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Synthesis of 3-Aryl-1,3,5-pentanetricarboxylic acid trialkylesters *via* a Tandem Addition-Rearrangement-Addition Reaction

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Summary. In the presence of anhydrous potassium carbonate as base, triethylbenzylammonium chloride as phase transfer catalyst, and dimethylformamide as solvent, 4-nitrophenylsulfonylacetate was treated with alkyl acrylate at 70°C to afford the unexpected 3-aryl-1,3,5-pentanetricarboxylic acid trialkylesters *via* a tandem addition-rearrangement-addition reaction. A possible mechanism was suggested.

Keywords. Addition-rearrangement-addition reaction; Mechanism; 3-Aryl-1,3,5-pentanetricarboxylic acid trialkylesters.

Introduction

The *Michael* reaction is an important method for carbon–carbon bond formation [1, 2]. Until now, many reports have appeared on using the conjugate addition of active methylene with α,β-unsaturated carbonyl compounds in the presence of a phase-transfer catalyst [3, 4]. In addition, aryl, β-keto, and vinyl sulfones are interesting in synthesis because they can undergo desulfonylation to give various important compounds [5–7]. Pentanetricarboxylic acids and their derivatives have been shown to be useful intermediates for the access to agricultural chemicals, pharmaceutical products, or crosslinking agents of polymers [8–10]. However, methods for preparing 1,3,5-pentanetricarboxylic acid derivatives involve rare starting materials, such as ethyl pentanehexacarboxylate, require relatively harsh conditions, and therefore, they lack adaptability to different substituent patterns [11–13]. In this paper, a particularly interesting and useful method for the preparation of 3-aryl-1,3,5-pentanetricarboxylic acid trialkylesters *via* a *Michael* reaction is described.

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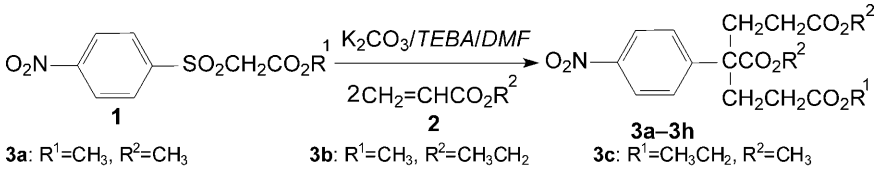
Results and Discussion

Like in recent studies on the reaction of β-ketosulfones [14, 15], we used 4-nitrophenylsulfonylacetate **1** as *Michael* donor, two equivalents of alkylacrylate **2** (R^2 = methyl or ethyl) as *Michael* acceptor, K_2CO_3 as base, and triethylbenzylammonium chloride (*TEBA*) as phase transfer catalyst (PTC) in *DMF*. However, the expected reaction did not occur. Instead, the addition-rearrangement-addition product, the 3-(4-nitrophenyl)-1,3,5-pentanetricarboxylic acid trialkylesters **3a**–**3h** were produced in good yields (Scheme 1).

In order to explain the formation of **3a**–**3h**, we suggest the mechanism shown in Scheme 2. Since the methylene group in 4-nitrophenylsulfonylacetate is activated by both the arylsulfonyl group and the carbonyl group, **1** generates the carbanion **I** in the presence of PTC and base. The *Michael* reaction of **I** with **2** results in the formation of **II**. Then the carbanion of **II** undergoes an intramolecular nucleophilic substitution on the aromatic ring and rearranges into **III**, which is expected to react with another equivalent of **2** to give **IV**. The carbanion **IV** further undergoes desulfonylation, looses sulfur dioxide, and then leads to the final products **3a**–**3h**.

In conclusion, no regular mono- or double-*Michael* addition products could be isolated. Thereby, this reaction procedure is more effective to prepare compounds of the structure **3a**–**3h**. In contrast to other synthetic methods involving the *Michael* reaction [16, 17], our method has the advantage of mild reaction conditions and good yields.

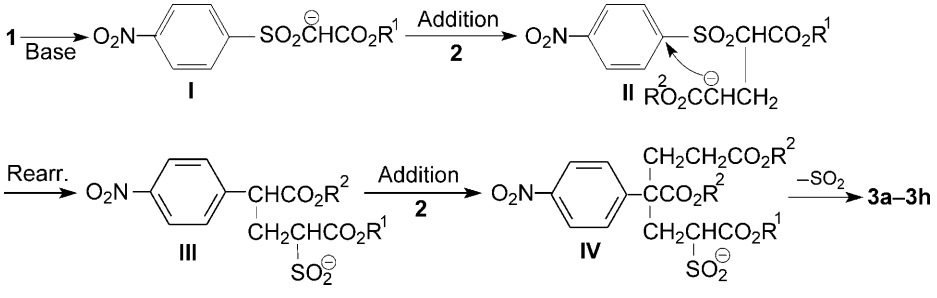


3a: R^1=CH_3, R^2=CH_3 **3b**: R^1=CH_3, R^2=CH_3CH_2 **3c**: R^1=CH_3CH_2, R^2=CH_3

3d: R^1=CH_3CH_2, R^2=CH_3CH_2 **3e**: R^1=$(CH_3)_2CH$, R^2=CH_3 **3f**: R^1=$(CH_3)_2CH$, R^2=CH_3CH_2

3g: R^1=$(CH_3)_2CHCH_2$, R^2=CH_3 **3h**: R^1=$(CH_3)_2CHCH_2$, R^2=CH_3CH_2

Scheme 1



Scheme 2

Experimental

Melting points were determined on a Kofler micro hot stage apparatus and are uncorrected. The IR spectra were recorded in KBr on a Nicolet 170 SX FT-IR spectrophotometer. ^{1}H NMR spectra were obtained on a Bruker WP-500SY (500 MHz) spectrometer with $CDCl_3$ as solvent and *TMS* as internal standard. Mass spectra were recorded on a ZAB-HS mass spectrometer with EI (70 eV). Elemental analyses were performed on a FOSS HEREAUS CHN-O-RAPID analyzer and provided results in good agreement with the calculated values. The 4-nitrophenylsulfonylacetates **1** (R^1 = methyl, ethyl, isopropyl, and isobutyl) were prepared by the method described in Ref. [18].

General Procedure for the Preparation of the Compounds **3a–3h**

A mixture of **1** (3.0 mmol), 0.83 g of anhydrous K_2CO_3 (6.0 mmol), 70 mg of triethylbenzylammonium chloride (0.3 mmol) and 5 cm^3 of *DMF* was stirred at room temperature for 10 minutes. The mixture was heated to 70°C, and 6.0 mmol of 2 were added dropwise to the mixture. Then the reaction mixture was stirred at 70°C for 2.5–5.5 h. After the reaction was complete, the mixture was diluted with 40 cm^3 of H_2O, acidified with 5% HCl, and then extracted with 2×15 cm^3 of CH_2Cl_2. The organic layer was washed with H_2O, dried with anhydrous $MgSO_4$, and filtered. The filtrate was concentrated and the residue was purified by column chromatography (silica gel, petroleum ether:ethyl acetate = 7:1) to give **3**.

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3,5-trimethylester (**3a**, $C_{17}H_{21}NO_8$)

Reaction time 2.5 h; yield 81%; mp 119–120°C; IR: $\bar{\nu}$ = 1727 (C=O), 1523 and 1350 (NO_2) cm^{-1}; ^{1}H NMR: δ = 1.95–2.65 (m, 2 CH_2CH_2), 3.66 (s, 2 CH_3O), 3.76 (s, CH_3O), 7.50 (d, J = 8.5 Hz, ArH), 8.21 (d, J = 8.5 Hz, ArH) ppm; MS: m/z (%) = 367 (0.6, M^+), 308 (35.7), 276 (28.0), 244 (100.0), 216 (68.0).

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3-diethyl-5-methylester (**3b**, $C_{19}H_{25}NO_8$)

Reaction time 3 h; yield 82%; mp 55–56°C; IR: $\bar{\nu}$ = 1731 (C=O), 1522 and 1349 (NO_2) cm^{-1}; ^{1}H NMR: δ = 1.30 (t, J = 7.1 Hz, 2 CH_3CH_2), 2.01–3.62 (m, 2 CH_2CH_2), 3.66 (s, CH_3O), 4.20 (q, J = 9.0 Hz, 2 OCH_2CH_3), 7.53 (d, J = 9.0 Hz, ArH), 8.26 (d, J = 9.0 Hz, ArH) ppm; MS: m/z (%) = 395 (0.4, M^+), 322 (34.0), 244 (100.0), 216 (64.8), 188 (53.3).

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3-dimethyl-5-ethylester (**3c**, $C_{18}H_{23}NO_8$)

Reaction time 3 h; yield 84%; mp 96–97°C; IR: $\bar{\nu}$ = 1730 (C=O), 1526 and 1352 (NO_2) cm^{-1}; ^{1}H NMR: δ = 1.20 (t, J = 7.0 Hz, CH_3CH_2), 1.90–2.60 (m, 2 CH_2CH_2), 3.63 (s, CH_3O), 3.76 (s, CH_3O), 4.08 (q, J = 7.0 Hz, OCH_2CH_3), 7.48 (d, J = 8.5 Hz, ArH), 8.26 (d, J = 8.5 Hz, ArH) ppm; MS: m/z (%) = 381 (0.6, M^+), 244 (100.0), 216 (66.1), 188 (57.8).

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3,5-triethylester (**3d**, $C_{20}H_{27}NO_8$)

Reaction time 3.5 h; yield 80%; IR: $\bar{\nu}$ = 1730 (C=O), 1523 and 1350 (NO_2) cm^{-1}; ^{1}H NMR: δ = 1.32 (t, J = 7.0 Hz, 3 CH_3CH_2), 1.95–2.65 (m, 2 CH_2CH_2), 3.93–4.50 (m, 3 CH_3CH_2O), 7.48 (d, J = 8.5 Hz, ArH), 8.26 (d, J = 8.5 Hz, ArH) ppm; MS: m/z (%) = 409 (0.2, M^+), 336 (37.5), 244 (100.0), 188 (46.9).

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3-dimethyl-5-isopropylester (**3e**, $C_{19}H_{25}NO_8$)

Reaction time 4.5 h; yield 82%; IR: $\bar{\nu}$ = 1733 (C=O), 1527 and 1349 (NO_2) cm^{-1}; ^{1}H NMR: δ = 1.26 (d, J = 7.6 Hz, $CH(CH_3)_2$), 1.85–2.56 (m, 2 CH_2CH_2), 3.61 (s, CH_3O), 3.75 (s, CH_3O), 4.66–4.96

(m, OCH), 7.50 (d, $J = 9.0$ Hz, ArH), 8.25 (d, $J = 9.0$ Hz, ArH) ppm; MS: m/z (%) = 395 (0.3, M^+), 276 (37.3), 244 (100.0), 216 (55.2), 188 (43.9).

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3-diethyl-5-isopropylester
(**3f**, $C_{21}H_{29}NO_8$)

Reaction time 4.5 h; yield 75%; IR: $\bar{\nu} = 1731$ (C=O), 1523 and 1349 (NO_2) cm^{-1}; ^1H NMR: $\delta = 1.16$–1.50 (m, 4 CH_3), 1.90–2.60 (m, 2 CH_2CH_2), 3.97–4.47 (m, 2 CH_2O), 4.76–5.00 (m, OCH), 7.57 (d, $J = 9.0$ Hz, ArH), 8.30 (d, $J = 9.0$ Hz, ArH) ppm; MS: m/z (%) = 423 (1.4, M^+), 336 (49.3), 290 (40.1), 244 (100.0), 216 (54.8), 188 (61.8).

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3-dimethyl-5-isobutylester
(**3g**, $C_{20}H_{27}NO_8$)

Reaction time 5 h; yield 75%; IR: $\bar{\nu} = 1735$ (C=O), 1523 and 1350 (NO_2) cm^{-1}; ^1H NMR: $\delta = 0.90$ (d, $J = 7.0$ Hz, $CH(CH_3)_2$), 1.60–2.60 (m, 2 CH_2CH_2 and $CH(CH_3)_2$), 3.63 (s, CH_3O), 3.73 (s, CH_3O), 3.80 (d, $J = 7.0$ Hz, OCH_2), 7.51 (d, $J = 9.0$ Hz, ArH), 8.26 (d, $J = 9.0$ Hz, ArH) ppm; MS: m/z (%) = 409 (0.7, M^+), 308 (20.4), 276 (34.6), 244 (100.0), 216 (55.8), 188 (45.1).

3-(4-Nitrophenyl)-1,3,5-pentanetricarboxylic acid-1,3-diethyl-5-isobutylester
(**3h**, $C_{22}H_{31}NO_8$)

Reaction time 5.5 h; yield 70%; IR: $\bar{\nu} = 1734$ (C=O), 1523 and 1350 (NO_2) cm^{-1}; ^1H NMR: $\delta = 1.00$ (d, $J = 7.0$ Hz, $CH(CH_3)_2$), 1.32 (t, $J = 7.0$ Hz, 2 CH_2CH_3), 1.70–2.70 (m, 2 CH_2CH_2 and $CH(CH_3)_2$), 3.76–4.50 (m, 3 CH_2O), 7.56 (d, $J = 9.0$ Hz, ArH), 8.27 (d, $J = 9.0$ Hz, ArH) ppm; MS: m/z (%) = 437 (0.8, M^+), 336 (30.5), 244 (100.0), 216 (64.8), 188 (63.3).

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