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Trichloro-(trans-2,4-pentadienyl)stannane as a Less Electron-rich Diene and Its Application to Tandem Michael/Diels-Alder Reaction. Formal Total Synthesis of 11-Deoxydaunomycinone[1)]

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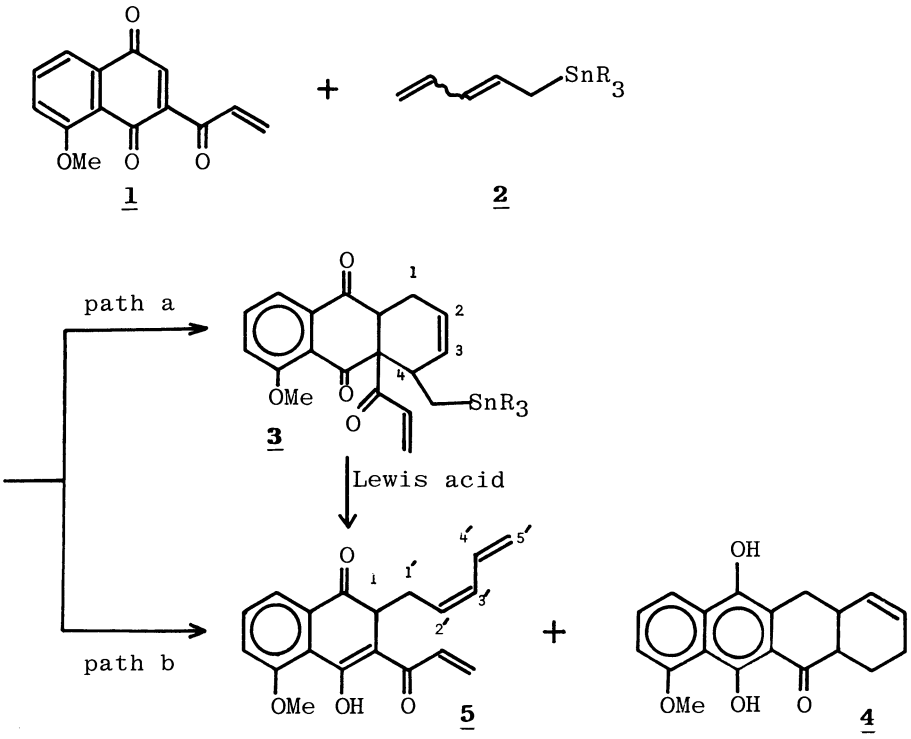
Trichloro-(trans-2,4-pentadienyl)stannane effectively reacted with an acryloylnaphthoquinone to afford tandem Michael/Diels-Alder adduct in excellent yield. The obtained tetracyclic quinone was converted to 11-deoxydaunomycinone precursor.

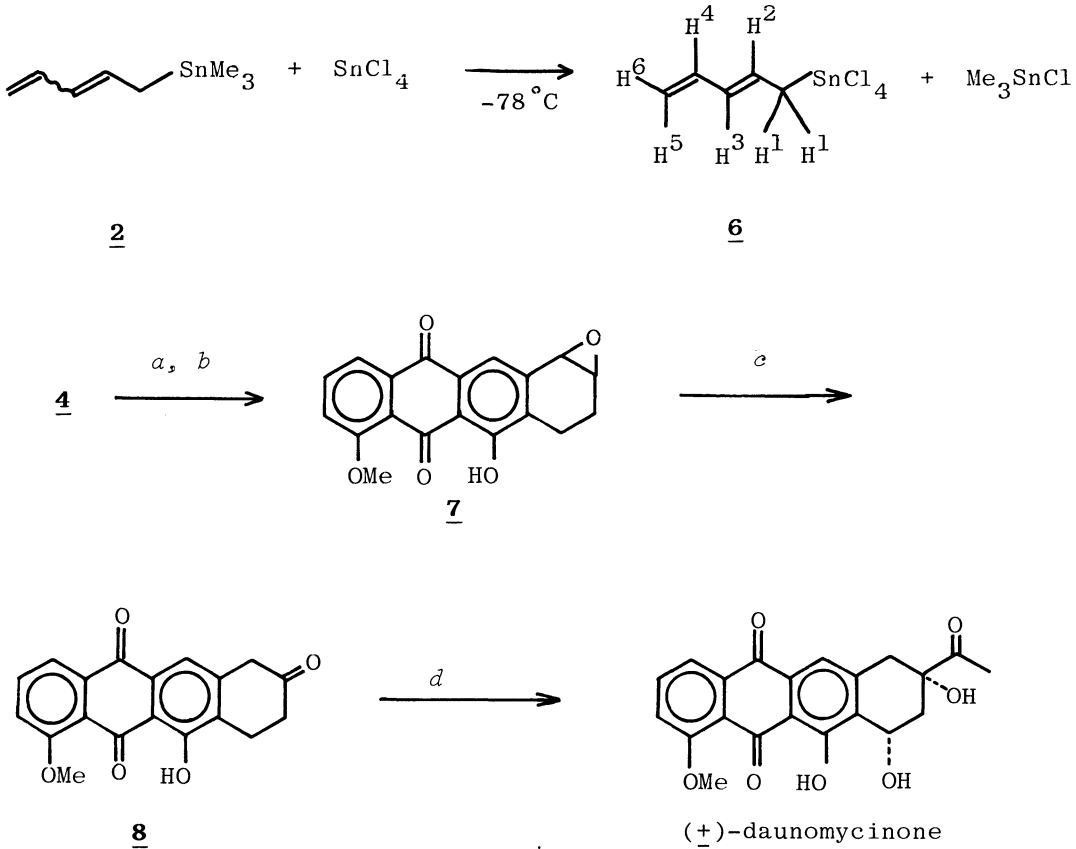
Recently, we reported tandem Michael/Diels-Alder addition of 2,4-pentadienyltrimethylstannane (2) to acryloylnaphthoquinone (1) relevant to 11-deoxydaunomycinone synthesis (Scheme 1).[2-4)] The major problem in this reaction was the concomitant formation of acyclic dienylated side product (5) in comparable yield to the desirable one (4). The detailed analysis of 5 revealed that the dienyl side chain had cis configuration,[5,12)] which could prevent further cyclization to the tetracyclic product 4. Further study on the formation of the cis isomer 5 clarified the presence of the following two possible pathways (paths a and b).



Scheme 1.

Without any Lewis acid, Diels-Alder cyclization between the quinone 1 and pentadienylstannane 2 quantitatively gave a cyclized product (3),[5] of which treatment with Lewis acid transformed 3 to the acyclic product 5 in quantitative yield without formation of the tetracyclic product 4 (path a in Scheme 1). The other possibility for the formation of 5 comes from intrinsic structure of the diene 2. The applied trimethyl-2,4-pentadienylstannane is a mixture of E- and Z-isomers (ratio E/Z=69/31).[6] In the presence of Lewis acid, the first step of this conjugate addition should be Michael reaction (path b). If the stereochemistry of the applied diene was preserved in the course of the initial addition, the product ratio (4/5) will reflect the isomeric ratio of 2. The observed ratio in the $SnCl_4$ mediated reaction[7] was 4/5=45/55, and the both pathways (a and b) would be involved in this reaction. Various reaction conditions were examined for the maximization of the yield of the tandem reaction.

We found stereospecific transmetallation of the stereoisomeric mixture of pentadienylstannane to trichloro-trans-2,4-pentadienylstannane (6). The solution of 2 (R=Me) at -78 °C instantaneously afforded 6 without contamination of the corresponding cis isomer by the addition of $SnCl_4$.[8,13] The tandem reaction was done as follows. To a dichloromethane solution of 6 (1.1 mmol) prepared in situ,[8]



Scheme 2.†

† *a*, O_2, DMF, Δ; *b*, MCPBA, CH_2Cl_2; *c*, TfOTMS, lutidine, $PhCH_3$, CH_2Cl_2, 80 °C; *d*, see Ref. 11.

the quinone 1 (1.0 mmol) in CH_2Cl_2 was added at -78 °C. After stirring for 10 min at the same temperature and subsequent workup, a mixture of 4 and 5 was quantitatively obtained in high selectivity (4/5=94/6). After chromatographic purification, pure 4 was isolated in 76% yield. Conclusively, the high product selectivity would be realized (1) by decrease of the electron density of 6, which is considered to be a less reactive diene toward Diels-Alder reaction, and (2) by efficient isomerization of the dienyl stannane to a pure trans isomer.

Next, we applied the tandem adduct 4 to the synthesis of 11-deoxydaunomycinone. Dehydrogenative oxidation of 4 under an oxygen atmosphere in DMF gave the corresponding anthraquinone derivative, of which epoxidation with MCPBA provided 7 in 75% yield from 4 The successive isomerization of the epoxide 7 to the ketone 8 has been reported by Hauser et al.,[9] while by the reported procedures (H_2, Pd/C; PCC) 8 could not be obtained in acceptable yield. After examination of several isomerization reaction by acid catalysis,[10] trimethylsilyl triflate in the presence of lutidine gave the ketone 8 in 90% yield. Conclusively, 8 was efficiently prepared in 51% overall yield from the quinone 1. Since 11-deoxydaunomycinone has already prepared in three steps from 8,[11] this is one of the promising route to it.

References

1) Synthesis of Naturally Occurring Quinones. Part 18; Part 17, Y.Naruta, N.Nagai, T.Yokota, and K.Maruyama, Chem. Lett., 1986, 1185.

2) Y.Naruta, M.Kashiwagi, Y.Nishigaichi, H.Uno, and K.Maruyama, Chem. Lett., 1983, 1687.

3) J.-P.Gesson, J.C.Jacquesy, and B.Renoux, Tetrahedron Lett., 24, 2757 (1983); idem., Tetrahedron, 40, 4743 (1984); J.P.Gesson, J.C.Jacquesy, and M.Mondon, Nouv. J. Chim., 7, 205 (1983); J.C.Bauman, R.B.Barber, R.D.Gless, and H.Rapoport, Tetrahedron Lett., 21, 4777 (1980); J.Alexander, D.L.Flynn, L.A.Mitscher, and T.Veysoglu, ibid., 22, 3711 (1981); J.Yadav, P.Corey, C.T.Hsu, K.Perlman, and C.J.Sih, ibid., 22, 811 (1981); S.D.Kimball, D.R.Walt, and F.Johnson, J. Am. Chem. Soc., 103, 1561 (1981); A.V.R.Rao, V.H.Deshpande, and N.L.Reddy, Tetrahedron Lett., 23, 775 (1982); A.V.R.Rao, A.R.Mehendale, and K.B.Reddy, ibid., 23, 2415 (1982); J. Chem. Soc. Chem. Commun., 1983, 564 ; A.S.Kende and J.P.Rizzi, Tetrahedron Lett., 22, 1799 (1981); A.S.Kende, and S.D. Boettger, J. Org. Chem., 46, 2799 (1981); M.E.Jung, J.A.Lowe, III, M.A.Lyster, M.Node, R.W.Pflunger, and R.W.Brown, Tetrahedron, 40, 4751 (1984); F.M.Hauser and D.Mal, J. Am. Chem. Soc., 105, 5688 (1983); R.M.Hauser, S.Prassana, and D.W.Combs, J. Org. Chem., 48, 1328 (1983); F.M.Hauser and V.M.Baghdanov, Tetrahedron, 40, 4719 (1984); E.Vedejs, W.H.Miller, and J.R.Pribish, J. Org. Chem., 48, 1167 (1983); Y.Tamura, S.Akai, M.Sasho, and Y.Kita, Tetrahedron Lett., 25, 1167 (1984); J.-M.Tornare and P.Vogel, Helv. Chim. Acta, 68, 1069 (1985); W.D.Wulff, P.-C.Tang, K.-S.Chan, J.S.McCallum, D.-C.Yang, and S.R.Gilbertson, Tetrahedron, 41, 5813 (1985).

4) A similar strategy in anthracyclinone synthesis appeared recently, G.A.Kraus and B.S.Fulton, J. Org. Chem., 50, 1782 (1985).

5) 400 MHz ^{1}H-NMR spectra (in $CDCl_3$); 3, δ 0.70(dd, 1H, J=11.5, 5.5 Hz,

diastereotopic H of CH_2Sn), 0.83(dd, 1H, H=13.3, 11.5 Hz, diastereotopic H of CH_2Sn), 2.21(dm, 1H, J=18.6 Hz, diastereotopic H at C-1), 2.81(d, 1H, J=18.6 Hz, diastereotopic H at C-1), 3.15(d, 1H, J=13.3 Hz, H^4), 3.88(dd, 1H, J=7.5, 4.2 Hz, ring COCH), 3.96(s, 3H, MeO), 5.60(m, 1H, H^2), 5.67(dd, 1H, J=10.7, 1.0 Hz, $COCH=CH_2$), 5.69(m, 1H, H^3), 6.31(dd, 1H, J=16.9, 2.0 Hz, $COCH=CH_2$), 6.85(dd, 1H, J=16.9, 10.7 Hz, $COCH=CH_2$), 7.28 and 7.61(each d, 2H, J=8.1 Hz, arom. H), 7.67(t, 1H, J=8.1 Hz, arom. H).

5, δ 2.55(t, 2H, J=7.5 Hz, $H^{1'}$), 3.73(t, 1H, J=7.5 Hz, H^1), 4.02(s, 3H, MeO), 5.02(d, 1H, J=10.0 Hz, (E)-$H^{5'}$), 5.14(d, 1H, J=17 Hz, (Z)-$H^{5'}$), 5.22(dd, 1H, J=11.0, 7.5 Hz, $H^{2'}$), 5.76(dd, 1H, J=10.5, 2.0 Hz, $COCH=CH_2$), 5.97(t, 1H, J=11.0 Hz, $H^{3'}$), 6.25(dt, 1H, J=17.0, 10.5 Hz, $H^{4'}$), 6.46(dd, 1H, J=17.0, 2.0 Hz, $COCH=CH_2$), 6.60(dd, 1H, J=17.0, 10.5 Hz, $COCH=CH_2$), 7.31(each d, 2H, J=8.0 Hz, arom. H), 7.62(t, 1H, J=8.0 Hz, arom. H), 17.13(s, 1H, OH).

6) Y.Naruta, N.Nagai, Y.Arita, and K.Maruyama, Chem. Lett., 1983, 1683.

7) Trimethylpentadienylstannane 2 was added to a solution of the quinone 1 and $SnCl_4$ at -78 °C.

8) Trichloropentadienylstannane 6 was prepared by the treatment of trimethyl derivative 2 with six equivalents of $SnCl_4$ at -78 °C. The formation of 6 was instantaneous and the isomeric purity of the trans isomer was well characterized by means of ^{119}Sn- and ^1H-NMR.
^{119}Sn-NMR ($CDCl_3$; -50 °C; Me_4Sn as a standard) δ -43(s).
^1H-NMR ($CDCl_3$; -50 °C) δ 3.22(d, 2H, J=8.2 Hz, J_{Sn-H}=122Hz, H^1), 5.19(d, 1H, J=8.9 Hz, H^6), 5.27(d, 1H, J=15.9 Hz, H^5), 5.79(dt, 1H, J=14.0, 8.2 Hz, J_{Sn-H}=69 Hz, H^2), 6.30(ddd, 1H, J=15.9, 16.3, 8.9 Hz, H^4), 6.35(dd, 1H, J=14.0, 11.3 Hz, H^3).

9) F.M.Hauser, S.Prasanna, and D.W.Combs, J. Org. Chem., 48, 1328 (1983).

10) Trifluoromethanesulfonic acid was moderately effective for this conversion.

11) J.-P.Gesson and M.Mondon, J. Chem. Soc., Chem. Commun., 1982, 421.

12) The stereochemistry of the dienyl side chain of the acyclic product 5 was not specified in the previous report.[2]

13) Under the previous reaction conditions,[2] there remains the possibility of the concomitant formation of 6, while the competition with other processes, i.e. Diels-Alder reaction or Michael reaction, would decrease the selectivity of the formation of the tandem addition product 5.

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