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

MELIHA BURCU GÜRDERE*, YAKUP BUDAK and MUSTAFA CEYLAN
Department of Chemistry, Faculty of Arts and Sciences
Gaziosmanpasa University, 60250 Tokat, Turkey
Fax: (90)(356)2521585, Tel: (90)(356)2521616; E-mail: burcugurdere@gmail.com

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 activities. They also play important roles in natural products, nonlinear optics and supermolecular chemistry. In particular, pyrroles are found in many naturally occurring compounds such as heme, chlorophyll and vitamin B12. Additionally, multi-substituted furan ring are important compounds for synthesis purpose and as starting materials to produce pharmaceutically and industrially important compounds. Therefore, many synthetic methods for the preparation of these systems have reported in the literature. These compounds are usually prepared from the 1,4-diketones.

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 13C 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 CCl4 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 MgSO₄ and evaporation of the solvent to dryness gave 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 I₂ 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 CHCl₃. The combine extracts were washed with water, dried over MgSO₄. The removal of the solvent in vacuum gave 1,2-diphenylethane (3) (1.43 g, 54%; white crystals mp 49 ºC, lit.¹⁴ 52 ºC). ¹H NMR (200 MHz, CDCl₃) δ = 2.99 (s, 4H), 7.23-7.39 (m, 10H). ¹³C NMR (50 MHz, CDCl₃) 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 CCl₄, 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 MgSO₄. 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, CDCl₃) δ = 3.59 (dd, 2H), 5.25 (t, 1H), 7.18-7.62 (m, 10H), ¹³C NMR (50 MHz, CDCl₃) 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 AgClO₄ (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 MgSO₄. The removal of the solvent in vacuo gave 1,2-diphenyl-ethane-1-ol (5) (1.52 g 88%; white crystals, mp 65 ºC, lit.¹⁶ 67 ºC). ¹H NMR (200 MHz, CDCl₃) δ = 3.09 (dd, 2H); 4.95 (t, 1H), 7.15-7.57 (m, 10H) ¹³C NMR (50 MHz, CDCl₃) 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 CH₂Cl₂. The mixture was cooled to 0 ºC and added 1,2-diphenylethane-1-ol (5) (1.5 g, 18.1 mmol) in CH₂Cl₂ (15 mL) for 0.5 h. The mixture was stirred at room temperature for 3 h. The solution was filtered for removal of the insoluble material. The removal of the solvent in vacuo gave 6 (1.4 g, 82%; white crystals, m.p. 60 ºC, lit.¹⁷ 58 ºC). ¹H NMR (200 MHz, CDCl₃) δ = 4.30 (s, 2H), 7.07-8.16 (m, 10H); ¹³C NMR (50 MHz, CDCl₃) 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 CCl₄ was added a solution of Br₂ (0.98 g 6.12 mmol) in 20 mL of CCl₄ at room temperature for 0.5 h. The mixture was washed with water (50 mL) and dried over MgSO₄. 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, CDCl₃) δ = 6.45 (s, 1H), 7.30-8.15 (m, 10H); ¹³C NMR (50 MHz, CDCl₃) δ = 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 I₂. 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 CHCl₃ (3 × 50 mL). The combined extracts were washed with water and dried over MgSO₄. 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, CDCl₃) δ = 8.07 (m, 4H), 7.53 (m, 4H), 7.30 (m, 12H), 4.32 (s, 2H); ¹³C NMR (50 MHz, CDCl₃) δ = 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, 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 P₂S₅ (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 MgSO₄ 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, CDCl₃) δ = 7.26-6.94 (m, 20H); ¹³C NMR (50 MHz, CDCl₃) δ = 140.24, 139.03, 137.26, 134.83, 131.44, 129.71, 128.43, 127.92, 127.27, 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-Tetraphenylfurane (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 MgSO₄ 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, CD₂Cl₂) δ = 7.25 (m, 20H); ¹³C NMR (50 MHz, CDCl₃) δ = 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-Tetraphenylpyrrole (11): A mixture of 1,2,3,4-tetraphenylbutane-1,4-dione and (8) (1 g, 25.6 mmol) and (NH₄)₂CO₃ (2.4 g, 25.6
mmol) were heated in the sealed tube at 210 °C 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 MgSO4 and evaporated. After removal of solvent, the crude was crystallized (0.8 g, 86 %, white crystals, mp 210-212 °C, lit.22 213-214 °C).

1H NMR (200 MHz, CDCl3) δ = 8.22 (1 H, NH), 7.44-6.87 (m, 20H); 13C NMR (50 MHz, CD2Cl2) 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 I2 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 AgClO4 in the acetone/H2O (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 I2 at 65 ºC resulted in the 1,2,3,4-tetraphenylbutane-1,4-dione (8) via wurtz-like self condensation (Scheme-I).

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 °C 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 P2S5
and (NH₄)₂CO₃, 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).

![Chemical structures of compounds 9-11](image)

**Scheme-II**  Reagent and conditions: (i) P₂S₅, 210 ºC, 3 h, sealed tube (ii) DMSO, reflux, 3 h (iii) (NH₄)₂CO₃, 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.

**ACKNOWLEDGEMENT**

The authors are indebted to Department of Chemistry, Gaziosmanpasa University, Turkey.

**REFERENCES**


(Received: 7 March 2007; Accepted: 8 October 2007) A JC-5987