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ACID-CATALYZED CYCLIZATION OF OCTADIENYNE DERIVATIVES. FACILE FORMATION OF CYCLOPENTADIENE, ISOBENZOTHIOPHENE, AND 18-MEMBERED CYCLIC ETHER

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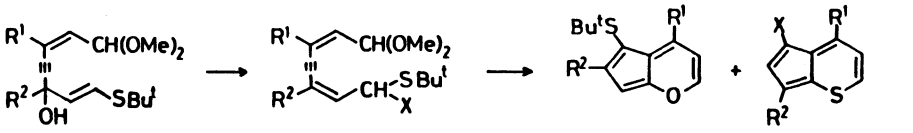
Treatment of substituted octa-2,6-dien-4-yne-1,8-dial derivatives with CF_3COOH gave cyclopentadiene, thiophene, or isobenzothiophene derivatives. Formation of an 18-membered cyclic ether was observed in the case of octa-2,7-dien-4-yne-1,6-diol derivative.

In previous papers,[1,2] we have reported the formation of cyclopenta[b]pyrans (3) and cyclopenta[b]thiopyrans (4) by the acid-catalyzed intramolecular cyclization of substituted octadienynedial derivatives (2) derived from 1 (Scheme 1). In order to clarify the mechanisms of this interesting reaction and also to obtain further information regarding the cyclization products, we have examined the reactions of other octadienyne derivatives with CF_3COOH. We now wish to report the formation of cyclopentadiene, isobenzothiophene, and 18-membered cyclic ether derivatives.



Scheme 1.

We have first examined the reactions of the t-butyl-methyl system (2, R^1=t-Bu, R^2=Me), because preliminary experiments revealed that the reactions of 1 or 2 (R^1=t-Bu, R^2=Me, X=S-t-Bu) gave no cyclopenta[b]pyran and cyclopenta[b]thiopyran derivatives (3 and 4: R^1=t-Bu, R^2=Me) in contrast to the reaction of the methyl-t-butyl system (2, R^1=Me, R^2=t-Bu, X=OMe or S-t-Bu) which yielded the corresponding pyran (3, R^1=Me, R^2=t-Bu) and thiopyran (4, R^1=Me, R^2=t-Bu, X=OMe or S-t-Bu).[2]

The reaction of the lithio derivative (5) derived from 3-t-butyl-2-penten-4-yn-1-al dimethyl acetal[3] with 4-(t-butylthio)-3-buten-2-one (6)[4] afforded the hydroxy acetal (7, viscous oil, 93%). Treatment of 7 with CF_3COOH-$CH(OMe)_3$ in CH_2Cl_2 in the presence of t-BuSH (-15 °C, 0.5 h) gave the acetal-thioacetal (8, colorless prisms, mp 50.5-51.5 °C, 23%)[5] and the cyclopentadiene derivative (9, pale yellow

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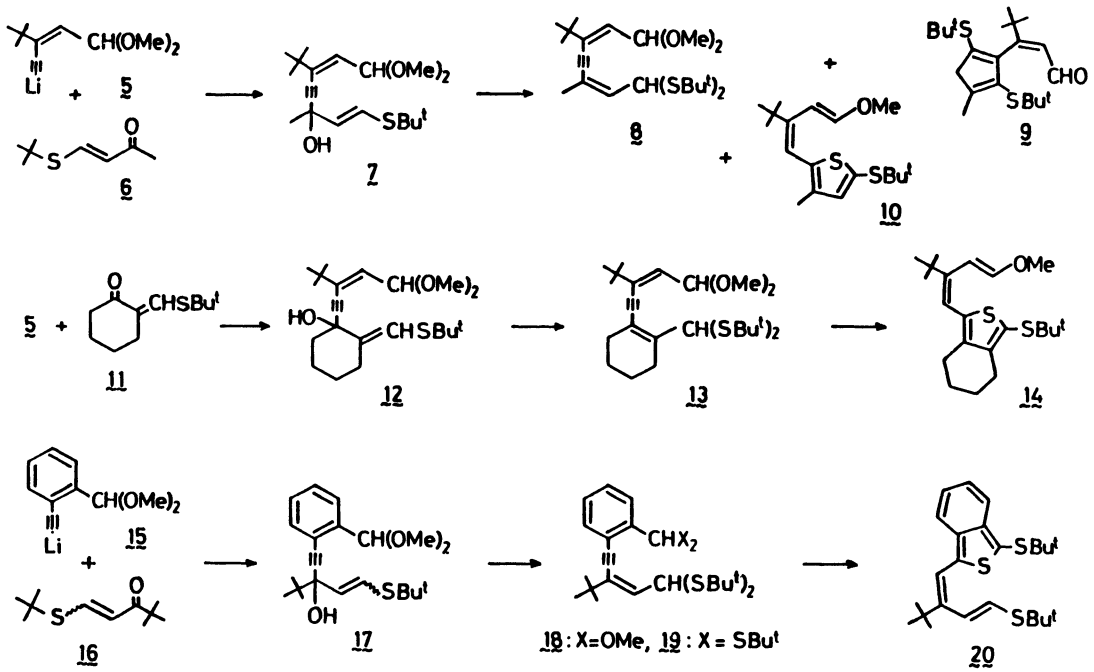
cryst., mp 79-83 °C, 17%),[6] and similar treatment of 7 at higher temperature gave the cyclopentadiene (9, 20%) and the thiophene derivative (10, yellow viscous oil, 42%). The similar thiophene formation was observed in the case of the acetal-thioacetal (13). The reaction of the hydroxy acetal (12) obtained from 5 and 11 with CF_3COOH-$CH(OMe)_3$ in CH_2Cl_2 in the presence of t-BuSH (-30 °C, 1.5 h) gave the acetal-thioacetal (13, colorless prisms, mp 56.5-57.0 °C, 54%). Treatment of 13 with CF_3COOH-$CH(OMe)_3$ in CH_2Cl_2 (-15 °C, 40 min) afforded the thiophene derivative (14, pale yellow prisms, mp 99.5-101.0 °C, 86%).

Above-mentioned observations show that the cyclization of 7 or 8 and 13 resulted in the formation of cyclopentadiene or thiophene derivatives, respectively, instead of the formation of cyclopenta[b]pyrans and cyclopenta[b]thiopyrans. In order to get further information on the cyclization mode of octadienynedial derivatives, we have investigated the acid-catalyzed cyclization of 18 and 19 containing a benzene ring in the system.

The reaction of the lithio derivative (15)[7] with 16[8] gave the hydroxy acetal (17, viscous oil, 99%). Treatment of 17 with CF_3COOH-$CH(OMe)_3$ in CH_2Cl_2 in the presence of t-BuSH (-15 °C, 1 h) gave the acetal-thioacetal (18, colorless cryst., mp 30.5-31.5 °C, 60%) and the similar treatment of 17 at higher temperature and for longer time (-15 °C, 22 h and then 5 °C, 4 h) gave the dithioacetal (19, colorless cryst., mp 95-98 °C, 17%). The reaction of 18 with CF_3COOH-$CH(OMe)_3$ in CH_2Cl_2 (-15 -0 °C, 5.5 h) proceeded slowly and resulted in the formation of the isobenzothiophene derivative (20, reddish brown cryst., mp 71.0-71.5 °C, 4%).[9] The formation of 20 could be explained by the cyclization of 19 which would be formed by the acetal-thioacetal exchange under the reaction conditions. Actually the reaction of 19 with CF_3COOH-$CH(OMe)_3$ in CH_2Cl_2 (-15 °C - rt, 4 h) gave 20 in 65% yield.

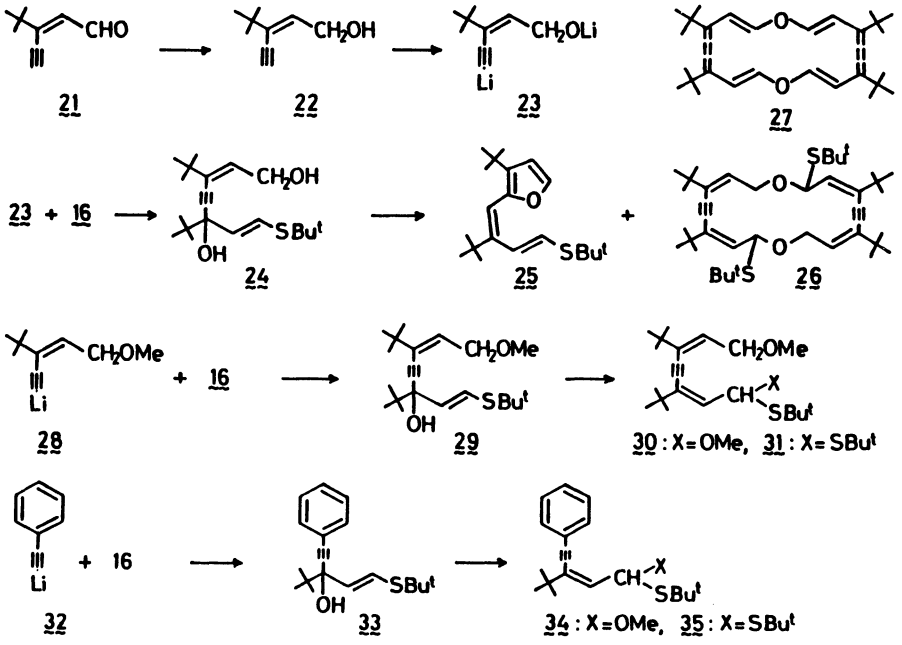
The facile formation of a variety of products by the cyclization reaction in acidic media of the octadienynedial derivatives containing acetal, hemithioacetal



Scheme 2.

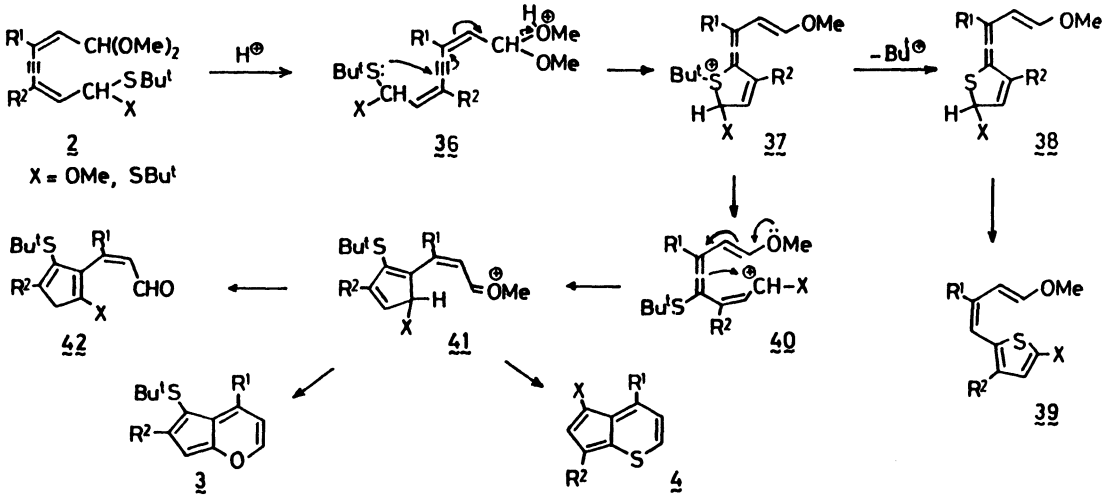
and thioacetal as terminal groups prompted us to investigate the cyclization of octadienynes bearing hydroxy or methoxy, and hemithioacetal or thioacetal parts as terminal groups.

The lithium salt (23) obtained from 21 via 22 was allowed to react with 16 and the reaction product was chromatographed on alumina to give 24 (colorless cryst., 96%), which was found to be unstable both in crystalline state and in solution. The crystals of 24 gradually changed at room temperature to give a dark brown oil, which was chromatographed to afford the furan derivative (25) and the 18-membered cyclic ether (26, colorless cryst., mp 185.5-186.5 °C).[10] The macrocyclic ether (26) may be converted into 1,10-dioxa-5,14-bisdehydro[18]annulene (27), an antiaromatic 20π-electron system, by the elimination of t-butylhydrosulfite. The compound (26) was also obtained in 12% yield together with 7% yield of 25 by standing a solution of 24 in CH_2Cl_2 at room temperature. This reaction proceeds by a mechanism different from that for the formation of cyclopenta[b]pyrans, cyclopenta[b]thiopyrans and thiophenes. The formation of 26 may be advantageously accelerated by the octadienyne structure containing an acetylene and two ethylene units [the dimer (26) possesses a strainless, relatively rigid structure as compared with the corresponding monomer and polymers]. In contrast to the instability of 24, the corresponding methyl ether (29) obtained from 28 and 16 was stable, and could be satisfactorily converted into the hemithioacetal (30, 77%) and the thioacetal (31, 70%) by similar procedure. Treatment of 30 and 31 with CF_3COOH-$CH(OMe)_3$ in CH_2Cl_2 gave no cyclization products. In the case of 30, the formation of the acetal and thioacetal was observed by the acid-catalyzed disproportionation of the hemithioacetal (30). However, the thioacetal (31) was stable under the reaction conditions and recovered unchanged from the reaction mixture after 3 days at room temperature. Attempts to obtain cyclization products of the hemithioacetal (34) and the thioacetal (35), which were prepared from 32 and 16 via 33, were also unsuccessful and the starting materials were recovered.



Scheme 3.

Taking into account the formation of the cyclopentadiene (9), the thiophenes (10 and 14), and the isobenzothiophene (20), the reaction mechanism may be rationalized by the sequence shown in Scheme 4. The acid-catalyzed elimination of methanol followed by the addition of sulfur atom in the thioether group in 36 to the acetylenic carbon gives 37, from which t-butyl cation or 2-methylpropene is eliminated to afford 39 via 38. When X in 37 is methoxy group, which stabilizes the adjacent carbonium ion, cleavage of C-S bond is facilitated to give 40. The interaction between the carbonium ion and allenic sp-carbon in 40 results in the formation of the cyclopentadiene (41). As reported previously,[2] cyclization of 41 with oxygen or sulfur forms cyclopenta[b]pyran (3) or cyclopenta[b]thiopyran (4), respectively. Formation of 42 can be explained by the isomerization of 41.



Scheme 4.

References

1) Y. Aso, M. Iyoda, S. Fujisawa, S. Yamaguchi, and M. Nakagawa, Tetrahedron Lett., 22, 3061 (1981).
2) M. Iyoda, Y. Aso, and M. Nakagawa, Heterocycles, 18, 137 (1982).
3) M. Iyoda and M. Nakagawa, Tetrahedron Lett., 1973, 4743.
4) S. Akiyama, S. Nakatsuji, T. Hamamura, M. Kataoka, and M. Nakagawa, Tetrahedron Lett., 1979, 2809.
5) All new crystalline compounds described in this paper gave IR, NMR, and mass spectral data consistent with the assigned structures and satisfactory elemental analyses were obtained.
6) 9: Mass (m/z) 366 (M^+); ^{1}H-NMR (MeOH-d_4) δ 9.38 (d, J=8.0 Hz, 1H, -CHO), 6.25 (d, J=8.0, 1H, =CH-), 3.58 (s, 2H, $-CH_2-$), 2.25 (s, 3H, Me), 1.39 (s, 9H, t-Bu), 1.21 (s, 18H, S-t-Bu); ^{13}C-NMR ($CDCl_3$) δ 194.2 (CHO), 171.7, 156.2, 148.4, 132.7, 132.2, 130.6 (sp^2-carbons), 51.4 ($-CH_2-$), 48.9, 46.6, 37.8 (-C-), 32.3, 32.2 (S-t-Bu), 30.6 (t-Bu), 16.6 (=C-Me). The cyclopentadiene structure in 9 was confirmed by the formation of the corresponding cyclopentadienide ion.
7) J. Ojima, T. Yokomachi, and T. Yokoyama, Chem. Lett., 1972, 633.
8) A mixture of (E)- and (Z)-isomers (83:17) was used.
9) 20: Mass (m/z) 418 (M^+); ^{1}H-NMR (CCl_4-CD_3COCD_3) δ 7.76-7.56 (m, 2H, aromatic), 7.15-6.91 (m, 2H, aromatic), 6.99 (s, 1H, =CH-), 6.45 (d, J=16.0, 1H, =CH-S), 6.26 (d, J=16.0, 1H, =CH-), 1.30 (s, 9H, t-Bu), 1.28 (s, 9H, t-Bu), 1.24 (s, 9H, t-Bu).
10) 26: Mass (m/z) 640 (M^+); ^{1}H-NMR ($CDCl_3$) δ 5.88 (dd, J=5.5, 7.0, 1H, =CH-CH_2), 5.82 (d, J=9.5, 1H, =CH-CH), 5.62 (d, J=9.5, 1H, -CH-S), 4.60 (dd, J=7.0, 11.0, 1H, $-CH_2-$), 4.23 (dd, J=5.5, 11.0, 1H, $-CH_2-$), 1.34 (s, 9H, t-Bu), 1.17 (s, 9H, t-Bu), 1.14 (s, 9H, t-Bu).

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