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Synthesis of 2,3,4,5-Tetraphenylfuran, -thiophene and -pyrrole from Toluene

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1,2,3,4-Tetraphenylbutane-1,4-dione (**8**) was synthesized from toluene in seven steps. Additionally, the 2,3,4,5-tetraphenylthiophene (**9**), -furan (**10**) and -pyrrole (**11**) were prepared using the modified of known methods in good yields.

Key Words: Synthesis, 2,3,4,5-Tetraphenylfuran/thiophene/pyrrole, Toluene.

INTRODUCTION

Heterocycles such as furan, pyrrole and thiophene are versatile pharmacophores possessing a variety of biological activites[1-3]. They also play important roles in natural products, non linear optics[4-6] and supermoleculer chemistry[7]. In particular, pyrroles are found in many naturally occuring compounds such as heme, chlorophyll and vitamin B_{12}[8-10]. Addition, multi-substitued furan ring are important compounds for synthesis purpose and as starting materials to produce pharmaceutically and industrially important compounds[11]. Therefore, many synthetic methods for the preparation of these systems have reported in the literature[3,12]. These compound are usually prepared from the 1,4-diketones[5,6].

In this article, we report the synthesis of 1,2,3,4-tetraphenylbutane-1,4-dione (**8**), which is the starting material for generating the 2,3,4,5-tetraphenylthiophene (**9**), -furan (**10**) and pyrrole (**11**), from toluene.

EXPERIMENTAL

All solvents were dried and distilled by standard procedures. ^1H and ^{13}C NMR spectra were recorded on 200 (50) MHz Varian spectrometers and reported in δ units with TMS as internal standard. All column chromatography was performed on silica gel (60 mesh, Merck).

Benzylbromide (2): To solution of toluene (**1**) (5 g, 5.4 mmol) in a 50 mL CCl_4 was added N-bromosuccinimide (NBS) (10.53 g, 58.86 mmol) and a little amount of AIBN. The reaction mixture was heated under reflux for 1 h. The mixture was cooled to room temperature and the solution was filtrated for the removal of insoluble materials and washed with 50 mL of water. The extracts were dried with anhydrous $MgSO_4$ and evaporation of the solvent to dryness give **2** (9 g, 96 %; b.p. 198-199 ºC, lit.[13] 198 ºC).

1,2-Diphenylethane (3): In a solution of benzyl bromide (**2**) (2.5 g 14.6 mmol) in a 50 mL anhydrous THF Mg (0.35 g. 14.6 mmol) dust and a small amount of I_2 were added. The reaction mixture was heated at a bath temperature of 65 ºC for 16 h. After the mixture was cooled to room temperature, the insoluble materials were separated by filtration. The filtrate was diluted with water and extracted with $CHCl_3$. The combine extracts were washed with water, dried over $MgSO_4$. The removal of the solvent *in vacuum* give 1,2-diphenylethane (**3**) (1.43 g, 54 %; white crystals mp 49 ºC, lit.[14] 52 ºC). ^1H NMR (200 MHz, $CDCl_3$) δ = 2.99 (s, 4H), 7.23-7.39 (m, 10H). ^{13}C NMR (50 MHz, $CDCl_3$) δ = 143.83, 130.49, 130.37, 127.95, 39.96.

1-Bromo-1,2-diphenylethane (4): In solution of 1,2-diphenylethane (**3**) (2 g, 10.9 mmol) in a 50 mL of CCl_4, NBS (1.95 g, 10.9 mmol) and a small amount of AIBN were added. The reaction mixture was heated under reflux temperature for 1 h. After the mixture was cooled to room temperature, the insoluble materials were separated by filtration. The mixture was washed with water and dried over $MgSO_4$. The removal of the solvent *in vacuo* give 1-bromo-1,2-diphenylethane (**4**) (2.5g, 87 %; colourless crystals m.p. 45-47 ºC, lit.[15] 46-48 ºC). ^1H NMR (200 MHz, $CDCl_3$) δ = 3.59 (dd, 2H), 5.25 (t, 1H), 7.18-7.62 (m, 10H), ^{13}C NMR (50 MHz, $CDCl_3$) δ = 143.61, 139.87, 131.52, 130.67, 130.45, 130.25, 129.62, 128.66, 58.25, 48.53.

1,2-Diphenyl-ethane-1-ol (5): 1-Bromo-1,2-diphenylethane (**4**) (2.3 g, 8.81 mmol) dissolved in 30 mL of acetone/water (9:1) and add $AgClO_4$ (1.8 g, 8.81 mmol). The reaction mixture was heated and refluxed temperature for 3 h. The mixture was cooled to room temperature and extracted with diethyl ether (3 × 50 mL). The organic layers were dried over $MgSO_4$. The removal of the solvent *in vacuo* give 1,2-diphenyl-ethane-1-ol (**5**) (1.52 g 88 %; white crystals, mp 65 ºC, lit.[16] 67 ºC). ^1H NMR (200 MHz, $CDCl_3$) δ = 3.09 (dd, 2H); 4.95 (t, 1H), 7.15-7.57 (m, 10H) ^{13}C NMR (50 MHz, $CDCl_3$) 145.88, 140.07, 131.53, 130.68, 130.48, 130.39, 128.59, 128.59, 127.92, 48.11.

1,2-Diphenylethanone (6): PCC (1,78 g, 18.1 mmol) was dissolved in 30 mL of CH_2Cl_2. The mixture was cooled to 0 ºC and added 1,2-diphenylethane-1-ol (**5**) (1.5 g, 18.1 mmol) in CH_2Cl_2 (15 mL) for 0.5 h. The mixture was stirred at room temperature for 3 h, the solution was filtrated for removal of the insoluble material. The removal of the solvent *in vacuum* gave **6** (1.4 g, 82 %; white crystals, m.p. 60 ºC, lit.[17] 58 ºC). ^1H NMR (200 MHz, $CDCl_3$) δ = 4.30 (s, 2H), 7.07-8.16 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 199.61, 138.74, 136.61, 135.11, 131.46, 130.63, 130.46, 128.87, 47.52.

2-Bromo-2-phenylacetophenone (7): To a solution of 1,2-diphenylethanone (**6**) (1.2 g 6.12 mmol) in 20 mL of CCl_4 was added a solution of Br_2 (0.98 g 6.12 mmol) in 20 mL of CCl_4 at room temperature for 0.5 h. The mixture was washed with water (50 mL) and dried over $MgSO_4$. The removal of the solvent *in vacuo* give 2-bromo-2-phenylacetophenone (**7**) (1.4 g, 83 %; white crystals, m.p. 54-55 ºC, lit.[18] 53 ºC). ^1H NMR (200 MHz, $CDCl_3$) $\delta = 6.45$ (s, 1H), 7.30-8.15 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) $\delta = 187.74$, 142.03, 130.95, 130.71, 129.91, 58.08.

1,2,3,4-Tetraphenylbutane-1,4-dione (8): To a stirred solution of 2-bromo-2-phenylacetophenone (**7**) (1.4 g 50.9 mmol) in anhydrous THF (30 mL) was added Zn dust (0.32 g 50.9 mmol) and a small amount of I_2. The reaction mixture was heated at a bath temperature of 65 ºC for 16 h. After the mixture was cooled to room temperature, the insoluble materials were separated by filtration. The filtrate was diluted with water and extracted with $CHCl_3$ (3 × 50 mL). The combined extracts were washed with water and dried over $MgSO_4$. After removal of the solvent, the crude product was crystallized (0.7 g, 70 %; white crystals, m.p. 158-161 ºC, lit.[19] 157-160 ºC). ^1H NMR (200 MHz, $CDCl_3$) $\delta = 8.07$ (m, 4H), 7.53 (m, 4H), 7.30 (m, 12H), 4.32 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) $\delta = 196.62$, 138.71, 136.64, 135.17, 132.95, 132.45, 131.93, 131.52, 131.08, 130.96, 130.89, 130.66, 130.43, 129.38, 129.23, 128.92, 127.91, 47.54.

2,3,4,5-Tetraphenylthiophene (9): A mixture of 1,2,3,4-tetraphenylbutane-1,4-dione (**8**) (1 g, 25.6 mmol) and P_2S_5 (5.68 g, 25.6 mmol) were heated in the sealed tube at 210 ºC for 3 h. The reaction mixture was cooled to room temperature and extracted with diethyl ether (3 × 50 mL) and washed with water. The combined organic layers was dried over $MgSO_4$ and evaporated. After removal of solvent, the crude product was crystallized (0.66 g, 68 %; needle crystals, m.p. 188 ºC, lit.[20] 188 ºC). ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.26$-6.94 (m, 20H); ^{13}C NMR (50 MHz, $CDCl_3$) $\delta = 140.24$, 139.03, 137.26, 134.83, 131.44, 129.71, 128.43, 127.92, 127.25.

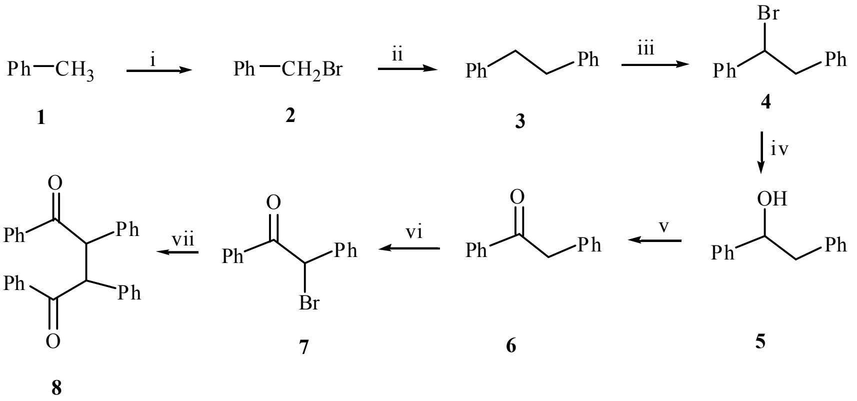
2,3,4,5-Tetraphenylfuran (10): A solution of 1,2,3,4-tetraphenylbutane-1,4-dione (**8**) (1 g, 25.6 mmol) in 30 mL DMSO was heated at reflux temperature for 3 h. The reaction mixture was cooled to room temperature and extracted with diethyl ether (3 × 50 mL) and washed with water. The organic layer was dried over $MgSO_4$ and evaporated. After removal of solvent, the crude product was crystallized (0.85 g, 89 %; m.p. 173-175 ºC, lit.[21] 175 ºC). ^1H NMR (200 MHz, CD_2Cl_2) $\delta = 7, 25$ (m, 20H); ^{13}C NMR (50 MHz, $CDCl_3$) $\delta = 147.75$, 133.25, 130.96, 130.43, 128.34, 127.27, 127.13, 125.88, 125.15; IR (KBr, cm^{-1}) 3040, 1595, 1485, 1440, 1150, 1107, 1070, 1055, 1028, 950, 800, 764, 750, 700, 688.

2,3,4,5-Tetraphenylpyrolle (11): A mixture of 1,2,3,4-tetraphenylbutane-1,4-dione and (**8**) (1 g, 25.6 mmol) and $(NH_4)_2CO_3$ (2.4 g, 25.6

mmol) were heated in the sealed tube at 210 ºC for 3 h. The reaction mixture was cooled to room temperature and extracted with diethyl ether (3 × 50 mL) and washed with water. The organic layers was dried over $MgSO_4$ and evaporated. After removal of solvent, the crude was crystallized (0.8 g, 86 %, white crystals, mp 210-212 ºC, lit.[22] 213-214 ºC). ^1H NMR (200 MHz, $CDCl_3$) δ = 8.22 (1 H, NH), 7.44-6.87 (m, 20H); ^{13}C NMR (50 MHz, CD_2Cl_2) δ = 136.52, 129.03, 128.54, 127.05, 115.01.

RESULTS AND DISCUSSION

The reaction of toluene (**1**) with N-bromosuccinimide (NBS) gave benzyl bromide (**2**). The treatment of benzyl bromide (**2**) with zinc dust in the presence of a small amount of I_2 at 65 ºC afforded the 1,2-diphenyl ethane (**3**) which convert to 1-bromo-1,2-diphenylethane (**4**) with NBS. Compound **4** was converted to the 1,2-diphenyl-ethene-1-ol (**5**) with $AgClO_4$ in the acetone/H_2O (9:1). Oxidation of 5 with PCC, followed bromination of 1,2-diphenylethanone (**6**) with molecular bromine yielded 2-bromo-2-phenylacetophenone (**7**). The reaction of 2-bromo-2-phenylacetophenone **7** with zinc dust in the presence of a small amount of I_2 at 65 ºC resulted in the 1,2,3,4-tetraphenylbutane-1,4-dione (**8**) *via* wurtz-like self condensation (**Scheme-I**).

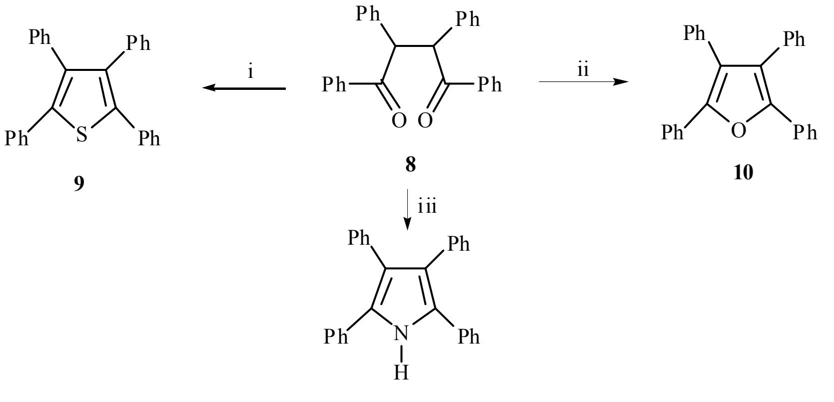


Scheme-I Reagent and conditions: (i) NBS, AIBN, CCl_4, 1 h reflux (ii) Mg, I_2, dry THF, 65 ºC, 16 h (iii) NBS, AIBN, CCl_4, reflux, 1 h (iv) $AgClO_4$, 9:1 acetone/water, reflux, 3 h (v) PCC, CH_2Cl_2, 3 h room temp. (vi) Br_2, CCl_4, r.t., 0.5 h (vii) Zn, I_2, THF, 65 ºC 16 h

The structures of the compounds **2-8** were determined on basis of the spectral data and comparison with their published data. All spectral findings are in accord with the purposed structures.

The heating of 1,2,3,4-tetraphenylbutane-1,4-dione (**8**) in DMSO at 190 ºC for 3 h gave the 2,3,4,5-tetraphenylfuran (**10**), in good yield (89 %). Addition, the heating of 1,2,3,4-tetraphenylbutane-1,4-dione (**8**) with P_2S_5

and $(NH_4)_2CO_3$, separately, in sealed tube at 210 ºC afforded the 2,3,4,5-tetraphenylthiophene (**9**) and 2,3,4,5-tetraphenyl-pyrrole (**11**), respectively (**Scheme-II**).



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Scheme-II Reagent and conditions: (i) P_2S_5, 210 ºC, 3 h, sealed tube (ii) DMSO, reflux, 3 h (iii) $(NH_4)_2CO_3$, 210 ºC, 3 h, sealed tube

The structures of the compounds **9-11** were determined on basis of the spectral data and comparison with their published data. All spectral findings are in accord with the proposed structures.

Conclusion

The 1,2,3,4-tetraphenylbutane-1,4-dione (**8**) was easily synthesized using the known and modified methods in seven step from starting the toluene. Additionally, the 2,3,4,5-tetraphenylthiophene (**9**), -furan (**10**) and -pyrrole (**11**) were prepared using the modified of known methods in good yields.

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