Base-Promoted Rearrangement of Methyl (2-Troponyloxy)acetate and 4-(2-Troponyloxy)-2-butenoate to Methyl 2-Hydroxy-2-(2-troponyl)-acetate and 4-Hydroxy-4-(2-troponyl)-2-butenoate

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https://doi.org/10.15017/17707

出版情報：九州大学大学院総合理工学報告. 10 (1), pp.19-23, 1988-06-30. 九州大学大学院総合理工学研究科
バージョン：
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(Received February 22, 1988)

Abstract. A base-catalyzed rearrangement of methyl 2-(2-troponyloxy)acetate and methyl 4-(2-troponyloxy)-2-butenoate gave methyl 2-hydroxy-2-(2-troponyl)acetate and methyl 4-hydroxy-4-(2-troponyl)-2-butenoate. From the latter, a formation of tropylidene derivatives via tautomerism was observed.

Introduction

Among the chemical properties of troponoids, base-promoted ring-contraction to benzenoid derivatives from various functionalized tropone derivatives has been one of the most outstanding feature.[1] However, in a synthetic view point, this instability of tropones towards alkaline has been a problem. During our synthetic study on the troponoid ethers, we have found a novel base-catalyzed rearrangement of 2-(nitrobenzyloxy)tropones to 2-[nitrophenyl(hydroxy)methyl] tropones. And the reaction could be extended to other electron-withdrawing benzyloxy derivatives,[2] as well as 2-(phenacyl)tropones.[3] We will herein describe further extention of this novel base-catalyzed reaction to 2-troponyl aliphatic ethers having an electron-withdrawing substituent on their α-position, such as 2-(methoxycarbonylmethoxy)tropone and 2-(4-methoxycarbonyl-2-propenyloxy)tropone.

Results and Discussion

When a hexamethylphosphoric triamide (HMPA) solution of potassium tropolonate (**1**) and methyl bromoacetate (**2a**) was stirred at 60 ℃ for 15 min, a product (**3a**) was isolated by silica-gel column chromatography in 81% yield. The strucure of **3a** was identified to be desired methyl (2-troponyloxy)acetate. While **3a** was treated with the base under similar conditions as in the condensation, two products (**4a** and **5a**) were obtained. The former **4a** was the rearranged methyl [hydroxy(2-troponyl)] acetate. The latter **5a** was highly polar and was difficult to liberate from a silica-gel column. Therefore, the mixture containing **5a** was treated with diazomethane prior to the chromatographic fractionations; a methyl ether (**6**), thus obtained, showed in its ^{1}H NMR spectrum a singlet methyl at 4.04 together with five consecutive protons in the aromatic region and was deduced to be 3-methoxycyclohepta-[*b*]furan-2-one. The UV spectrum of **6**, showing two strong λ_{max} at 255 and 379

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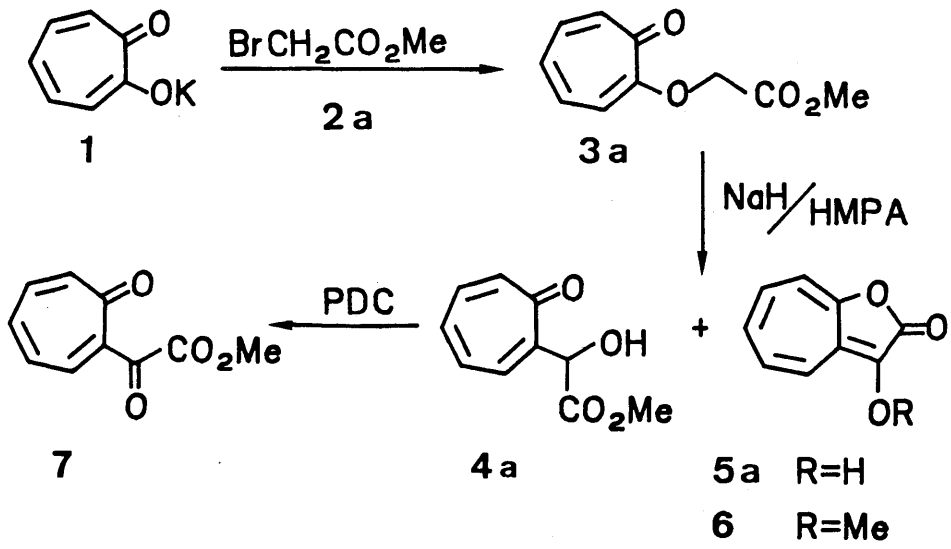
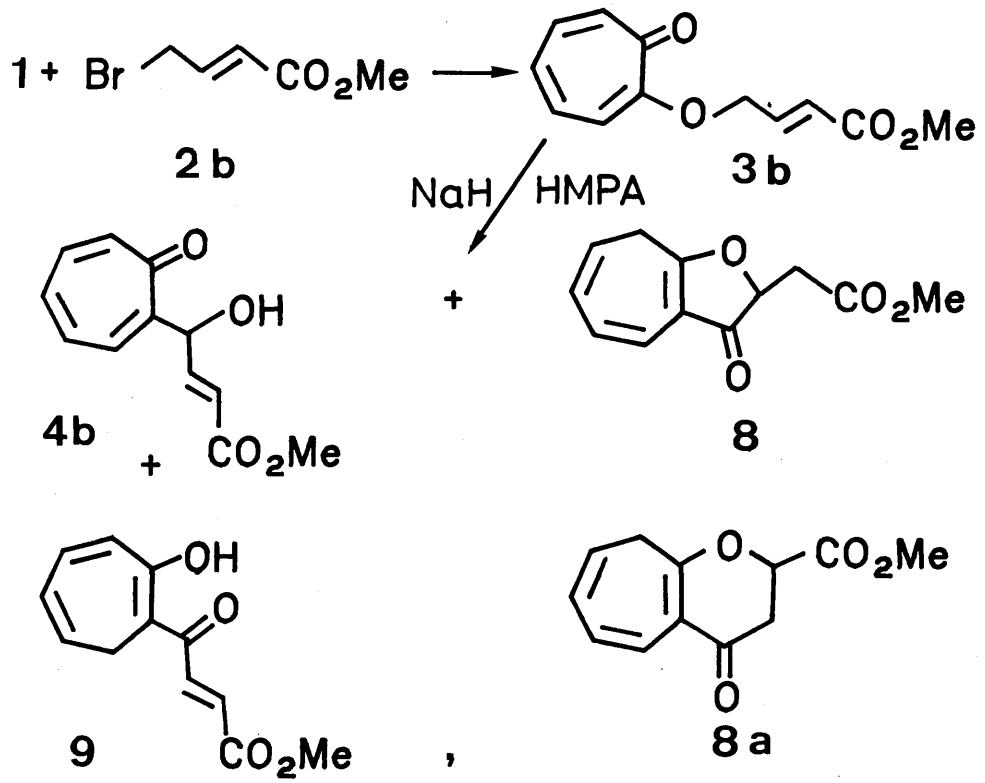


[**Scheme 1**]

nm, further confirmed its structure.[4] The pyridinium dichromate oxidation of **4a** gave an unstable methyl (2-troponyl)glyoxalate (**7**).

On the other hand, the condensate (**3b**) from **1** and **2b** afforded the expected rearrangement product (**4b**) and two other products (**8** and **9**). The major product, **4b**, was the expected methyl 4-hydroxy-4-(2-troponyl)-2-butenoate on the basis of the NMR spectral analysis. Two other compounds, **8** and **9**, were secondary products derived from **4b**. The IR spectrum of **8** exhibited a strong absorption peak at 1740 cm^{-1}, indicating a presence of an isolated ester group, and the ^1H NMR spectrum showed four olefinic proton signals whose chemical shifts are considerably high-field shifted, $\delta = 5.40$ (1H, dd, $J = 9.5$, 6 Hz) and 6.0 − 6.5 (3H, m), and methylene signal, 3.15 (2H, d, $J = 6$ Hz), indicating a presence of a tropyl group. From these findings, together with the λ_{max}, 284 nm,[5] **8** no longer possesses the fully conjugated troponoid system, and two alternative structures, **8** and **8a**, seem to be feasible. The dihydrocycloheptapyranone structure, **8a**, is, however eliminated on the basis of the coupling parameters in the ^1H NMR; the splitting patterns of ABX-system for the protons on the sp^3-carbons, $J_{AX} = 9.5$ Hz and $J_{BX} = 3.5$ Hz, were different to those of 4-oxo-2-phenylchromanes whose coupling patterns were $J_{AX} = 13.5$ Hz and $J_{BX} = 3.2$ Hz.[6] In addition, the absence of $\nu_{C=O}$ ca. 1630 cm^{-1} was also incompatible to the pyranone formula.[7] Hence, **8** is methyl (2,8(*2H*)-3-oxocyclohepta[*b*]furan-2-yl)acetate. Remaining product, **9**, was an enolyzed β-diketone derivative; its NMR exhibited the chelated proton signal at 15.9, as a broad peak. Other NMR features of **9** were an appearance of six vinylic protons; four of them are on the tropylidene ring, and two consisting systems are a part of the α, β-unsaturated ester function. Consequently, **9** is deduced to be methyl 4-oxo-4-(2-hydroxycyclohepta-1,3,5-trienyl)-2-butenoate.



[Scheme 2]

Now, it is interesting to note that **8** and **9** no longer have the tropone ring system. Such an easy deconjugation of the pseudo-aromatic system indicated that the aromaticity of tropones may be overestimated. For these days, reevaluation of the aromatic character of troponoid systems suggested that, contrary to general view of earlier studies, the tropones are essentially unsaturated ketones.[8] The present finding, an easy deconjugation of the tropone system to olefinic compounds, should constitute an experimental evidence for limited aromatic character of tropones.

Finally, we make a point that benzenoid analogs, salicylaldehyde or other phenolic compounds carrying electron-attractive substituents, gave no such rearrangement products. To date every attempt was unsuccessful.

Experimental

Condensation of 1 with 2a. Formation of 3a. a) An anhydrous HMPA solution (5 cm^3) of **1** (393 mg) and **2a** (460 mg) was stirred at 60 ℃ for 15 min. The mixture was then acidified with dil HCl and extracted with $CHCl_3$. Silica-gel column chromatography of the extract gave **3a** [an orange oil, 388.5 mg; 81%. Found: M. W., 194.0582. Calcd for $C_{10}H_{10}O_4$: 194.0579. ^{1}H NMR δ [9] = 3.75 (3H, s), 4.80 (2H, s), 6.6−7.1 (3H, m), and 7.1−

7.3 (2H, m). ^{13}C NMR δ =52.4, 66.1, 117.2, 129.8, 132.5, 136.7, 138.5, 163.8, 168.7, and 180.8. IR ν: 2960, 1760, 1630, 1600, 1560, 1495, 1475, and 1440 cm^{-1}. UV λ_{max}^{MeOH}: 236 nm (ε =21600), 320 (8000), 332 (7300), 343 (6200), and 359 (3600)].

Base-Catalyzed Rearrangement of 3a to 4a and 5a. Isolation of 5a as Methyl Ether (6). An anhydrous HMPA (1.6 cm^3) of **3a** (327 mg) and NaH (50%, 39.7 mg) was stirred at room temperature for 10 min. The mixture was then diluted with water, extracted with AcOEt, and dried on $MgSO_4$. To the organic solution, ethereal CH_2N_2 was added and kept in the refrigerator for 16 h. The mixture was then evaporated in vacuo and the residue was chromatographed on a silica-gel column to give **4a** [an orange oil, 94.1 mg; 29%. Found: M. W., 194.0564. Calcd for $C_{10}H_{10}O_4$: 194.0572. ^1H NMR δ =3.72 (3H, s), 5.00 (1H, s), 6.9−7.2 (4H, m), and 7.42 (1H, dd, J=6, 4 Hz). ^{13}C NMR δ =52.9, 75.0, 134.2, 135.5, 137.0, 137.4, 142.1, 150.3, 172.8, and 187.0. IR ν: 3400, 2960, 1740, 1630, 1560, 1520, 1470, and 1435 cm^{-1}. UV λ_{max}^{MeOH}: 231 nm (ε =20500), 306 (7000), and 313 (7000)] and **6** [red needles, mp 61−62 ℃, 21.9 mg; 7%. Found: C, 68.25; H, 4.64%. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58%. ^1H NMR δ =4.04 (3H, s), 6.4−6.8 (4H, m), and 6.9−7.1 (1H, m). ^{13}C NMR δ =59.1, 112.2, 129.7, 130.8, 131.0, 132.5, 134.1, 154.1 (2C), and 163.2. IR ν: 2960, 1750, 1645, 1610, 1570, 1525, 1485, 1450, 1420, 1330, 1270, 1215, 1200, 1160, 1080, 940, 900, 885, 755, and 695 cm^{-1}. UV λ_{max}^{MeOH}: 255 nm (ε = 17100) and 379 (13700)].

Oxidation of 4a to 7. To a CH_2Cl_2 solution (30 cm^3) of **4a** (91.2 mg) was added PDC (880 mg) at room temperature and the mixture was stirred for 2.5 d. The mixture was passed through Florisil column to give **7** [pale yellow crystals,[10] 13.2 mg; 15%. Found: m/z, 192. ^1H NMR δ =3.88 (3H, s), 7.1−7.3 (4H, m), and 7.7−7.9 (1H, m). ^{13}C NMR δ =53.0, 133.5, 136.8, 139.4 (2C), 144.4, 163.7, 186.4 (2C), and 188.0. IR ν: 1735, 1690, 1630, 1590, 1575, 1520, 1320, 1275, and 1135 cm^{-1}].

Condensation of 1 and 2b. An anhydrous HMPA solution (2 cm^3) of **1** (100 mg) was treated with anhydrous HMPA solution (2 cm^3) of **2b** (90%, 124.3 mg) at 50 ℃ for 3.5 h. The mixture was then diluted with water, acidified with dil HCl, extracted with AcOEt, and dried on $MgSO_4$. Organic fractions were chromatographed on a silica-gel column to give **3b** [light brown crystals, mp 119−121 ℃, 96.2 mg; 70%. Found: C, 65.29; H, 5.57%. Found: $C_{12}H_{12}O_4$: C, 65.44; H, 5.49%. ^1H NMR δ =3.72 (3H, s), 4.84 (2H, dd, J=4, 2 Hz), 6.18 (1H, dt, J=16, 2 Hz), and 6.6−7.3 (6H, m). ^{13}C NMR δ =51.8, 67.6, 115.0, 122.9, 129.0, 132.5, 136.7, 137.8, 141.0, 163.9, 166.3, and 180.6. IR ν: 3025, 1720, 1665, 1620, 1595, 1570, 1495, 1465, 1440, 1310, 1285, 1260, 1235, 1210, 1195, 1175, 1095, 1040, 1015, 960, 920, 870, 835, 770, 705, and 680 cm^{-1}. UV λ_{max}^{MeOH}: 235 nm (ε = 24000), 320 (8200), 346 (6500, sh), and 360 (4000, sh)] together with the recovered tropolone [0.4 mg; 1%].

Base-Catalyzed Rearrangement of 3b. An anhydrous HMPA solution (5 cm^3) of **3b** (530 mg) and NaH (50%, 86.8 mg) was stirred at room temperature for 3 min. The mixture was then diluted with dil HCl, extrated with AcOEt, and dried on $MgSO_4$. The organic layer was chromatographed on a silica-gel column to give **4b** [a dark orange oil, 74.4 mg; 14%. Found: M. W., 220.0738. Calcd for $C_{12}H_{12}O_4$: 220.0735. ^1H NMR δ =3.69 (3H, s), 4.2−4.5 (1H, br s), 5.42 (1H, dd, J=4, 2 Hz), 6.18 (1H, dd, J=16, 2 Hz), 6.9−7.2 (5H, m), and 7.3−7.5 (1H, m). ^{13}C NMR δ =51.7, 71.9, 120.8, 134.7, 135.1, 135.4, 136.8, 141.9,

147.9, 152.6, 167.2, and 187.0. IR ν : 3400, 2960, 1720, 1660, 1630, 1550, 1520, 1470, 1440, 1270, 1130, 1030, 985, and 790 cm^{-1}. UV λ_{max}^{MeOH}: 210 nm (ε =19500), 230 (21600), and 314 (6900)], **8** [an orange oil, 41.4 mg; 8%. Found: M. W., 220.0735. Calcd for $C_{12}H_{12}O_4$: 220.0735. ^1H NMR δ =2.63 (1H, dd, J=17, 9 Hz), 3.03 (1H, dd, J=17, 3.5 Hz), 3.15 (2H, d, J=6 Hz), 3.72 (3H, s), 4.91 (1H, dd, J=9.5, 3.5 Hz), 5.40 (1H, dd, J=9.5, 6 Hz), and 6.0－6.5 (3H, m). ^{13}C NMR δ = 30.1, 35.7, 52.3, 82.8, 114.6, 118.6, 119.0, 126.7, 130.1, 170.1, 180.5, and 198.7. IR ν : 3025, 2950, 1740, 1605, 1445, 1405, 1365, 1260, 1070, 995, and 665 cm^{-1}. UV λ_{max}^{MeOH}: 240 nm (ε = 10100) and 284 (6700)], and **9** [orange needles, mp 79－82 ℃, 12.2 mg; 2%. Found: M. W., 220.0734. Calcd for $C_{12}H_{12}O_4$: 220.0735. ^1H NMR δ =3.08 (2H, d, J=6.5 Hz), 3.80 (3H, s), 5.5－5.8 (1H, m), 6.1－6.3 (1H, m), 6.23 (1H, d, J=11 Hz), 6.70 (1H, d, J=11 Hz), 6.83 (1H, d, J=15 Hz), 7.55 (1H, d, J=15 Hz), and 15.9 (1H, br s). ^{13}C NMR δ =41.9, 52.1, 113.8, 118.4, 121.1, 124.0, 126.8, 128.9 (2C), 135.0, 170.9, and 197.1. IR ν : 3450, 1720, 1640, 1630, 1600, 1580, 1535, 1430, 1390, 1315, 1260, 1220, 1180, 1020, 975, 910, 740, and 685 cm^{-1}. UV λ_{max}^{MeOH}: 240 nm (ε =10400), 284 (7300), and 416 (400)].

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9) The NMR spectra were measured in $CDCl_3$ with FX 100 and GSX 270H Spectrometers.

10) The compound was extremely unstable; even at room temperature, the crystals turned black upon exposure to air. As a result, measurements of mp and elemental analysis were unsuccessful.