivatives to yield dinitroprehnitene in excellent yields.

2. Results and Discussion. – When 1 equiv. of hexamethylbenzene was treated with 6 (or more) equiv. of $NO_2^+BF_4^-$ in dry CH_2Cl_2, a deep dark solution was formed. After stirring the solution for a time, the color began to fade. The reaction mixture was stirred for 10 h. At this time, the solution was completely colorless. Upon aqueous workup, an almost quantitative yield of dinitroprehnitene was obtained *(Scheme 1)*.

Scheme 1



When hexamethylbenzene was treated with 5 to 3 equiv. of the $NO_2^+BF_4^-$, the product mixture revealed besides dinitroprehnitene also pentamethylnitrobenzene and unreacted starting material.

Similar reaction of pentamethylnitrobenzene, bromopentamethylbenzene, and pentamethylbenzoic acid with large excess (> 6 equiv.) of $NO_2^+BF_4^-$ also gave dinitroprehnitene in excellent isolated yields (see the *Table*). The relative product ratios varied as expected. Nitration of 1,2,3,5-tetramethyl-4-nitrobenzene and 1,2,3,4-tetramethyl-5-nitrobenzene also gave 1,2,3,5-tetramethyl-4,6-dinitrobenzene and dinitroprehnitene, respectively. Furthermore, pentamethylbenzaldehyde[2]) also reacts with excess NO_2^+ to give dinitroprehnitene. Based on these observations, one can propose a mechanism for the nitration of hexamethylbenzene (see *Scheme 2*).

No intermediates of the proposed *Scheme 2* could be isolated or observed. However, the mechanism proposed is reasonable based on earlier work of *Suzuki* [2] [3]. Moreover, cases of benzyl-nitrite formation [8] as well as related hydride abstraction [9] are documented in the literature. In fact, such side-chain nitration reactions have been employed recently for the preparation of some otherwise inaccessible compounds [10].

The observed *ortho*-selectivity from 1,2,3,4,5-pentamethyl-6-nitrobenzene to dinitroprehnitene in the reaction is probably due to initial complexation of NO_2^+ ion by the NO_2

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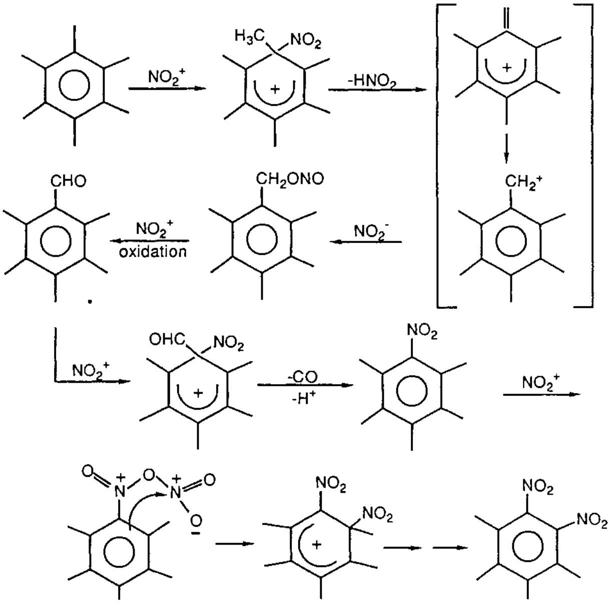
[2]) Prepared from pentamethylbenzyl chloride following the procedure in [7].

Scheme 2



group which facilitates attack by the NO_2^+ ion on the *ortho*-position of the aromatic ring. An alternative mechanistic pathway involving direct ring nitration followed by demethylation appears unlikely, since $^+CH_3$ would be an extremely unfavorable leaving group.

In conclusion, we have found a clean regioselective method for the preparation of dinitroprehnitene by the unexpected nitration of hexamethylbenzene and its derivatives with excess $NO_2^+BF_4^-$ in a single step.

Experimental Part

Hexamethylbenzene and its derivatives were purchased from *Aldrich* and used as received. $NO_2^+BF_4^-$ was also purchased from *Aldrich*. CH_2Cl_2 was rigorously dried over P_2O_5 and distilled before use. NMR spectra were obtained on a *Varian Associates* model *VXR-200* spectrometer. Mass spectra were obtained on a *Finnigan Incos-50* GC-MS instrument.

Typical Nitration Procedure. Hexamethylbenzene (0.324 g, 0.20 mmol) was added to a 30-ml *Nalgene* bottle containing 1.73 g of $NO_2^+BF_4^-$ (13 mmol) in 20 ml of dry CH_2Cl_2 under Ar. After shaking the bottle for 10 h, the mixture was quenched with H_2O (30 ml), extracted with CH_2Cl_2 (2 × 50 ml), washed with H_2O, and dried ($MgSO_4$). The solid residue was recrystallized from EtOH to obtain pure dinitroprehnitene as white crystalline solid: 0.425 g (95%). M.p. 179–181° ([2]: 176–177°). ^{1}H-NMR ($CDCl_3$): 2.31 (*s*, 6 H); 2.24 (*s*, 2.24). ^{13}C-NMR ($CDCl_3$): 142.2; 140.5; 127.7; 17.1, 15.5. GC-MS: 224 (55.9, M^+), 207 (43.9), 190 (2.31), 177 (86.3), 162 (10.7), 148 (10.4), 131 (31.1), 115 (61.6), 106 (45.6), 91 (98.7), 77 (100).

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REFERENCES

[1] G. A. Olah, T. Yamato, N. Trivedi, A. Tsuge, J. A. Olah, *Rend. Fis. Acc. Lincei*, in press.

[2] H. Suzuki, *Bull. Soc. Chem. Jpn.* **1970,** *43,* 879.

[3] a) H. Suzuki, *Synthesis* **1977,** 217; b) H. Suzuki, H. Koide, Y. Taki, E. Ohbayashi, T. Ogawa, *Chem. Lett.* **1987,** 891.

[4] G. A. Olah, H. C. Lin, Y. K. Mo, *J. Am. Chem. Soc.* **1972,** *94,* 3667.

[5] V. I. Mamatyuk, B. G. Derendyaev, A. N. Detsina, V. A. Koptyug, *J. Org. Chem. (USSR)* **1974,** *10,* 2506.

[6] G. A. Olah, R. Malhotra, S. C. Narang, 'Nitration: Methods and Mechanism', VCH Publishers Inc., Weinheim, 1989.

[7] Prepared from pentamethylbenzyl chloride following the procedure: N. Kornblum, W. J. Jones, G. J. Anderson, *J. Am. Chem. Soc.* **1959,** *81,* 4113.

[8] S. R. Hartshorn, *Chem. Soc. Rev.* **1974,** *3,* 167.

[9] G. A. Olah, B. G. B. Gupta, *J. Org. Chem.* **1980,** *45,* 3532; G. K. S. Prakash, Q. Wing, X-Y. Li, G. A. Olah, submitted to *New J. Chem.*

[10] a) T. Keumi, T. Inagaki, N. Nakayama, M. Taniguchi, T. Morita, H. Kitajima, *J. Org. Chem.* **1989,** *54,* 4034; b) T. Keumi, T. Inagaki, N. Nakayama, T. Morita, H. Kitajima, *J. Chem. Soc., Chem. Commun.* **1987,** 109; c) T. Keumi, T. Morita, K. Teramoto, H. Takahashi, H. Yamamoto, K. Ikeno, M. Hanaki, T. Inagaki, H. Kitajima, *J. Org. Chem.* **1986,** *51,* 3439.