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# THE DI-t-BUTYLSILYLENE PROTECTING GROUP FOR DIOLS

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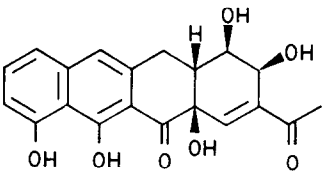
ABSTRACT: Di-t-butyldichlorosilane reacts with diols to yield the corresponding di-t-butylsilylene derivatives. This useful protecting group is readily removed by treatment with pyridinium hydrofluoride.

In conjunction with our synthetic efforts directed toward pillaromycinone (1), we required a diol protecting group having the following properties: 1) stability to Lewis acids, 2) ability to be removed chemoselectively in the presence of ester and t-butyldimethylsilyl ether functions, 3) ability to be removed under non-acidic or, at most, mildly acidic conditions, and 4) stability to chromatography. While dihydroxy compound 2 (see




1

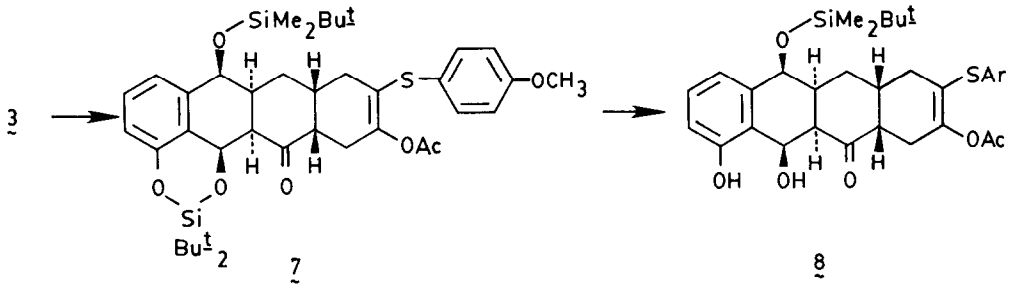
Table) readily yields the corresponding isopropylidene derivative,[1] this method of protection proved to be unsatisfactory for subsequent transformations. The use of dialkylsilylene derivatives was therefore investigated.[2] Preliminary experiments utilizing imidazole in DMF indicated that adducts readily formed between compound 2 and dimethyldichlorosilane, as well as between 1,8-dihydroxynaphthalene and diphenyldichlorosilane. Unfortunately, these adducts failed to survive chromatography. On the other hand, di-t-butyldichlorosilane[3] yielded adducts which fully satisfy all of our requirements.

The Table summarizes our results. While triethylamine or imidazole in DMF can serve to give quite good results in some cases, the best and most general approach utilized triethylamine as base and 1-hydroxybenzotriazole as a catalytic agent for silyl transfer.[4] Qualitatively, reactions performed in acetonitrile appear to be cleaner than the same

reactions in DMF. In cases with at least one of the hydroxyl groups being phenolic or primary, reactions proceeded rapidly at 25 to 65°; with both hydroxyl groups being secondary and aliphatic, more forcing conditions (0.2 eq. of 1-hydroxybenzotriazole, 95°C in a sealed tube) were required for optimum yields (see entries 4 and 5).

The properties exhibited by the di-t-butylsilylene derivatives are attractive. While the isopropylidene derivative of 2 was only sparingly soluble in THF at temperatures below 25°C, solutions of the silicon-protected compound 3 were readily obtained. Although the solubility of these derivatives in most ether and hydrocarbon solvents was very good, recrystallization from acetonitrile provided an efficient method of purification. NMR spectra are uncluttered, with the protecting group adding only one or two sharp singlets in the range of δ0.70 - 1.20.

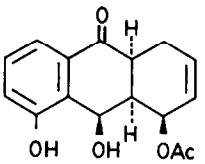
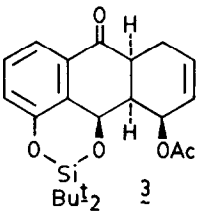
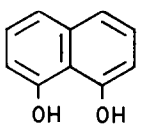
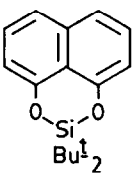
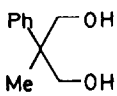
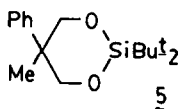
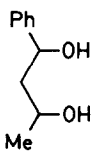
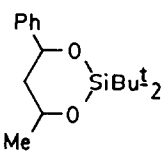
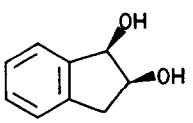
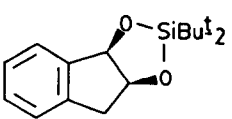
The selective removal of the di-t-butylsilylene group in the presence of other functionality is demonstrated in the deprotection of substrate 7 (derived from 3, see Table) to give dihydroxy compound 8. The use of tetra-n-butylammonium fluoride in THF




at 25°C with or without various amine/benzoic acid buffers gave mixtures of products, apparently due to the lability of the benzylic hydroxyl group of 8. In contrast to these results, treatment of 7 with pyridinium hydrofluoride[5] (4 eq. in THF, 25°C) gave 8 in 88% yield after recrystallization. Not only is the sensitive β-hydroxycarbonyl system undisturbed, but the diol protecting group is cleanly removed even in the presence of a t-butyldimethylsilyl ether. A stock solution (∿1 N) of this reagent is conveniently prepared by addition of pyridinium poly(hydrogen fluoride) to an excess (2-3 eq.) of pyridine in THF and can be stored in a polyethylene bottle in a dessicator for 2-3 weeks with no apparent loss of effectiveness. Application of the same procedure to 4, 5, and 6 returned the corresponding diols in 87, 85, and 92% yields, respectively.

In a representative procedure, 1-hydroxybenzotriazole hydrate (546 mg, 4.0 mmol) was dried overnight at 0.5 mm and 25°C. The resulting 502 mg of material was dissolved with 11.50 g (39.9 mmol) of diol 2 in 56 ml of acetonitrile. Triethylamine (28 ml, 20 g, 200 mmol) and 9.3 g (44 mmol) of di-t-butyldichlorosilane were added sequentially and the resulting solution was warmed in a 65°C oil bath. After 10 min, a white precipitate formed and the reaction was complete within 30 min. The reaction mixture was partitioned between

TABLE. Reactions of Diols with Di-t-butyldichlorosilane.

| Entry | Diol | Solvent | Conditions[a] | Yield(%) | Product[b] |
|---|---|---|---|---|---|
| 1 |  2 | DMF | 2.5 Imidazole, 50°C, 48 h | 55 |  3 |
| | | | 4.6 $Et_3N$, 45°C, 24 h | 36 | |
| | | $CH_3CN$ | 6 Imidazole, 70°C, 4 h | 31 | |
| | | | 3 DMAP,[c] 70°C, 2.75 h | 45 | |
| | | | 6.7 $Et_3N$, 70°C, 3 h | 53 | |
| | | | 4 $Et_3N$, 2 DMAP,[c] 70°C, 1 h | 65 | |
| | | | 5 $Et_3N$, 0.1 HOBt,[d] 65°C, 0.5 h | 84 | |
| 2 |  | DMF | 4.3 $Et_3N$, 25°C, 12 h | 84 |  4 |
| 3 |  | DMF | 5 Imidazole, 60°C, 18 h | 64 |  5 |
| 4 |  | DMF | 5 Imidazole, 60°C, 7 h | 13 |  |
| | | $CH_3CN$ | 5 $Et_3N$, 0.1 HOBt,[d] 60°C, 40 h | 65 | |
| | | | 3 $Et_3N$, 0.2 HOBt,[d] 95°C, 5 h | 85 | |
| 5 |  | $CH_3CN$ | 3 $Et_3N$, 0.2 HOBt,[d] 95°C, 5 h | 81 |  6 |
| | | | 3 $Et_3N$, 0.2 NHSu,[e] 95°C, 5 h | 71 | |

(a) The number indicated is the reagent/diol ratio.
(b) All products have been fully characterized by spectral analysis and elemental composition determined by combustion analysis and high resolution mass spectroscopy.
(c) 4-(Dimethylamino)pyridine.
(d) 1-Hydroxybenzotriazole.
(e) N-Hydroxysuccinimide.

water and chloroform, and the chloroform layer was washed with water, aqueous sodium bicarbonate, and aqueous sodium chloride. After drying and removal of the solvent under reduced pressure, the solid product 3 was recrystallized from hexane to give a total of 14.42 g (84%) of white crystals, mp 184-5°C. The product has been fully characterized by $^{1}H$ and $^{13}C$ NMR, IR, and mass spectroscopy and combustion analysis.

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2. While this work was in progress, other interesting silylene derivatives have been described. (a) Ryu, I.; Murai, S.; Shinonaga, A.; Horüke, T.; Sonoda, N. J. Org. Chem. 1978, 43, 780. (b) Markiewicz, W.T. J. Chem. Res. (M). 1979, 181. (c) Markiewicz, W.T.; Samek, Z.; Smrt, J. Tetrahedron Lett. 1981, 21, 4523. (d) Verdegaal, C.H.M.; Jansse, P.L.; de Rooij, J.F.M.; van Boom, J.H. ibid. 1980, 21, 1571. (e) van Boeckel, C.A.A.; van Boom, J.H. ibid. 1980, 21, 3705. (f) Jenner, M.R.; Khan, R. J. Chem. Soc. Chem. Commun. 1980, 50.

3. Commercially available from Petrarch Systems, Inc., Levittown, PA, or conveniently prepared by formation of di-t-butylchlorosilane[6] followed by chlorination ($Cl_2$, carbon tetrachloride, 8-10°C).[7]

4. We believe this is the first report of the use of this reagent for transfer of silyl groups. For its catalytic use in peptide synthesis, see (a) Konig, W.; Geiger, R. Chem. Ber. 1973, 106, 3626. (b) Klausner, Y.S.; Chorev, M. J. Chem. Soc. Chem. Commun. 1975, 973. (c) Khan, S.A.; Sivanandaiah, K.M. Tetrahedron Lett. 1976, 199.

5. The use of pyridinium hydrofluoride to cleave an allylic t-butyldiphenylsilyl ether has been independently reported. Nicolaou, K.C.; Seitz, S.P.; Pavia, M.R.; Petasis, N.A. J. Org. Chem. 1979, 44, 4011.

6. Weidenbruch, M.; Pesel, H.; Peter, W.; Steichen, R. J. Organometal. Chem. 1977, 141, 9. The controlled addition of t-butyllithium to the volatile trichlorosilane is hampered by the formation of a crust of lithium chloride around the tip of the addition funnel. We therefore added trichlorosilane to the t-butyllithium, although the resulting yield (50-54%) was somewhat lower.

7. For similar conditions, see Doyle, M.P.; West, C.T. J. Am. Chem. Soc. 1975, 97, 3777.

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