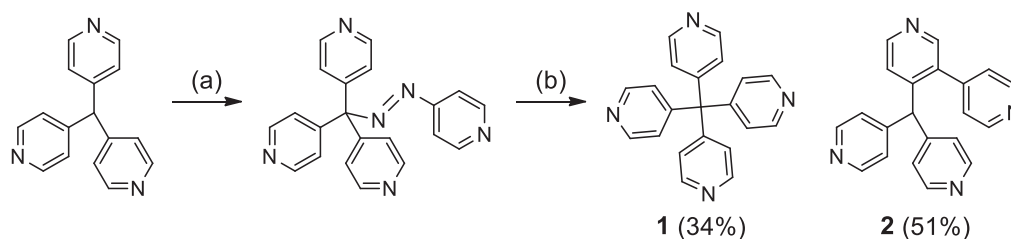


## Autoxidation of Di-4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)methane

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**Abstract.** The corresponding methanol was obtained by the autoxidation of di-4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)methane. This tertiary alcohol derivative was further converted to di-4-pyridylketone, 4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)ketone or 5,5-di-4-pyridyl-6-oxa-5,6-dihydro-2,8-phenanthroline under the ambient conditions.

Tetra-4-pyridylmethane (**1**) was firstly synthesized by aromatic nucleophilic substitution of 4-chloropyridine with tri-4-pyridylmethyl anion.<sup>[1]</sup> But the yield of the reaction was very low (3%) and to be improved. We reported the efficient synthesis of **1** by the pyrolysis of tri(4-pyridyl)-4-pyridylazomethane,<sup>[2]</sup> which was synthesized from tri-4-pyridylmethane<sup>[3]</sup> in one step (Scheme 1). Another main product in this pyrolysis was di-4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)methane (**2**), an isomer of **1**, which would be formed through the coupling between 4-pyridyl radical and tri-4-pyridylmethyl radical at 3-position of the 4-pyridyl group followed by the migration of hydrogen atom. Compounds **1** and **2** could be hardly separated each other by the column chromatography on alumina, but **1** was fortunately isolated by washing thoroughly with ethyl acetate because **2** was much more soluble in ethyl acetate than **1**.



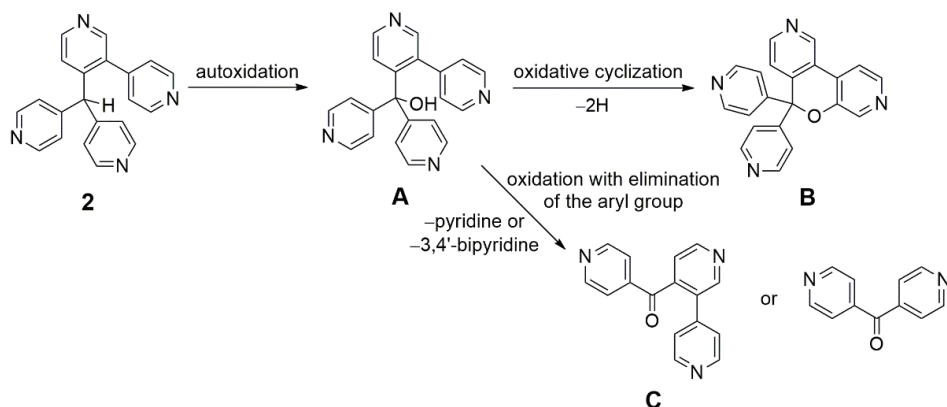
Scheme 1. Synthesis of **1** through the pyrolysis of tri(4-pyridyl)-4-pyridylazomethane. *Reagents and conditions:* (a) 4-pyridyldiazonium chloride (5.0 equiv), 2M HCl, 0 °C, 1 h. (b) 130 °C, 2 h, under N<sub>2</sub>.

We performed this pyrolysis reaction in several times and obtained the gram quantity of **1**. On the other hand, the ethyl acetate washings, in which the isomer **2** was mainly contained, was stored under the ambient conditions after the concentration. After several years, the sample of **2** turned red probably due to the effects of the acidic vapor. We investigated this sample and found that the autoxidation of **2** partially occurred. Furthermore, two new compounds, which would be formed by further conversion of the autoxidation product of **2**, were also isolated. Now we report the isolation and characterization of these compounds.

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The experimental details of the isolation was as follows: the sample (ca. 1.4 g) of crude **2** was dissolved in 20 mL of 1M HCl. The deep red solution was alkalized with 40 mL of 14% ammonia solution and the solution turned yellow. The solution was extracted with 30 mL of chloroform two times and the combined organic layers were dried over anhydrous sodium sulfate. After the filtration, the filtrate was concentrated and dried under the flow of nitrogen gas. First recrystallization from ethyl acetate gave a mixture of **1** and the unknown compound **A** (150 mg) and the second recrystallization from the same solvent afforded the different mixture of **1** and the unknown compound **B** (500 mg). The filtrate of the second recrystallization was concentrated and dried. The residue was purified the column chromatography on alumina eluting with 200 mL of methylene chloride–ethyl acetate (1:1 v/v), 200 mL of ethyl acetate, and then 400 mL of ethyl acetate–methanol (20:1 v/v). Small amount of di-4-pyridylketone (ca. 10 mg) was eluted firstly. Second, the fraction of the unknown compound **C** (50 mg) was collected. After the elution of the compound **C**, the fraction of the mixture of **1** and **2** (500 mg) were eluted together. The unknown compound **A** was purified by column chromatography on alumina eluting with methylene chloride–methanol (50:1 v/v). The unknown compound **B** was purified by the iterative recrystallization from ethyl acetate. The unidentified compound **C** was purified by the recrystallization from chloroform–hexane.

The structure of the unknown compounds **A**, **B**, and **C** were characterized<sup>[4-6]</sup> and eventually determined by X-ray crystallographic analyses.<sup>[7-9]</sup> The unknown compound **A** was di-4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)methanol, the autoxidation product from **2**. The unknown compound **B** was 5,5-di-4-pyridyl-6-oxa-5,6-dihydro-2,8-phenanthroline, which would be formed by the oxidative cyclization of **A**. The compound **C** was 4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)ketone, which might be formed by the oxidation of **A** with the elimination of the aryl group. Whereas the elimination of 4-pyridyl group afforded **C**, the elimination of 3-(4-pyridyl)-pyridin-4-yl group gave di-4-pyridylketone (Scheme 2).



Scheme 2. Plausible formation of unknown compounds **A**-**C** and di-4-pyridylketone.

Figure 1 shows the <sup>1</sup>H NMR chemical shifts of **2**, **A**, and **B**. The comparison of the chemical shifts of tri-4-pyridylmethane (δ 8.59 (Py-2,6H), 7.02 (Py-3,5H), 5.43 (C-α)) and tri-4-pyridylmethanol (δ 8.50 (Py-2,6H), 7.21 (Py-3,5H), 6.82 (OH)), the high-field shifts of the protons on the 3,4'-bipyridyl moiety are characteristic. The <sup>13</sup>C NMR

chemical shift of the  $sp^3$  carbon atom in **A** was observed at 81.0 ppm, which was much lower than that of **2** (51.6 ppm) and comparable with that of tri-4-pyridylmethanol (79.4 ppm).

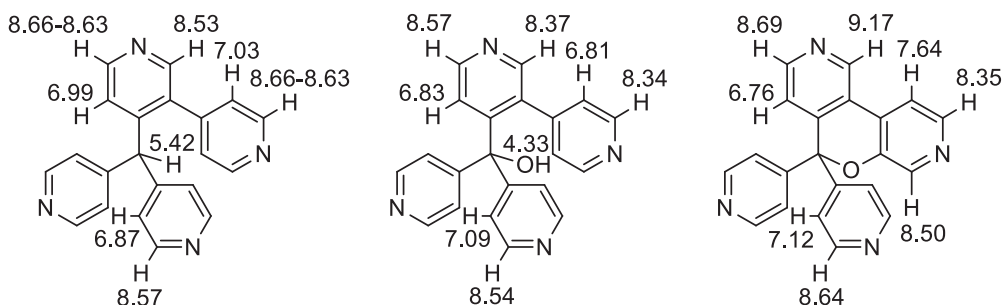


Figure 1.  $^1\text{H}$  NMR chemical shifts of **2** (left), **A** (center), and **B** (right).

Figure 2 shows the result of the X-ray crystallographic analysis of **A**. The intermolecular hydrogen bond between the central hydroxyl group and the nitrogen atom of 4-pyridyl group was observed ( $\text{N1}\cdots\text{H1}$  1.84(3) Å,  $\text{N1}\cdots\text{O1}$  2.782(2) Å). The similar hydrogen bond was also observed in tri-4-pyridylmethanol ( $\text{N1}\cdots\text{H1}$  1.80(2) Å,  $\text{N1}\cdots\text{O1}$  2.775(2) Å).<sup>[10]</sup> The angle between the two pyridyl rings in bipyridyl moiety was 85.6°, which was larger than that in **2** (57.7°). This was due to the steric congestion around the  $sp^3$  carbon atom and would cause the high-field shifts of the protons in bipyridyl moiety in **A**.

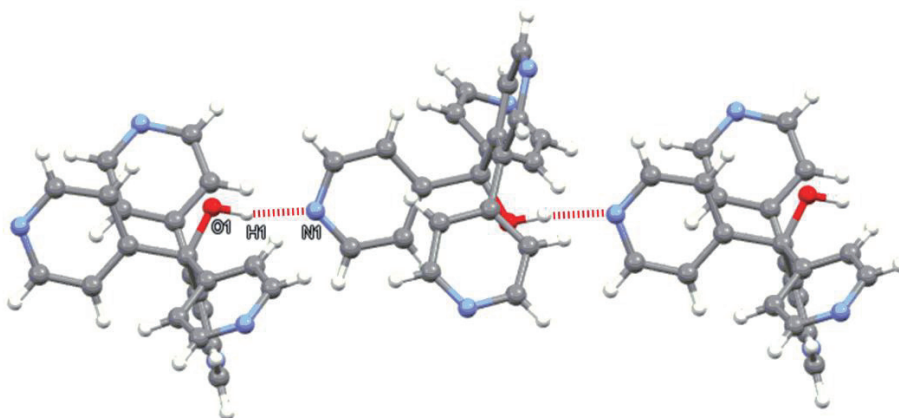


Figure 2. Molecular structure of **A**. The red hashed lines show the hydrogen bonds.

The most characteristic feature of the  $^1\text{H}$  NMR chemical shift of **B** is lower-field shifts of the protons in bay region of 6-oxa-2,8-phenanthroline moiety ( $\delta$  9.17 at 1-position and 7.64 at 10-position). While the  $^{13}\text{C}$  NMR chemical shift of  $sp^3$  carbon was observed at 83.9 ppm, comparable with that of **A**. Figure 3 shows the X-ray crystallographic analysis of **B**. There are three symmetrically independent molecules in the crystal. By the intramolecular cyclization the angle between the two pyridine rings in phenanthroline moiety is decreased (14.4°, 16.3°, and 20.8°). This would cause the

lower-field shift of  $^1\text{H}$  NMR chemical shifts described above. Also by the intramolecular cyclization the absorption at longer wavelength region at 311 nm is observed. The central six-membered ring of pyran take a half chair conformation in which the oxygen atom and the 5-carbon atom are the out of plane of the other four carbon atoms.

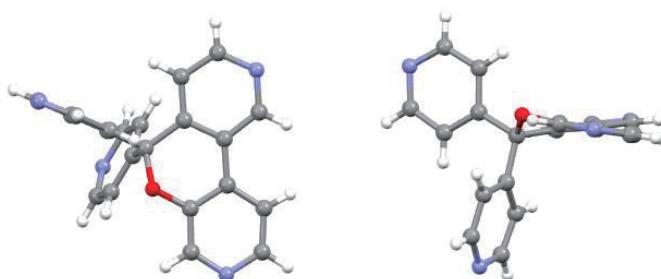


Figure 3. Molecular structure of **B**. Although there are three symmetrically independent molecules, only one of them is represented. Left; top view, right; side view.

The carbonyl group of **C** is characterized by  $^{13}\text{C}$  NMR, IR, and X-ray crystallographic analysis. The  $^{13}\text{C}$  NMR chemical shift of the carbonyl group is observed at 195.0 ppm and the C=O stretching is observed at  $1676\text{ cm}^{-1}$  in IR spectrum. The C=O bond lengths in crystal is  $1.217(2)\text{ \AA}$ . The angle between the two pyridine rings of bipyridyl moiety is  $41.1^\circ$ .

In summary, we have obtained the autoxidation product of **2** and this compound is further converted to 6-oxa-2,8-phenanthroline derivative or diarylketone through the elimination of the aryl group. To the best of our knowledge, the ring system of **B** is unknown. The investigation of other tri-4-pyridylmethane derivative containing the reactivity of tri-4-pyridylmethyl anion is now in progress.

## Reference

- [1] (a) K. Matsumoto, M. Kannami, D. Inokuchi, H. Kurata, T. Kawase, M. Oda, *Org. Lett.*, **2007**, *9*, 2903–2906. (b) K. Matsumoto, D. Inokuchi, Y. Hirao, H. Kurata, T. Kubo, *Cryst. Growth Des.*, **2010**, *10*, 2854–2856.
- [2] D. Inokuchi, K. Matsumoto, K. Kobayashi, K. Onishi, Y. Hirao, H. Kurata, T. Kubo, *Chem. Lett.*, **2015**, *44*, 32–34.
- [3] The spectroscopic data for tri-4-pyridylmethane was reported.<sup>[1a]</sup> Furthermore, we have performed its X-ray crystallographic analysis. Crystal data for tri-4-pyridylmethane:  $\text{C}_{16}\text{H}_{13}\text{N}_3$ ,  $M_r = 247.29$ , monoclinic,  $P2_1/n$  (No. 14),  $a = 9.1869(3)$ ,  $b = 15.6984(4)$ ,  $c = 9.7757(3)\text{ \AA}$ ,  $\beta = 114.2637(17)^\circ$ ,  $V = 1285.31(7)\text{ \AA}^3$ ,  $Z = 4$ ,  $D_{\text{calcd}} = 1.278\text{ g cm}^{-3}$ ,  $T = 83\text{ K}$ , total reflection collected = 22305, unique reflection = 2349 ( $R_{\text{int}} = 0.0551$ ), final  $R$  factor = 0.0432 ( $R_w = 0.1057$  for all data) for 2038 reflections ( $I > 2\sigma(I)$ ), GOF = 1.057. The structure was solved by direct method and refined by full-matrix least squares by using the SHELXL-97 program. The C–H hydrogen atoms were positioned geometrically and allowed to ride on their parent atoms, with C–H =  $0.95\text{ \AA}$  and  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$  for aromatic H atoms. CCDC-2210593 contains the supplementary crystallographic data. These data can be obtained

free of charge from the Cambridge Crystallographic Data Centre at [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

- [4] Spectroscopic data for di-4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)methanol (**A**); mp > 250 °C (dec., methanol–acetonitrile);  $R_f$  value 0.18 (methylene chloride–ethyl acetate–methanol 2:1:0.2 (v/v), on alumina); MS (EI)  $m/z$  (rel intensity) 340 ( $M^+$ , 100), 262 ( $[M^+ - C_5H_4N]^+$ , 59), 185 ( $[M^+ - C_5H_4N - C_5H_4N]^+$ , 46); UV/Vis (in methanol)  $\lambda_{max}$  / nm (log  $\epsilon$ ) 267sh (3.92), 261 (3.98); IR (KBr disk,  $cm^{-1}$ ): 2812 (brs, OH);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  / ppm 8.57 (d,  $J$  = 5.2 Hz, 1H, 3-(4Py)-4Py-6H), 8.54 (dd,  $J$  = 4.4, 2.0 Hz, 4H, 4Py-2,6H), 8.37 (s, 1H, 3-(4Py)-4Py-2H), 8.34 (dd,  $J$  = 4.4, 1.6 Hz, 2H, 3-(4Py)-4Py-2,6H), 7.09 (dd,  $J$  = 4.4, 2.0 Hz, 4H, 4Py-3,5H), 6.83 (d,  $J$  = 5.2 Hz, 1H, 3-(4Py)-4Py-5H), 6.81 (dd,  $J$  = 4.4, 1.6 Hz, 2H, 3-(4Py)-4Py-3,5H), 4.33 (brs, 1H, OH);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  / ppm 152.5, 152.1, 150.2, 149.8, 149.6, 149.2, 146.6, 134.4, 124.6, 123.2, 122.1, 81.0; Anal Calcd for  $C_{21}H_{16}N_4O$ : C; 74.10, H; 4.74, N; 16.46. Found: C; 73.84, H; 4.80, N; 16.27.
- [5] Spectroscopic data for 5,5-di-4-pyridyl-6-oxa-5,6-dihydro-2,8-phenanthroline (**B**); mp 246–247 °C (ethyl acetate);  $R_f$  value 0.55 (methylene chloride–ethyl acetate–methanol 2:1:0.2 (v/v), on alumina); MS (EI)  $m/z$  (rel intensity) 338 ( $M^+$ , 30), 260 ( $[M^+ - C_5H_4N]^+$ , 100); UV/Vis (in methylene chloride)  $\lambda_{max}$  / nm (log  $\epsilon$ ) 311 (3.71), 259 (4.20);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  / ppm 9.17 (s, 1H, Phen-1H), 8.69 (d,  $J$  = 5.2 Hz, 1H, Phen-3H), 8.64 (dd,  $J$  = 4.8, 1.6 Hz, 4H, 4Py-2,6H), 8.50 (s, 1H, Phen-7H), 8.35 (d,  $J$  = 5.2 Hz, 1H, Phen-9H), 7.64 (d,  $J$  = 5.2 Hz, 1H, Phen-10H), 7.12 (dd,  $J$  = 4.8, 1.6 Hz, 4H, 4Py-2,6H), 6.76 (d,  $J$  = 5.2 Hz, 1H, Phen-7H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  / ppm 151.0, 150.3, 148.4, 147.8, 145.4, 144.6, 142.6, 141.2, 126.5, 122.9, 122.8, 121.6, 116.0, 83.9; Anal Calcd for  $C_{21}H_{14}N_4O$ : C; 74.54, H; 4.17, N; 16.56. Found: C; 74.55, H; 4.32, N; 16.71.
- [6] Spectroscopic data for 4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)ketone (**C**); mp 173–174 °C (chloroform–hexane);  $R_f$  value 0.64 (methylene chloride–ethyl acetate–methanol 2:1:0.2 (v/v), on alumina); MS (EI)  $m/z$  (rel intensity) 261 ( $M^+$ , 100), 183 ( $[M^+ - C_5H_4N]^+$ , 97); UV/Vis (in methylene chloride)  $\lambda_{max}$  / nm (log  $\epsilon$ ) 278 (3.79); IR (KBr disk,  $cm^{-1}$ ): 1676 (C=O);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  / ppm 8.88 (d,  $J$  = 4.8 Hz, 1H, 3-(4Py)-4Py-6H), 8.82 (s, 1H, 3-(4Py)-4Py-2H), 8.71 (dd,  $J$  = 4.8, 1.6 Hz, 2H, 4Py-2,6H), 8.55 (dd,  $J$  = 4.8, 1.6 Hz, 2H, 3-(4Py)-4Py-2,6H), 7.44 (d,  $J$  = 4.8 Hz, 1H, 3-(4Py)-4Py-5H), 7.42 (dd,  $J$  = 4.8, 1.6 Hz, 2H, 4Py-3,5H), 7.19 (dd,  $J$  = 4.8, 1.6 Hz, 2H, 3-(4Py)-4Py-3,5H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  / ppm 195.0, 151.0, 150.5, 150.3, 150.2, 144.0, 143.7, 141.4, 132.5, 123.5, 122.0, 121.8; Anal Calcd for  $C_{16}H_{11}N_3O$ : C; 73.55, H; 4.24, N; 16.08. Found: C; 73.47, H; 4.37, N; 15.84.
- [7] Crystal data for di-4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)methanol (**A**):  $C_{21}H_{16}N_4O$ ,  $M_r$  = 340.38, monoclinic,  $P2_1/n$  (No. 14),  $a$  = 8.1649(2),  $b$  = 15.2759(3),  $c$  = 13.6770(3) Å,  $\beta$  = 104.3487(13)°,  $V$  = 1652.67(6) Å<sup>3</sup>,  $Z$  = 4,  $D_{calcd}$  = 1.368 g cm<sup>-3</sup>,  $T$  = 200 K, total reflection collected = 30560, unique reflection = 2975 ( $R_{int}$  = 0.0345), final  $R$  factor = 0.0435 ( $R_w$  = 0.1131 for all data) for 2589 reflections ( $I > 2\sigma(I)$ ), GOF = 1.196. The structure was solved by direct method and refined by full-matrix least squares by using the SHELXL-97 program. The N–H hydrogen atom H1 was located in a difference Fourier map and refined freely. The C–H hydrogen atoms were positioned geometrically and allowed to ride on their parent atoms, with C–H = 0.95 Å and  $U_{iso}(H)$  = 1.2 $U_{eq}(C)$  for aromatic H atoms, with C–H = 0.98 Å and  $U_{iso}(H)$  = 1.5 $U_{eq}(C)$  for methyl H atoms. CCDC-2210594 contains the supplementary crystallographic data.

- [8] Crystal data for 5,5-di-4-pyridyl-6-oxa-5,6-dihydro-2,8-phenanthroline (**B**):  $C_{21}H_{14}N_4O$ ,  $M_r = 338.36$ , monoclinic,  $C2/c$  (No. 15),  $a = 16.7190(3)$ ,  $b = 13.9522(3)$ ,  $c = 42.0082(9)$  Å,  $\beta = 91.797(2)^\circ$ ,  $V = 9794.3(3)$  Å<sup>3</sup>,  $Z = 24$ ,  $D_{\text{calcd}} = 1.377$  g cm<sup>-3</sup>,  $T = 81$  K, total reflection collected = 86581, unique reflection = 8949 ( $R_{\text{int}} = 0.1018$ ), final  $R$  factor = 0.1004 ( $R_w = 0.2315$  for all data) for 7115 reflections ( $I > 2\sigma(I)$ ), GOF = 1.063. The structure was solved by direct method and refined by full-matrix least squares by using the SHELXL-97 program. The C–H hydrogen atoms were positioned geometrically and allowed to ride on their parent atoms, with C–H = 0.95 Å and  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$  for aromatic H atoms. CCDC-2210595 contains the supplementary crystallographic data.
- [9] Crystal data for 4-pyridyl-(3-(4-pyridyl)-pyridin-4-yl)ketone (**C**):  $C_{16}H_{11}N_3O$ ,  $M_r = 261.28$ , monoclinic,  $P2_1/c$  (No. 14),  $a = 5.8015(2)$ ,  $b = 29.1008(10)$ ,  $c = 7.4031(3)$  Å,  $\beta = 98.5352(19)^\circ$ ,  $V = 1236.01(8)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calcd}} = 1.404$  g cm<sup>-3</sup>,  $T = 81$  K, total reflection collected = 21961, unique reflection = 2247 ( $R_{\text{int}} = 0.0585$ ), final  $R$  factor = 0.0462 ( $R_w = 0.1061$  for all data) for 2043 reflections ( $I > 2\sigma(I)$ ), GOF = 1.063. The structure was solved by direct method and refined by full-matrix least squares by using the SHELXL-97 program. The C–H hydrogen atoms were positioned geometrically and allowed to ride on their parent atoms, with C–H = 0.95 Å and  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$  for aromatic H atoms. CCDC-2210596 contains the supplementary crystallographic data.
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