Simple and efficient synthesis of new tricarboxylic acids bearing cyclohexane and norbornane fragments

A. A. Firstova, * E. R. Kofanov, G. G. Krasovskaya, and A. S. Danilova

Yaroslavl State Technical University, 88 Moskovskii prosp., 150023 Yaroslavl, Russian Federation. Fax: +7 (485) 244 1360. E-mail: firstova.a.a@mail.ru

A synthesis new aryl alicyclic tricarboxylic acids bearing two carboxyl groups at either cyclohexane or norbornane fragment and one carboxyl group at the benzene ring was developed. Tricarboxylic acids of this type are promising monomers for the synthesis of heterocyclic polymers.

Key words: tricarboxylic acids, cyclohexane and norbornane fragments.

Heat-resistant polymers, particularly, aromatic poly-(imide)s and poly(amidoimide)s, possess unique properties and widely used in different fields as engineering plastics, thermal and radiation resistant films, binding agents, membrane materials, etc. Modern high technologies (manufacturing of the display devices, solar cells, etc.) show strong demand for polymers having not only high heat resistance but also optical transparency. It is known that the optical absorption of aromatic polyimides at $\lambda < 450$ nm is caused by the intra- and intermolecular donor-acceptor interactions between aromatic and heterocyclic fragments of polymer chain regions with increased and decreased electron density. Replacement of the fragments of aromatic anhydrides by cycloaliphatic units is the efficient approach to reduce or even completely suppress this effect.¹⁻⁶ Such polymers can be synthesized from tricarboxylic acids 7,8 containing alicylic fragments.

The aim of the present work is the development of the synthetic procedure towards aryl alicyclic tricarboxylic acids bearing two carboxyl groups at either cyclohexane or norbornane fragment and one carboxyl group at benzene ring. These compounds are regarded as perspective monomers for the synthesis of poly(amidoimide)s.

Results and Discussion

Tricarboxylic acids were synthesized from commercially available anhydrides **1a** and **1b** in four steps (Scheme 1). Hydrolysis of anhydrides **1a,b** in refluxing water gives the corresponding acids **2a,b**. Phenyl-substituted dicarboxylic

Scheme 1



 $X = absent (a), CH_2 (b)$

Reagents and conditions: i. H₂O, reflux; ii. C₆H₆, AlCl₃, 5 h; iii. MeCOCl, AlCl₃, 5 h; iv. NaOH, Br₂.

Published in Russian in Izvestiya Akademii Nauk. Seriya Khimicheskaya, No. 5, pp. 0867-0869, May, 2017.

1066-5285/17/6605-0867 © 2017 Springer Science+Business Media, Inc.

acids 3a,b were synthesized in 80-90% yields by the modified procedure published earlier⁹ (see Experimental).

Earlier, in communication¹⁰ we have described synthesis of compounds 4a, b by Friedel-Crafts electrophilic aromatic substitution (AlCl₃-catalyzed acylation with acetyl chloride in tetrachloroethane). Tetrachloroethane is a common solvent for these reactions; however, in the present work transformation $3a, b \rightarrow 4a, b$ was performed in chloroform, which significantly facilitated the isolation of the target products. When the reaction was carried out in tetrachloroethane, the product yields do not exceed 40%, but in chloroform compounds **4a**,**b** were obtained in 70-75% yields. Tricarboxylic acids 5a,b were synthesized by oxidation of the acetyl group of compounds 4a,b preliminary converted into the corresponding sodium salts. Oxidation was enabled using freshly prepared aqueous solution of sodium hypobromite. Compounds 5a,b were obtained in $\sim 60\%$ yields.

Structures of the synthesized compounds were confirmed by IR and NMR spectroscopy and high resolution electrospray ionization mass spectrometry.



Presence of well-resolved cross peaks in ${}^{1}H$ — ${}^{1}H$ NOESY spectra of compounds **5a**,**b** indicates the couplings between the aryl and alicyclic protons. This in turn is indicative of the equatorial positions of the carboxyphenyl substituents in these compounds. The couplings of the alicyclic protons confirmed that two carboxyl groups are *syn*-axial.

In summary, we elaborated simple and versatile procedure to access new aryl alicyclic tricarboxylic acids, promising monomers for the synthesis of poly(amidoimide)s and other heterocyclic polymers.

Experimental

¹H and ¹³C NMR spectra were recorded with a Bruker DRX-500 instrument (working frequencies of 500 and 125 MHz,

respectively). ${}^{1}H^{-1}H$ NOESY experiments were carried out with a Bruker DRX-300 instrument. All NMR spectra were recorded in DMSO-d₆, the chemical shifts are given in the δ scale and referenced to Me₄Si (an internal standard).

IR spectra were run on a Perkin Elmer Spektrum RX-1 spectrophotometer in Nujol mulls applied to KBr crystal plate. For (4-carboxyphenyl)cycloalkanedicarboxylic acids **4a**,**b**, IR spectra were also measured in KBr pellets.

High resolution electrospray ionization (ESI) mass spectrometry was performed on a Bruker micrOTOF II instrument.

Following commercially available reagents (pure and chemically pure) produced in Russia were used: maleic anhydride, divinyl, cyclopentadiene. Aluminum chloride was purchased from Sigma-Aldrich. Solvents were dried and distilled prior to use by the known procedures.¹¹

For compounds 3a,b, physicochemical properties absent in publication⁸ are given.

(1*R**,2*S**,4*S**)-4-Phenylcyclohexane-1,2-dicarboxylic acid (3a). Yield 82%, m.p. 170–173 °C. IR, ν/cm^{-1} : 2520, 930 (OH); 1695 (C=O, acid); 1255 (C–O–C); 700 (Ar). ¹H NMR (DMSO-d₆), δ : 1.47 (m, 1 H, H_f); 1.77 (m, 2 H, H_b, H_b·); 1.95 (m, 1 H, H_e·); 2.21 (m, 1 H, H_b·); 2.45 (m, 2 H, H_e); 2.58 (m, 1 H, H_d); 3.18 (m, 1 H, H_c); 3.37 (m, 1 H, H_a); 7.17 (d, 2 H, Ar, *J*=7.5 Hz); 7.25 (t, 3 H, Ar, *J*=14.8 Hz); 12.02 (s, 2 H, COOH).

(1*R**,2*R**,3*S**,4*S**,5*S**)-5-Phenylbicyclo[2.2.1]heptane-2,3-dicarboxylic acid (3b). Yield 90%, m.p. 175–178 °C. IR, v/cm^{-1} : 2530, 930 (OH); 1690 (C=O, acid), 1240 (C–O–C); 740, 710 (Ar). ¹H NMR (DMSO-d₆), δ : 1.37 (m, 1 H, H_g'); 1.56 (m, 2 H, H_f', H_g); 2.01 (m, 1 H, H_f); 2.44 (m, 1 H, H_b); 2.60 (m, 1 H, H_e); 2.90 (m, 1 H, H_d); 3.06 (m, 1 H, H_c); 3.48 (m, 1 H, H_a); 7.17 (d, 2 H, Ar, *J* = 7.0 Hz); 7.25 (d, 3 H, Ar, *J* = 7.0 Hz), 11.87 (s, 2 H, COOH).

Synthesis of (4-acetylphenyl)cycloalkanedicarboxylic acids 4a,b (general procedure). Dicarboxylic acid 2a,b (0.1 mol) was dissolved in chloroform (15 mL) in a three-neck flask fitted with reflux condenser and thermometer. Then aluminum chloride (0.4 mol) was added by portions followed by addition of acetyl chloride (0.1 mol). The reaction mixture was heated at 60 °C for 5 h. After the reaction completion, the mixture was poured into ice-water (100 mL) and the product was precipitated by adding 36% HCl (5 mL). The product was collected by filtration, recrystallized from aqueous acetic acid, washed with water, and dried at 50 °C.

(1*R**,2*S**,4*S**)-4-(4-Acetylphenyl)cyclohexane-1,2-dicarboxylic acid (4a). Yield 75%, m.p. 173–176 °C. IR, v/cm⁻¹: 2728, 2678, 2643, 934 (OH); 1713 (C=O, acid); 1698, 1255 (C=O, ketone); 1600 (Ar); 1291 (C–O–C). ¹H NMR (DMSO-d₆), δ : 1.54 (m, 1 H, H_f); 1.62 (m, 2 H, H_b, H_f'); 1.86 (m, 1 H, H_e'); 1.96 (m, 1 H, H_b); 2.17 (m, 1 H, H_e); 2.54 (m, 3 H, CH₃C(O)); 2.57 (m, 1 H, H_c); 3.19 (m, 1 H, H_a); 7.35 (d, 2 H, Ar, *J* = 8.1 Hz); 7.88 (d, 2 H, Ar, *J* = 8.4 Hz); 12.00 (s, 2 H, COOH). MS (ESI), *m/z*: found 291.1227 [M + H]⁺. Calculated for C₁₆H₁₉O₅: 291.1233.

(1*R**,2*R**,3*S**,4*S**,5*S**)-5-(4-Acetylphenyl)bicyclo[2.2.1]heptane-2,3-dicarboxylic acid (4b). Yield 70%, m.p. 127–130 °C. IR, v/cm⁻¹: 2746, 2651, 2557, 930 (OH); 1703 (C=O, acid); 1688, 1240 (C=O, ketone); 1602 (Ar); 1309 (C–O–C). ¹H NMR (DMSO-d₆), δ : 1.37 (m, 1 H, H_g'); 1.56 (m, 2 H, H_f', H_g); 2.07 (m, 1 H, H_f); 2.41 (m, 2 H, H_b); 2.51 (m, 3 H, CH₃C(O)); 2,61 (m, 1 H, H_e); 2.91 (m, 1 H, H_d); 3.02 (m, 1 H, H_c); 3.47 (m, 1 H, H_a); 7.16 (d, 2 H, Ar, *J* = 8.1 Hz); 7.30 (d, 2 H, Ar, *J* = 8.4 Hz; 12.00 (s, 2 H, COOH). MS (ESI), m/z: found 303.1227 [M + H]⁺. Calculated for C₁₇H₁₉O₅: 303.1233.

Synthesis of (4-carboxyphenyl)cycloalkanedicarboxylic acids 5a,b (general procedure). Sodium hydroxide (0.1 mol) was charged into a three-neck flask equipped with dropping funnel and thermometer and dissolved in water (20 mL) under vigorous stirring and cooling. Then bromine (0.03 mol) was added dropwise maintaining the reaction temperature below 10 °C. After cooling the reaction mixture to 0 °C, an aqueous solution of compound **4a**,b (0.01 mol, compounds **4a**,b were preliminary converted into the corresponding water-soluble sodium salts) was added dropwise. The mixture was stirred at ~20 °C for 1 h, then the reaction temperature was gradually raised to 50-60 °C over a period of 5 h. Bromoform was separated, the alkali solution was treated with 10% aqueous sodium pyrosulfite and acidified with HCl. The precipitate formed was collected by filtration, washed with water, and dried at 50 °C.

(1R*,2S*,4S*)-4-(4-Carboxyphenyl)cyclohexane-1,2-dicarboxylic acid (5a). Yield 60%, m.p. 203–205 °C. IR (Nujol), v/cm⁻¹: 2734, 2639, 2567, 939 (OH); 1694, 1679 (C=O, acid); 1599 (Ar); 1449 (CH₂); 1260 (C–O). IR (KBr), v/cm⁻¹: 3067, 3030, 2663, 2558 (OH); 2942 (CH₂, v^{as}); 2871 (CH₂, v^s); 1701 (C=O); 1610, 1574, 1489 (Ar); 1451, 1420 (CH₂, d); 1287, 1259, 1230, 1185 (C–O); 935 (OH, δ). ¹H NMR (DMSO-d₆), δ : 1.47 (m, 1 H, H_f); 1.82 (m, 2 H, H_b, H_f'); 1.95 (m, 1 H, H_e'); 2.14 (m, 1 H, H_b); 2.49 (m, 1 H, H_e); 2.57 (m, 1 H, H_d); 3.20 $(m, 1 H, H_c)$; 3.37 $(m, 1 H, H_a)$; 7.33 $(d, 2 H, H_o, H_{o'}, J = 8.4 Hz)$; 7.85 (d, 2 H, H_m , $H_{m'}$, J = 8.6 Hz); 12.39 (s, 3 H, COOH). ¹³C NMR, δ: 174.7 (C(1)), 174.6 (C(2)), 174.5 (C(13)), 167.1 (C(12)), 151.3 (C(9)), 129.5 (C(11)), 129.4 (C(11r)), 128.7 (C(10)), 126.8 (C(10r)), 41.8 (C(6)), 41.3 (C(3)), 40.3 (C(4)),34.7 (C(5)), 32.5 (C(8)), 24.0 (C(7)). MS (ESI), m/z: found 293.102 $[M + H]^+$. Calculated for C₁₅H₁₇O₆: 293.094.

(1*R**,2*R**,3*S**,4*S**,5*S**)-5-(4-Carboxyphenyl)bicyclo[2.2.1]heptane-2,3-dicarboxylic acid (5b). Yield 60%, m.p. 223–225 °C. IR (Nujol), v/cm⁻¹: 2730, 2640, 2568, 940 (OH); 1695, 1680 (C=O, acid); 1600 (Ar); 1450 (CH₂); 1257 (C–O). IR (KBr), v/cm⁻¹: 3143, 3026, 2750, 2554 (OH); 2966 (CH₂, v^{as}); 2882 (CH₂, v^s); 1720 (C=O); 1603, 1490 (Ar); 1449, 1417 (CH₂, δ); 1232, 1201 (C–O); 908 (OH, δ). ¹H NMR (DMSO-d₆), δ : 1.42 (m, 1 H, H_{gr}); 1.54 (m, 2 H, H_{fr}, H_g); 2.06 (m, 1 H, H_f); 2.41 (m, 1 H, H_b); 2.61 (m, 1 H, H_e); 2.91 (dd, 1 H, H_d, J_1 = 3.7 Hz, J_2 = 3.7 Hz); 3.09 (dd, 1 H, H_c, J_1 = 4.6 Hz, J_2 = 4.6 Hz); 3.54 (t, 1 H, H_a, J = 15.5 Hz); 7.34 (d, 2 H, H_o, H_o', J = 7.8 Hz); 7.85 (d, 2 H, H_m, H_{mr}, J = 7.1 Hz); 12.29 (s, 3 H, COOH). ¹³C NMR, δ: 173.5 (C(1)), 173.3 (C(2)), 167.4 (C(14)), 146.7(C(13)), 131.5 (C(12)), 130.6 (C(12r)), 128.6 (C(11)), 127.7 (C(11r)), 126.5 (C(10)), 47.2 (C(6)), 45.9 (C(3)), 45.3 (C(4)), 41.1 (C(9)), 36.5 (C(5)), 33.1 (C(8)), 21.0 (C(7)). MS (ESI), m/z: found 305.102 [M + H]⁺. Calculated for C₁₆H₁₇O₆: 305.094.

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Received July 5, 2016; in revised form December 8, 2016