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SHORT COMMUNICATIONS

Double Acylation Product in the $SnCl_4$-promoted Reaction of 4,5-Dichlorocyclopent-4-en-1,3-dione with 1,3,5-Trimethoxybenzene

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Abstract—The reaction of 4,5-dichlorocyclopent-4-en-1,3-dione with 1,3,5-trimethoxybenzene under Friedel–Crafts reaction conditions gave, along with the expected 5-(2,4,6-trimethoxyphenyl)-4-chlorocyclopent-4-ene-1,3-dione, a disubstituted product—3,4-bis-(2,4,6-trimethoxyphenyl)-2-chlorocyclopent-2-en-1-one.

Keywords: chlorocyclopentenones, 1,3,5-trimethoxybenzene, Friedel–Crafts reaction, 5-aryl-4-chlorocyclopentene-1,3-dione, substitution

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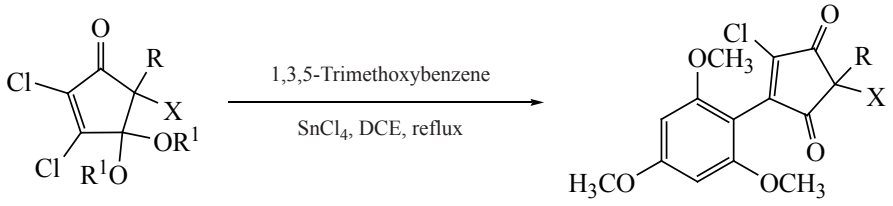
Previously, we made use of the Friedel–Crafts acylation of 1,3,5-trimethoxybenzene with di- and trichlorocyclopentenones **1a** and **1b** to obtain cyclopentenediones **2a** and **2b** substituted at C^3 (Scheme 1) [1–3]. Therewith, the reaction of compound **1b** with a 2-fold excess of trimethoxybenzene under prolonged reflux, resulted in the isolation, along with compound **4** [2], of a double substitution product **5** (Scheme 2).

The formation of compound **5** can be explained by the reduction of one of the keto groups of compound **4** and the subsequent replacement of the OH group by a second trimethoxybenzene molecule by the Friedel–Crafts reaction. To obtain evidence for the suggested pathway, we reacted the previously prepared hydroxyketone **6** [4, 5] with trimethoxybenzene under prolonged reflux and obtained a mixture of compounds **7** and **5** (Scheme 3). Apparently, under the acidic conditions, alcohol **7** initially forms carbocation **A** is formed, and the latter then attacks the aromatic substrate (Scheme 4).

Reaction of compound 3 with 1,3,5-trimethoxybenzene. Tin(IV) chloride, 0.51 mL, was added to a stirred solution of 0.36 g (2.18 mmol) of compound **3** in 40 mL of dichloroethane and 0.77 g (4.60 mmol) of 1,3,5-trimethoxybenzene in 10 mL of dichloroethane. The reaction mixture was refluxed until the starting compounds were completely consumed (36 h, TLC monitoring) and allowed to cool down to room temperature, after which 20 mL of distilled water and 30 mL of $CHCl_3$ were added. The organic layer was

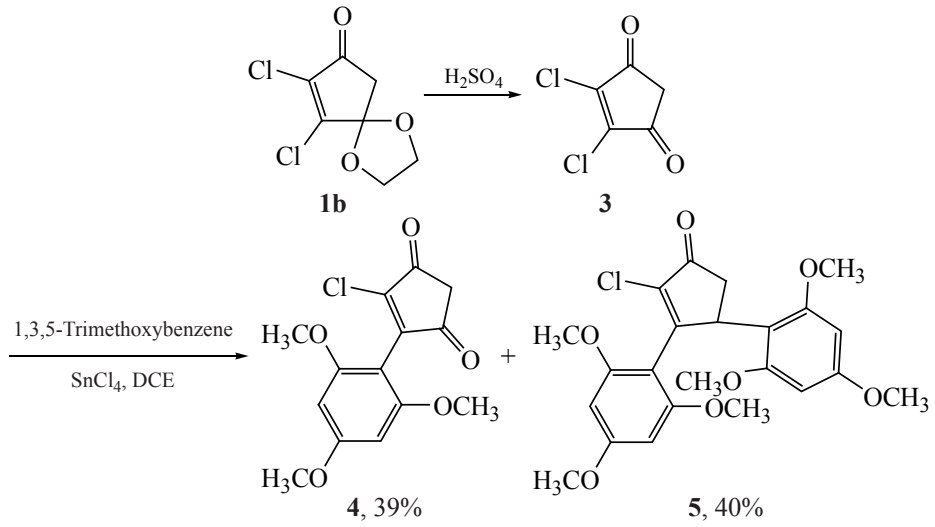
Scheme 1.



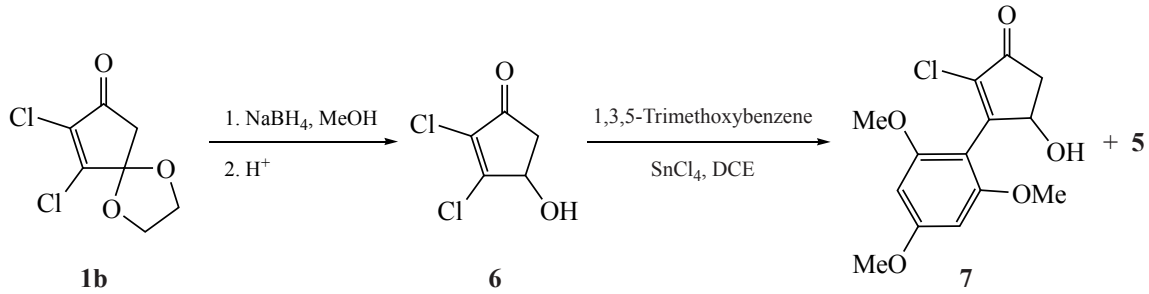
1a, **1b** **2a**, **2b**

1, R = $CH_2CH{=}CH_2$, X = Cl, R^1 = CH_2 (**a**), R = H, X = H, R^1–R^1 = $(CH_2)_2$ (**b**);
2, R = $CH_2CH{=}CH_2$, X = Cl (**a**), R = H, X = H (**b**).

Scheme 2.



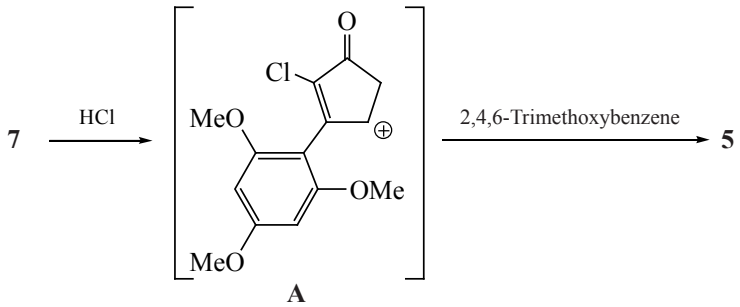
Scheme 3.



separated, washed with a saturated $NaHCO_3$ solution (2 × 15 mL), and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by column chromatography on a silica gel column (eluent petroleum ether–EtOAc, 10 : 1) to obtain 0.39 g (40%) of compound **5** and 0.251 g (39%) of compound **4** [2].

3,4-Bis(2,4,6-trimethoxyphenyl)-2-chlorocyclopen-2-en-1-one (5). Yellow crystals, mp 223–225°C. IR spectrum, ν, cm^{-1}: 2925, 2854, 1701, 1607, 1594, 1496, 1462, 1457, 1377, 1341, 1230, 1207, 1188, 1156, 1145, 1126, 1059, 1033, 951, 822, 808, 791. ^1H NMR spectrum, δ, ppm: 2.81 d.d (1H, CH_2, *J* 2.9, 18.0 Hz), 2.95 d.d (1H, CH_2, *J* 7.2, 18.1 Hz), 3.70 s (3H, OCH_3), 3.75 s (3H, OCH_3), 3.77 s (3H, OCH_3), 3.82 s (6H, OCH_3), 3.85 s (3H, OCH_3), 4.87 d.d (1H, C^4–H, *J* 2.9, 7.2 Hz), 6.11 s ($1H_{arom}$), 6.12 s ($1H_{arom}$), 6.18 s ($1H_{arom}$), 6.19 s ($1H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 39.48 (CH_2), 41.69 (C^4), 55.14 (OCH_3), 55.32 (OCH_3), 55.38 (OCH_3), 55.83 (OCH_3), 55.91 (OCH_3), 56.17 (OCH_3), 90.58, 90.88, 91.00 and 91.08 (C^3_{arom}, C^5_{arom}), 104.15 and 107.37 (C^1_{arom}), 135.18 (C^2), 158.93,

Scheme 4.



159.25, 160.05, 160.69, 161.85 (C^2_{arom}, C^6_{arom}, C^4_{arom}), 170.29 (C^3), 203.80 (C=O). Mass spectrum (EI), *m/z* (I_{rel}, %): 449 (450, 451) (100) $[M + H]^+$. Found, %: C 61.88; H 5.39; Cl 8.19. $C_{23}H_{25}ClO_7$. Calculated, %: C 61.54; H 5.61; Cl 7.90.

Reaction of compound 6 with 1,3,5-trimethoxybenzene was performed under the same conditions as with compound **3**, from 0.1 g (0.59 mmol) of keto alcohol **6** and 0.2 g (1.2 mmol) of 1,3,5-trimethoxybenzene in the presence of 0.14 mL (1.2 mmol) of $SnCl_4$. After the above-described workup, the products were separated on a silica gel column (eluent petroleum ether–EtOAc, 10 : 1), 61 mg (23%) to obtain 61 mg (23%) of compound **5** and 53 mg (30%) of compound **7**.

4-Hydroxy-3-(2,4,6-trimethoxyphenyl)-2-chlorocyclopen-2-en-1-one (7). Colorless crystals, mp 181–182°C. IR spectrum, ν, cm^{-1}: 3389, 2926, 2853, 1703, 1607, 1584, 1495, 1454, 1435, 1418, 1377, 1344, 1335, 1281, 1285, 1225, 1204, 1155, 1132, 1121, 1072, 1042, 968, 961, 806. ^1H NMR spectrum, δ, ppm: 2.48 d.d (1H, CH_2, *J* 2.1, 18.3 Hz), 2.62 br.s (1H, OH), 2.94–2.99 m (1H, CH_2), 3.79 s (3H, OCH_3), 3.84 s (6H, OCH_3), 5.31 d.d (1H, C^4–H, *J* 2.0, 6.3 Hz), 6.18 s ($2H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 43.33 (CH_2), 55.50 (OCH_3), 55.90 (OCH_3), 69.88 (C^4), 90.99 (C^3_{arom}, C^5_{arom}), 101.78 (C^1_{arom}), 135.33 (C^2), 163.06, 163.26 (C^2_{arom}, C^4_{arom}, C^6_{arom}), 163.89 (C^3), 197.81 (C=O). Mass spectrum (EI), *m/z* (I_{rel}, %): 299 (300, 301) (100) $[M + H]^+$. Found, %: C 56.58; H 5.29; Cl 11.49. $C_{14}H_{15}ClO_5$. Calculated, %: C 56.29; H 5.06; Cl 11.87.

The IR spectra were obtained on a Shimadzu IR Prestige-21 spectrophotometer for thin films. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-500 spectrometer at 500.13 and 125.77 MHz, respectively, internal standard TMS. The mass spectra were obtained on a Shimadzu LCMS-2010EV system (syringe injection of a chloroform–acetonitrile sample solution at a flow rate of 0.1 mL/min, eluent acetonitrile–water, 95 : 5, positive ion rmode, needle potential 4.5 kV; interface capillary temperature 250°C, interface capillary voltage 5 V). The elemental analyses were obtained on an EuroVector EuroEA-3000 CHNS analyzer. The reaction progress was monitored by TLC on Sorbfil plates, visualization with alkaline potassium permanganate. The synthesis products were isolated by column chromatography on silica gel (30–60 g of adsorbent per 1g of substance).

CONCLUSIONS

The reactions of 4,5-dichlorocyclopent-4-ene-1,3-dione and 2,3-dichloro-4-hydroxycyclopent-2-en-1-one with a double excess of 1,3,5-trimethoxybenzene was studied. Unlike the above-described substitution at the C^5 atom [1, 2], double substitution took place.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

OPEN ACCESS

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