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Intramolecular Disproportionation Reactions of 4,6-Bis(chloromethyl)-2,5-dimethoxytropone via Heptafulvene Intermediates

Shun-ichi HIRAYAMA, Akira MORI, and Hitoshi TAKESHITA*

Abstract: Acetolysis of 4,6-bis(chloromethyl)-2,5-dimethoxytropone, prepared from 5-hydroxytropolone in a three-step sequence, with silver acetate caused a facile disproportionation via heptafulvene intermediates.

In connection with another synthetic project, we synthesized 4,6-bis(chloromethyl)-2,5-dimethoxytropone (**1**) via Mannich reaction[1] of 5-hydroxytropolone (**2**) with morpholine giving 5-hydroxy-4,6-bis(morpholinomethyl)tropolone (**3**),[2] followed by methylation with diazomethane and treatment with ethyl chloroformate.[3] Silver ion-mediated solvolysis of **1** in acetic acid formed an intramolecular disproportionation product via heptafulvene intermediates; expected mono- and bis-(acetoxymethyl) derivatives were minor products. The results will be described herein.

When **1** was refluxed in acetic acid with silver acetate for 4 h, two compounds (**4**[a yellow oil. ^{1}H NMR[4] δ=2.13(3H, s), 2.16(3H, s), 3.74(3H, s), 3.90(3H, s), 5.09(2H, d, J=1 Hz), 5.14(2H, s), 6.75(1H, s), and 7.31(1H, t, J=1 Hz). ^{13}C NMR δ=21.0(2C), 56.3, 62.9, 63.0, 63.8, 113.2, 131.0, 134.9, 142.5, 155.7, 161.8, 170.9, and 179.0] and **5**[a yellow oil. ^{1}H NMR δ=2.12(6H, s), 2.35(3H, d, J=1 Hz), 3.74(3H, s), 3.92(3H, s), 6.77(1H, s), 7.26(1H, q, J=1 Hz), and 8.03(1H, s). ^{13}C NMR δ=20.9(2C), 22.4, 56.3, 61.9, 87.0, 109.1, 129.0, 139.1, 145.4, 157.0, 162.0, 168.5(2C), and 178.9]) were obtained in 23 and 51% yields, respectively. A presence of moisture as a contaminant sharply dropped a material balance to furnish **4** and **5** in 5 and 29% yields, respectively, and additionally isolated was **6**[brown crystals, mp 62-63 °C, ^{1}H NMR δ=2.18(6H, s), 3.78(3H, s), 5.18(4H, s), and 7.39(2H, s). ^{13}C NMR δ=21.2(2C), 62.8, 63.1 (2C), 123.0(2C), 140.5(2C), 155.7, 169.2(2C), and 170.7(2C)], in 15% yield. Under more mild conditions, heating at 80 °C for 2 h, 4-(acetoxymethyl)-6-(chloromethyl)-2,5-dimethoxytropone (**7**) [a yellow oil. ^{1}H NMR δ=2.14(3H, s), 3.83(3H, s), 3.90(3H, s), 4.52(2H, s), 5.16 (2H, s), 6.77(1H, s), and 7.42(1H, s). ^{13}C NMR δ=20.6, 44.8, 55.9, 63.2, 63.5, 113.2, 131.4, 138.3, 143.3, 155.4, 161.7, 170.5, and 178.4] was obtained in quantitative yield. Therefore, **7** should be

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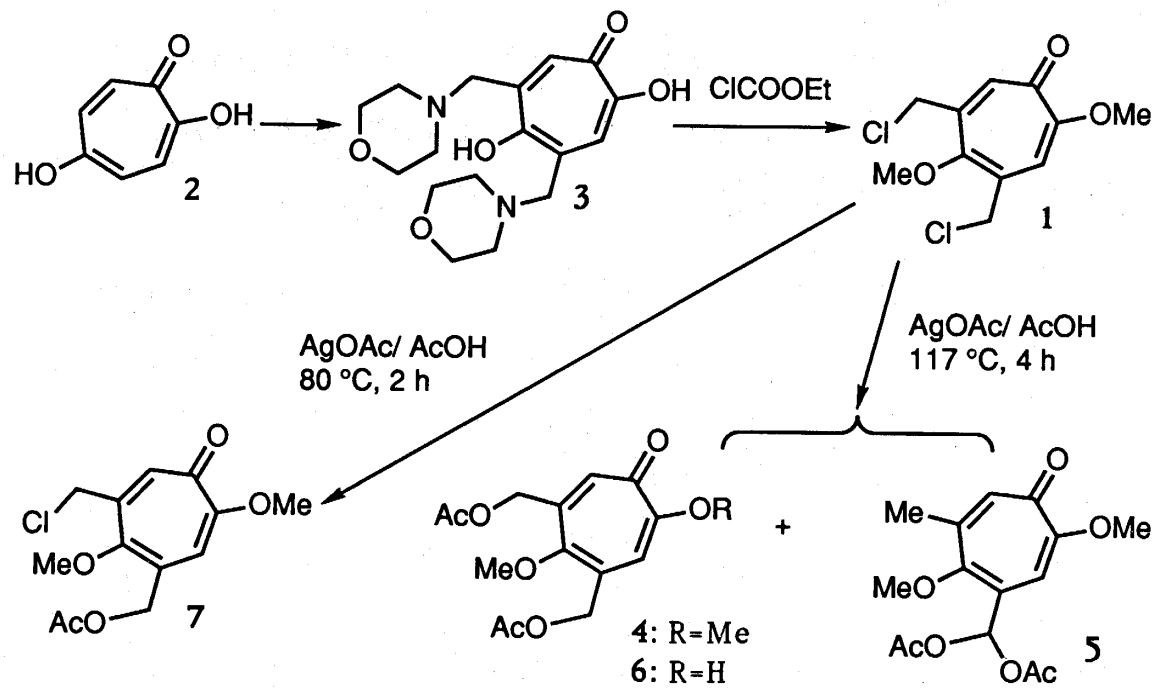
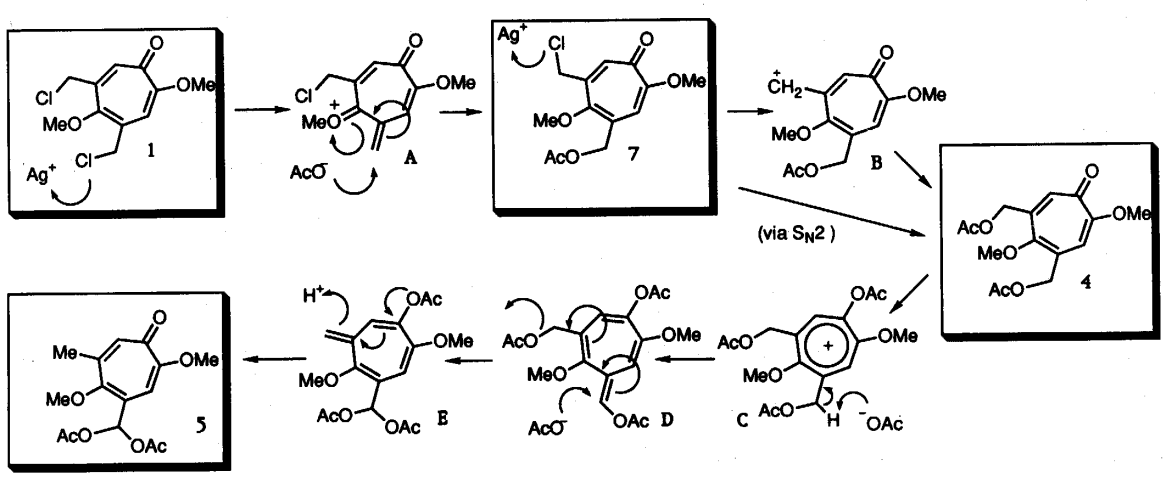


〔Scheme 1〕



〔Scheme 2〕

a common precursor of others. Their NMR spectra were fully consistent to the structures depicted. Particularly, appearance of the allyl couplings between the C-7 proton signals and C-6 methyl and methylene protons in the ^1H NMR spectra eliminated other possibilities.

Formation of **5**, showing a newly generated methyl group, is worth to comment. The first step of the solvolysis must be an elimination of chloride ion on the C-4 substituent assisted by electromeric effect from 5-methoxy group to form **A**, to which a nucleophilic attack of an acetoxy anion gives **7**. The second step of substitution[5] at 6-chloromethyl group to **4** via **B** should require more severe conditions due to no assistance from the methoxy group of C-2 or C-5. It is evident that only taking a heptafulvene intermediate into account, one can rationalize the formation of **5** from **4**, where disproportionation occurred functional groups on the *meta*-relationship. Thus, subsequent steps, **4** to **5**, are an acetylation of tropone carbonyl to form a tropylium ion (**C**), deprotonation to a heptafulvene (**D**), nucleophilic displacement of acetoxy group to form another heptafulvene (**E**), and the troponization via hydrolysis of 1-acetoxy group to form **5**.

Recently, we have isolated 3,4-diacetoxy-8,8-dimethylheptafulvene as a derivative having electron-releasing substituents at the exocyclic C=C in the first time.[6] Therefore, an intermediary occurrence of heptafulvenes should also be quite reasonable.

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3) H. Takeshita, S. Hirayama and A. Mori, *Kyushu Daigaku Kinou Busshitsu Kagaku Kenkyusho Hokoku,* **1**, 29 (1987).
4) The NMR spectra were measured in $CDCl_3$ solution with JEOL FX 100 and GSX 270H spectrometers.
5) We did not attempt to differentiate whether this step is solvolysis or ordinary S_N2-type displacement process.
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和 文 概 要

5－ヒドロキシトロポロンから三行程で得られる4，6－ビス(クロロメチル)－2，5－ジメトキシトロポンをアセトリシスすると，正常な加溶媒分解生成物と共に，ヘプタフルベン中間体を経る分子内不均化生成物が得られた。