Method of preparation of alkylated 1,3-diphenylpropan-2-ones, the components for assembly of graphene nanostructures

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Long-chain alkylated 1,3-diphenyl-2-propanones are used in the synthesis of graphene nanostructures (graphene nanoribbons and quantum dots). A reliable procedure to obtain mono- or dialkylated diphenyl-2-propanones in 26 and 38% yields has been proposed. The method includes the dioxolane protection of the keto group in 1,3-di-(4-bromophenyl)-2-propanone, then a palladium-catalyzed cross-coupling reaction of the obtained dioxolane with one-and-a-half- or four-fold excess of dodecyl magnesium bromide that leads to a predominant formation of mono- or dialkylation products respectively, followed by hydrolysis of dioxolanes at the last stage to form the desired diphenyl-2-propanones.

Key words: Grignard reagents, cross-coupling reactions, alkylation, long-chain 1,3-dialkylphenyl-2-propanones.

Molecular design of graphene nano-dimensional structures is a new, rapidly developing field of research focused on preparation of graphene nanoribbons and graphene quantum dots with specified electronic, optical, and magnetic properties.[1—9] To achieve this goal, it is necessary to create a fundamental basis for reproducible preparation of graphene materials with desired characteristics *via* identification of multiple structure — properties correlations. This, in turn, sets a challenge of developing a synthetic approach to prepare graphene nanostructures of the given geometry with exactly defined both electronic and functional edge states. The first successes on this way demonstrate the exclusive advantages of organic chemistry, giving the opportunity to perform an efficient step-by-step assembly of graphene nanosystems with atomic-level precision both on the surface and in solution.[10—12] The most notable achievement in this field is the synthesis of graphene nanoribbons with various widths wherein the key step comprises the Diels—Alder polymerization of acetylenyl-substituted cyclopentadienones (graphene assembly of the **GNR** nanoribbon from cyclopentadienone is illustrated in Scheme 1).[13,14] This approach allowed to obtain and study long (up to 600 nm) graphene nanoribbons with the width varying from 0.8 to 2 nm, in particular ribbons substituted with alkyl or alternating alkyl and other functionalities including stable radical groups on their edges.[15—18] Key cyclopentadienones **3a,b** (see Scheme 1) were synthesized by condensation of α-diketone **1** with 1,3-diphenylpropan-2-ones **2a,b** in the presence of KOH followed by deprotection of the acetylene moiety by treatment with tetrabutylammonium fluoride (TBAF).

The known synthetic procedure to obtain **2a** consists in the reaction between dibromide **4** and organozinc compound $C_{12}H_{25}ZnBr$ in the presence of $Pd(dppf)Cl_2$ (see Ref. 7). According to our experience, application of this procedure showed that it is poorly reproducible and, moreover, that the yields of mono- and dialkylated products depend heavily on the physical form of zinc in use, the composition of trace impurities therein, as well as on the method for zinc activation which is actually the removal of an oxide film from the surface. Many researches used zinc as a reactant faced these challenges.[19,20] Since it is necessary to accumulate a certain amount of **2a** and the analogs thereof in order to prepare various graphene nanoribbons including functionalized ones, we have focused on elaboration of a reliable method to obtain 1,3-diphenylpropan-2-ones **2a,b** in the present study. Such method was shown to be a three-step synthesis comprising protection of the keto group by reacting dibromide **4** with ethylene glycol in the presence of *para*-toluenesulfonic acid (*p*-TSA) followed by palladium-catalyzed cross-coupling of dioxolane **5** with dodecylmagnesium bromide to give mono- or dialkyl derivatives **6a,b** depending on the reagent ratio, and hydrolysis of the said derivatives with hydrochloric and trifluoroacetic acids (Scheme 2). Thus, using a four-fold excess of $C_{12}H_{25}MgBr$ resulted in an exhaustive (according to the NMR data) alkylation of dioxolane **5** and formation of compound **6b** isolated in

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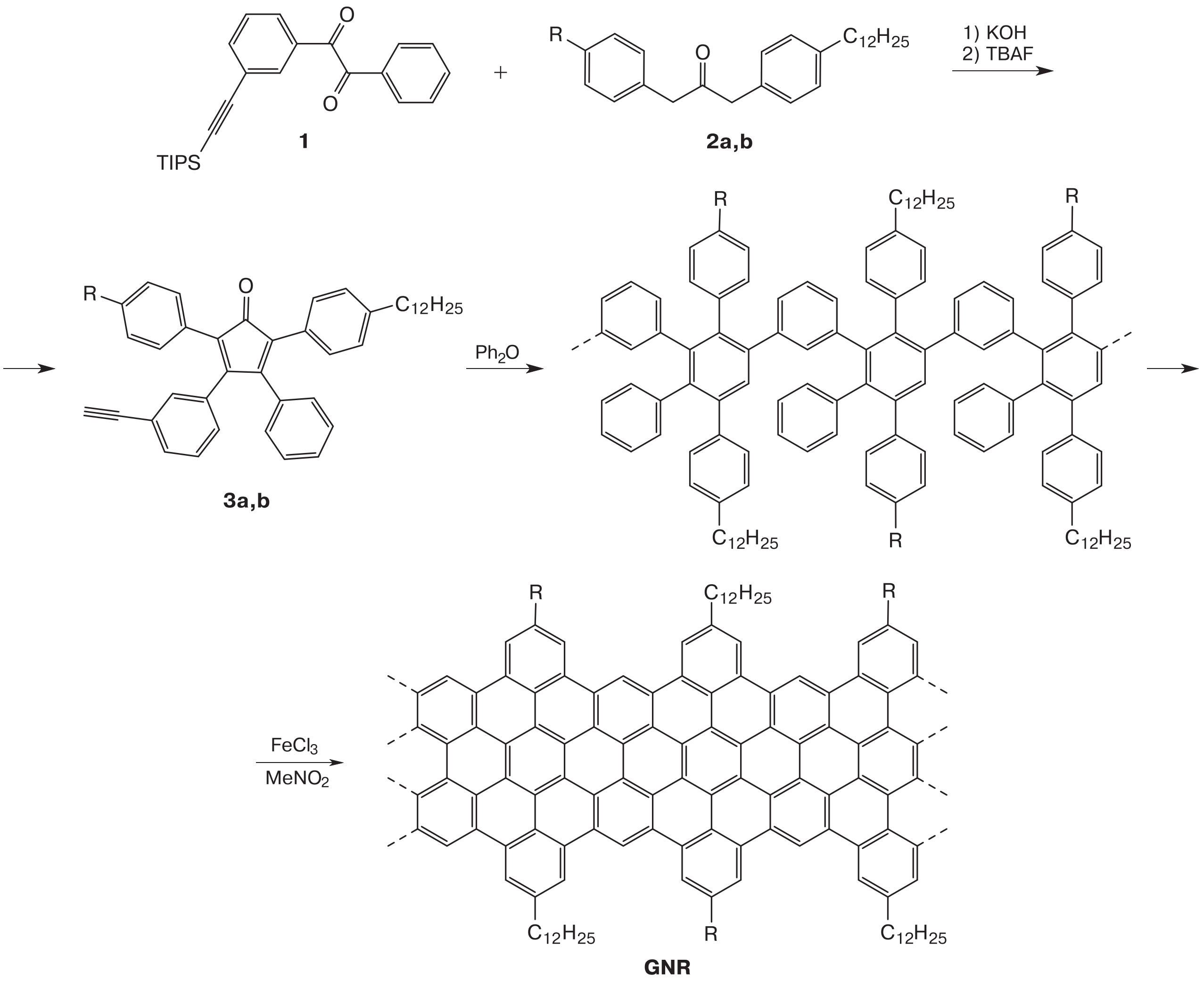
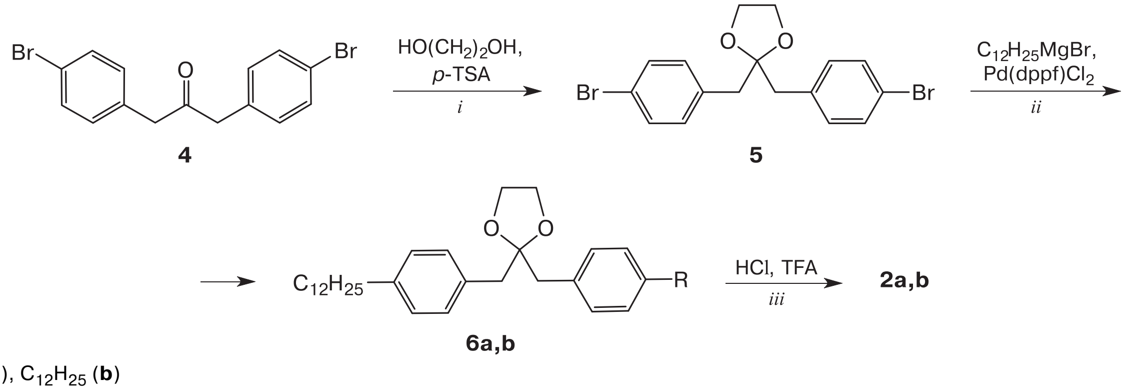
Scheme 1



R = Br (**a**), $C_{12}H_{25}$ (**b**)

TIPS is tri(isopropyl)silyl.

Scheme 2



R = Br (**a**), $C_{12}H_{25}$ (**b**)

Reagents and conditions: *i*. Toluene, 110 °C (the bath temperature is 165 °C), 8 h; *ii*. THF, 65 °C (the bath temperature is 85 °C), 24 h (dppf is 1,1′-bis(diphenylphosphino)ferrocene); *iii*. THF, 12 h.

Product yields based on dioxolane **5** (%): 26 (**2a**), 38 (**2b**).

59% yield. Hydrolysis of the latter compound made it possible to synthesize the desired propanone **2b** in 64% yield. With one-and-a-half excess of the Grignard reagent, a hard-to-separate mixture of dioxolanes **5**, **6a**, and **6b** was obtained, which was further hydrolyzed to give a mixture of compounds **2a**, **2b**, and **4**, wherefrom monobromide **2a** was isolated in 26% yield based on dioxolane **5**.

To summarize, we have developed a method of reproducible synthesis of the desired **2a,b** in the yields of 26 and 38% respectively based on dibromide **5**, thus allowing to produce monalkyl- (**2a**) and dialkylderivative (**2b**) in amounts required for the further experiments. Moreover, this method can be adapted to obtain unsymmetrically substituted ketones **2**, what opens an approach to functionalized derivatives of graphene nanoribbons.

Experimental

Compounds **4**[21] and **5**[22] were synthesized according to the known procedures. The following commercially available reagents were used: 1 *M* solution of $C_{12}H_{25}MgBr$ in Et_2O, $4-BrC_6H_4-CH_2CO_2H$, *p*-TSA, ethylene glycol, $Pd(dppf)Cl_2$ (all from Sigma-Aldrich) and TFA ("REAKHIM"). Solvents were purified according to the standard procedures; THF was dehydrated with calcium hydride and distilled over sodium-benzophenone.

^1H and ^{13}C NMR spectra were recorded on Bruker Avance-300 (300.13 MHz for ^1H), Bruker Avance-400 (400.13 MHz for ^1H, 100.62 MHz for ^{13}C) spectrometers in $CDCl_3$, chemical shifts are given in the δ-scale relative to the signals of residual protons of the corresponding deuterated solvents. IR-spectra were obtained on a Bruker Vector-22 apparatus for sample pellets in KBr. Masses of molecular ions were determines on a high resolution mass spectrometer DFS Thermo scientific instrument (EI, 70 eV) for compound **2b**, and on a high resolution chromate-mass spectrometer Agilent 7200 Accurate Mass Q-TOF GC/MS (EI, 70 eV, column HP-5MS) for compound **2a**. Melting points were determined on Mettler Toledo Thermosystem with FP 900 measuring cell. Column chromatography was performed on silica gel KSK 50—160 μm of OOO «IMID». Thin-layer chromatography was carried out on silica gel Merck (60 PF_{254}).

1-(4-Bromophenyl)-3-(4′-dodecylphenyl)-propan-2-one (2a).[7] To a stirred solution of 2,2-bis(4-bromobenzyl)-1,3-dioxolane **5** (824.24 mg, 2 mmol) in THF (6 mL) in argon, $Pd(dppf)Cl_2$ (73 mg, 0.1 mmol) was added. 1 *M* solution of $C_{12}H_{25}MgBr$ (3 mL) was added dropwise with a syringe. The resulting mixture was stirred with a reflux condenser at 65 °C for 24 h. After cooling, the mixture was treated with MeOH (10 mL). The resulting suspension was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent was hexane). The obtained dioxolane **6a** (1.370 g) was dissolved in THF(40 mL), conc. HCl (20 mL) and TFA (1 mL) were added, the mixture was stirred for 12 h. Solvents were evaporated under reduced pressure, the residue was neutralized with a saturated $NaHCO_3$ solution, and extracted with chloroform. The organic layer was dried over $MgSO_4$, the solvent was evaporated, the residue (1.350 g) was purified using preparative TLC (hexane—CH_2Cl_2, 80 : 20). Yield of propanone **2a** 0.234 g (26%), **2b** < 5%. ^1H NMR (400 MHz, $CDCl_3$), δ: 0.86 (t, 3 H, CH_3, $J = 6.8$ Hz); 1.22—1.26 (m, 18 H, CH_2); 1.54—1.61 (m, 2 H, CH_2); 2.56 (t, 2 H, CH_2, $J = 7.6$ Hz); 3.65, 3.67 (both s, 2 H, CH_2); 6.96 (d, 2 H, $J = 8.4$ Hz); 7.05 (d, 2 H, $J = 7.8$ Hz); 7.12 (d, 2 H, $J = 7.8$ Hz); 7.4 (d, 2 H, $J = 8.4$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.00, 22.56, 29.20, 29.23, 29.38, 29.47, 29.51, 29.54, 31.34, 31.79, 35.45, 47.82, 49.04, 120.89, 128.73, 129.18, 130.65, 131.08, 131.55, 132.84, 141.84, 205.17. IR (KBr), ν/cm^{-1}: 2917, 2448, 1716, 1488, 1469, 1342, 1064, 1010, 815, 719, 522, 487. Found, *m/z*: 456.2021 $[M]^+$. $C_{27}H_{37}BrO$. Calculated: 456.2022 [M].

2,2-Bis(4-dodecyl)-1,3-dioxolane (6b) was obtained similar to **6a** using compound **5** (1.442 g, 3.50 mmol), 1 *M* solution of $C_{12}H_{25}MgBr$ (14 mL), $Pd(dppf)Cl_2$ (0.128 g, 0.175 mmol), and anhydrous THF (27 mL). The product was purified by preparative TLC (hexane—ethyl acetate, 97 : 3), $R_f = 0.5$, m.p. 38.4—39.1 °C. Yield 1.23 g (59%). ^1H NMR (300 MHz, $CDCl_3$), δ: 0.88 (t, 6 H, CH_3, $J = 6.6$ Hz); 1.17—1.40 (m, 36 H, CH_2); 1.52—1.66 (m, 4 H, CH_2); 2.52—2.61 (m, 4 H, CH_2); 2.89 s, 4 H, CH_2); 3.45 (s, 4 H, CH_2); 7.07 (d, 4 H, $J = 8.0$ Hz); 7.17 (d, 4 H, $J = 8.0$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.01, 22.58, 29.23, 29.24, 29.41, 29.49, 29.53, 29.55, 29.56, 31.42, 31.81, 35.49, 44.07, 65.25, 110.84, 127.76, 130.47, 133.59, 140.71. IR (KBr), ν/cm^{-1}: 2954, 2920, 2848, 1516, 1466, 1323, 1184, 1149, 1070, 1032, 1011, 953, 833, 779, 723, 661, 484. Found, *m/z*: 589.4970 $[M - H]^+$. $C_{41}H_{65}O_2$. Calculated: 589.4979 [M − H].

1,3-Bis(4-dodecylphenyl)propan-2-one (2b) was synthesized using a modified procedure[22]. A solution of compound **6b** (0.648 g, 1.1 mmol), conc. HCl (13 mL), and TFA (0.7 mL) in THF (30 mL) was stirred for 12 h at room temperature. The solvent was partially evaporated at reduced pressure, the precipitate was filtered, washed with aqueous $NaHCO_3$ and water. Yield 0.388 g (64%). Spectral characteristics of compound **2b** were identical to those reported in literature[23].

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