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# A NOVEL ACID-CATALYZED TRANSFORMATION OF OCTADIENYNEDIAL DERIVATIVES TO CYCLOPENTA[b]-THIAPYRANS AND CYCLOPENTA[b]PYRAN.

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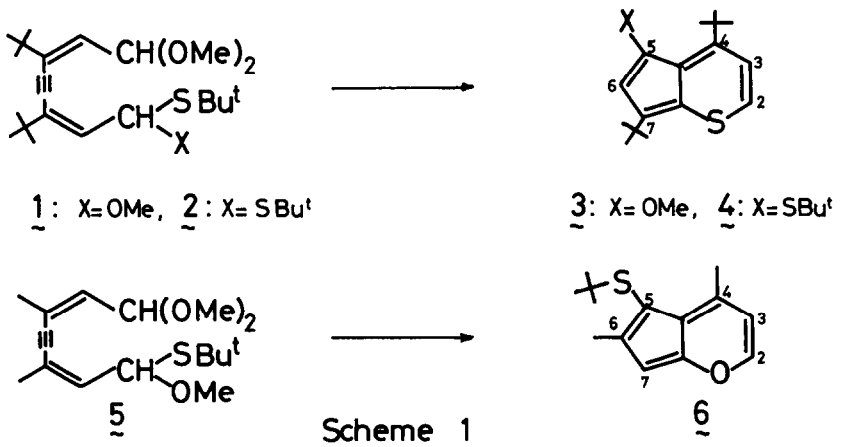
Summary: Substituted 2,6-octadien-4-ynedial derivatives were synthesized, which give cyclopenta[b]thiapyran or cyclopenta[b]pyran derivatives by intramolecular cyclization.

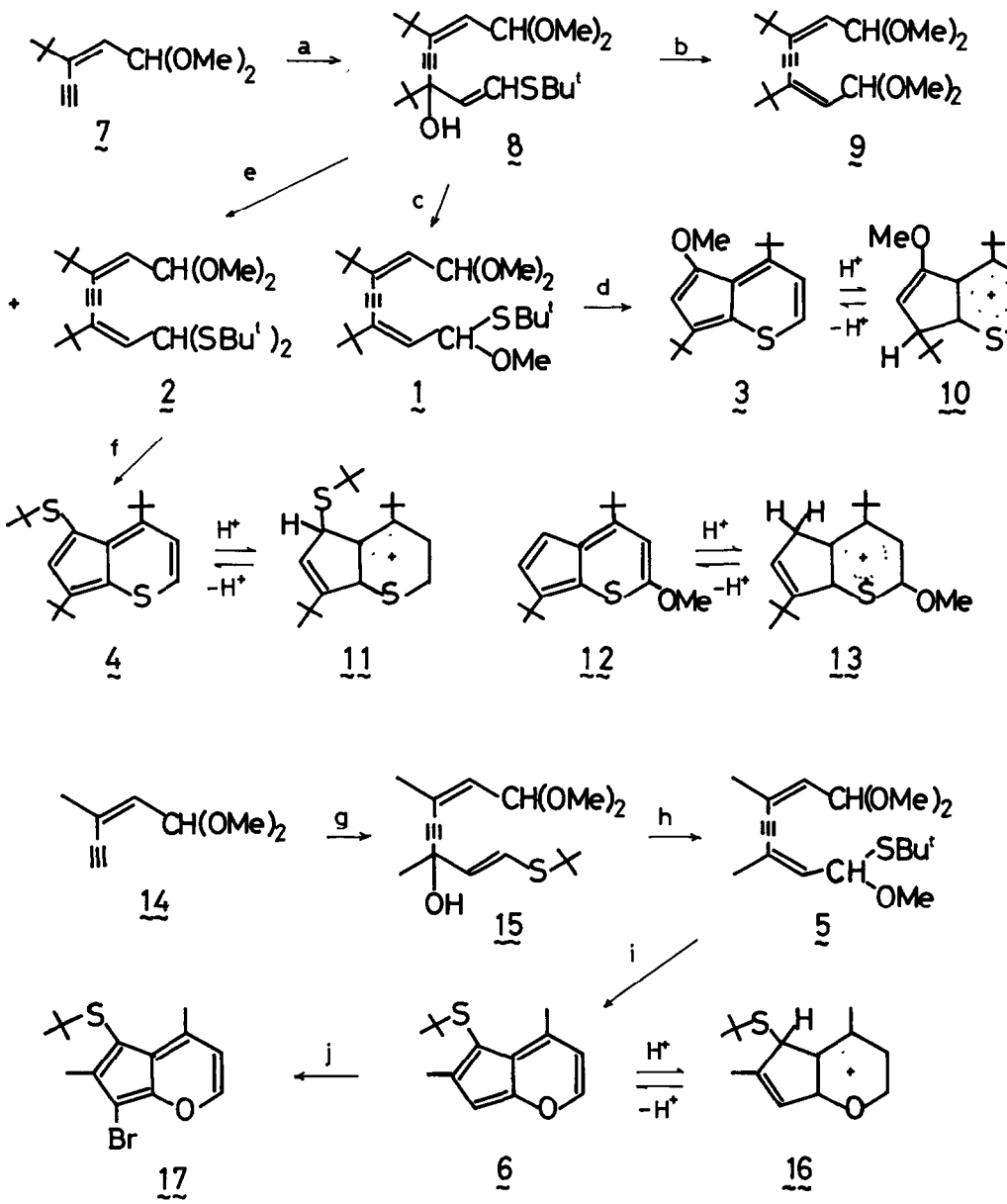
During the course of studies on dehydroannulenes[1], we have investigated the synthesis of substituted octadienynedial derivatives which seemed to be potential precursors of dehydroannulenes. It was found that the acetal-hemithioacetals or acetal-thioacetals of octadienynedial derivatives give readily cyclopenta[b]thiapyran or pyran derivatives by acid-catalyzed reaction. The previous work on cyclopenta[b]thiapyrans[2] and cyclopenta[b]pyrans[3] demonstrated these 10π-electron systems to be iso-π-electronic with azulene so as to show similar electronic spectra and electrophilic substitution reactions.

In this paper, we wish to report the acid-catalyzed transformation of substituted 2,6-octadien-4-ynedial derivatives (1, 2, and 5) to substituted cyclopenta[b]thiapyrans (3 and 4) or cyclopenta[b]pyran (6) by intramolecular cyclization (Scheme 1). The structure of 4 was unambiguously determined by means of X-ray crystallographic analysis[4].




Scheme 1

As outlined in Scheme 2, the starting materials are the enynealdehyde dimethyl acetals (7[5] and 14[6]). The dimethyl acetal (7) was treated with butyllithium to give the lithio derivative. The reaction of the lithio derivative with the thiovinylketone (18)[7] gave the hydroxy acetal (8, yellow viscous oil, 90%)[8]. Treatment of 8 with *p*-TsOH-$CH(OMe)_3$ at 31°C[9] gave a mixture of 9 and 3, which were separated by column chromatography on alumina (9, pale yellow viscous oil, 38%;

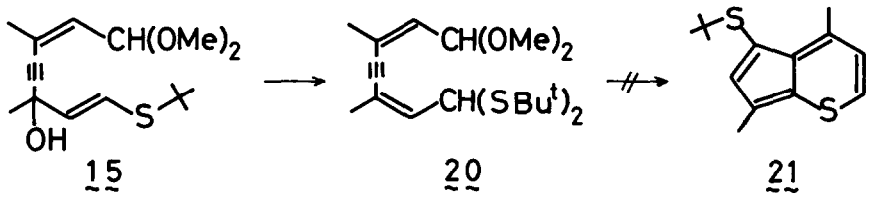


Scheme 2

Reagents a: (i) *n*-BuLi, THF, -40°C; (ii) *t*-BuCO-CH=CH-S-*t*-Bu (18). b: *p*-TsOH, $CH(OMe)_3$, 31°C, 13 h. c: $CF_3COOH$, $CH(OMe)_3$, -15°C, 2.5 h. d: $CF_3COOH$, $CH(OMe)_3$, $CH_2Cl_2$, 0°C, 1.5 h. e: $CF_3COOH$, *t*-BuSH, $CH(OMe)_3$, $CH_2Cl_2$, 0°C to rt, 3 h. f: $CF_3COOH$, $CH(OMe)_3$, $CH_2Cl_2$, 0°C to rt 3 h. g: (i) *n*-BuLi, THF, -40°C; (ii) $CH_3CO$-CH=CH-S-*t*-Bu[10] (19). h: $CF_3COOH$, $CH(OMe)_3$, -15°C, 50 min. i: $CF_3COOH$, $CH(OMe)_3$, $CH_2Cl_2$, -15°C, 30 min. j: $Br_2$, $CH_2Cl_2$, -60°C, 10 min.

3, deep blue plates, mp 117.0-117.9°C, 13%, Mass(m/e): 276($M^+$), 261; ES: $\lambda_{max}^{cyclohexane}$(ε) 273(14000), 349sh(3390), 364(4210), 378sh(2940), 634(610) nm). In order to get scope of the formation of the cyclopenta[b]thiapyran (3), the hydroxy acetal (8) was converted into the acetal-hemithioacetal (1, pale yellow viscous oil, 85%) with $CF_3COOH$-$CH(OMe)_3$. Treatment of 1 with *p*-TsOH-$CH(OMe)_3$ gave the diacetal (9, 42%) and the cyclopenta[b]thiapyran (3, 6%). Cyclization of 1 proceeded more readily with stronger acid. The hemithioacetal (1) underwent smooth cyclization with $CF_3COOH$-$CH(OMe)_3$-$CH_2Cl_2$ to afford 3 in 17% yield. Furthermore, treatment of 8 with $CF_3COOH$-$CH(OMe)_3$-$CH_2Cl_2$ in the presence of *t*-butylmercaptan gave 3 in 19% yield and 2 (colorless prisms, mp 55.9-57.3°C, 66%), respectively. Cyclization of the acetal-thioacetal (2) with $CF_3COOH$-$CH(OMe)_3$-$CH_2Cl_2$ yielded the *t*-butylthio-substituted cyclopenta[b]-thiapyran (4, deep blue prisms, mp 75.7-77.5°C, 44%, Mass(m/e): 334($M^+$), 278; ES: $\lambda_{max}^{cyclohexane}$ (ε) 243.5(13400), 296.5(16400), 362(4110), 592(1090) nm). Similar treatment of 2 at low temperature (-15°C, 100 min, 0°C, 3.5 h) gave a mixture of 2, 4 (33%[11]), and 12 (2.3%[11]), which could be separated by chromatography. Thus, cyclopenta[b]thiapyran (12, reddish violet needles, mp 132.6-133.5°C, Mass(m/e): 276($M^+$), 261, 245; ES: $\lambda_{max}^{cyclohexane}$(ε) 234.5(15500), 277(9800), 374 (7470), 525(1100) nm), an isomer of 3, could be obtained. The cyclopenta[b]thiapyrans (3, 4, and 12) were reversibly protonated ($CF_3COOH$ in $CH_2Cl_2$) on the five membered rings to yield the thiopyrylium ions (10, 11, and 13), respectively. The site of protonation in 3, 4, and 12 was found to be at C-7 in 3 and at C-5 in 4 and 12. Electronic spectra of 3, 4 and 12 show extremely broad absorption bands in the long wavelength region exhibiting characteristic feature of 10π-electron system isoelectronic with azulene.

The similar reaction of dimethyl derivative (5) was also examined to obtain further information regarding on the cyclization mechanism. The dimethyl acetal (14) was converted into the hydroxy acetal (15, pale yellow viscous oil, 76%) in the same manner as 7. Treatment of 15 with $CF_3COOH$-$CH(OMe)_3$ gave the acetal-hemithioacetal (5, viscous oil, 88%). Under the similar reaction used for 3 ($CF_3COOH$-$CH(OMe)_3$-$CH_2Cl_2$), 5 yielded unexpectedly the cyclopenta-[b]pyran derivative (6, deep red plates, mp 50.6-51.6°C, 30%, Mass(m/e): 234($M^+$), 145; ES: $\lambda_{max}^{cyclohexane}$(ε) 231sh(10800), 264(14300), 279sh(8300), 329(9700), 468(610) nm; $^1H$ NMR ($CD_2Cl_2$) δ 7.60 d(J=5.0, $H_2$), 6.24 d(J=5.0, $H_3$), 6.10 s($H_7$), 2.91 s($C_4$-Me), 2.46 s($C_6$-Me), 1.19 s(*t*-Bu)). Electronic spectrum of 6 shows extremely broad absorption band in the long wavelength region. The cyclopenta[b]pyran (6) was reversibly protonated on the five membered ring to yield the pyrylium ion (16, $^1H$ NMR ($CD_2Cl_2$-$CF_3COOH$, -30°C) δ 8.65 d(J=5.0, $H_2$), 7.51 d(J=5.0, $H_3$), 7.01 m (J=1.1, 1.2, $H_7$), 4.58 d(J=1.1, $H_5$), 2.91 s($C_4$-Me), 2.65 d(J=1.2, $C_6$-Me), 1.44 s(*t*-Bu)). The structure of 6 was confirmed by the long-range coupling in the five membered ring of 16, *i.e.*, first-order $AMX_3$-pattern. Bromination of 6 afforded the bromo derivative (17, deep red needles, 92%, mp 65.2-66.8°C, Mass(m/e): 314, 312($M^+$); $^1H$ NMR ($CDCl_3$) δ 7.69 d(J=5.0, $H_2$), 6.29 d(J=5.0, $H_3$), 2.92 s($C_4$-Me), 2.48 s($C_6$-Me), 1.22 s(*t*-Bu)). In order to obtain the dimethylcyclopenta[b]-thiapyran (21), cyclization of the acetal-thioacetal (20), prepared from the hydroxy acetal (15)[12], was attempted under the similar reaction conditions used for 2 (Scheme 3). Treatment of 20 with $CF_3COOH$-$CH(OMe)_3$-$CH_2Cl_2$ gave no identifiable product on the contrary to our expectation. Further investigation elucidating the cyclization mechanism of octadienynedial derivatives is now in progress.




15 20 21

Scheme 3

Acknowledgement

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References and Notes

1) a) M. Nakagawa, *Pure. Appl. Chem.*, 44, 885 (1975); b) M. Nakagawa, *Angew. Chem.*, 91, 215 (1979); *Angew. Chem. Int. Ed. Engl.*, 18, 202 (1979).

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3) a) G. V. Boyd, *J. Chem. Soc.*, 1979 (1958); 55 (1959); b) G. V. Boyd and A. W. Ellis, *J. Chem. Soc. (B)*, 349 (1966); c) G. V. Boyd and F. W. Clark, *J. Chem. Soc. (C)*, 859 (1966).

4) The following paper.

5) M. Iyoda and M. Nakagawa, *Tetrahedron Lett.*, 4743 (1973).

6) 3-Methyl-2-penten-4-yn-1-al was converted into the corresponding dimethyl acetal (14) in the usual way.

7) Thiovinylketone (18) was prepared by the reaction of hydroxymethylene-pinacolone with *t*-butylmercaptan in 84% yield. 18, colorless crystals, mp 89.4-89.9°C. A ratio of *cis* and *trans* isomer is 17 : 83.

8) All new compounds described in this paper gave satisfactory spectroscopic and analitical data.

9) The reaction of 1 with *p*-TsOH-$CH(OMe)_3$ was performed under more mild conditions (18°C, 12 h) to give a mixture of octadienynedial derivatives and the cyclopenta[b]thiapyran (1, 26%; 2, 14%; 9, 9%; 3, 6%).

10) S. Akiyama, S. Nakatsuji, T. Hamamura, M. Kataoka, and M. Nakagawa, *Tetrahedron Lett.*, 2809 (1979).

11) The yield based on consumed 2.

12) Treatment of 15 with $CF_3COOH$-$CH(OMe)_3$-$CH_2Cl_2$ in the presence of *t*-butylmercaptan gave 6 in 2.1% yield and 20 in 34% yield.

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