Efficient synthesis of furo[2,3-d]pyrimidin-4(3H)-ones

Yang-Gen Hu, a,b Gui-Hua Li, b and Ming-Wu Ding a, *

a Key Laboratory of Pesticide & Chemical Biology of Ministry of Education, Central China Normal University, Wuhan 430079, China
b Department of Medicinal Chemistry, Yunyang Medical College, Shiyan 442000, China
E-mail: ding5229@yahoo.com.cn

Abstract
The carbodiimides 4, obtained from reactions of iminophosphorane 3 with aromatic isocyanates, reacted with amines or phenols to give 2-substituted furo[2,3-d]pyrimidin-4(3H)-ones 6 in the presence of catalytic amount of sodium alkoxide or solid potassium carbonate in good yields.

Keywords: Furo[2,3-d]pyrimidin-4(3H)-one, iminophosphorane, aza-Wittig reaction, isocyanate

Introduction
The derivatives of fused pyrimidinones are valued not only for their rich and varied chemistry, but also for many important biological properties. Among them, the thienopyrimidinone ring system, because of a formal isoelectronic relationship with purine, is of special biological interest. 1-4 However, there are few reports on furopyrimidinones. 5-10 This is probably due to the instability of the furan ring especially under harsh reaction conditions. Therefore, the development of an efficient method for the preparation of furo[2,3-d]pyrimidinone derivatives under mild conditions is desirable. A key requirement for the facile synthesis of furo[2,3-d]pyrimidinones is the use of an effective electron-withdrawing group in order to protect the electron-rich furans from polymerization reactions. The ester group is a very useful electron-withdrawing protecting group since carboxylic ester furans are relatively easy to prepare and are extremely stable. Such protection allows for further functionalization of the furan ring.

The aza-Wittig reactions of iminophosphoranes have received increased attention in view of their utility in the synthesis of nitrogen heterocyclic compounds under mild conditions. 11-16 Recently we have been interested in the synthesis of quinazolinones, thienopyrimidinones and imidazolinones via aza-Wittig reaction. 17-21 Here we wish to report an efficient approach to the synthesis of furo[2,3-d]pyrimidin-4(3H)-ones under mild conditions.
Results and Discussion

Diethyl 2-amino-5-methylfuran-3,4-dicarboxylate 2 was prepared from reaction of ethyl 2-chloroacetoacetate 1 with ethyl cyanoacetate in the presence of sodium ethoxide in only 58% yield according to literature report\textsuperscript{22}. However, we found that when triethylamine was used as a base in place of sodium ethoxide, compound 2 was obtained in 88% yield. The good yield may be due to the mild conditions as weak base triethylamine was used. Compound 2 was further converted to iminophosphorane 3 via reaction with triphenylphosphine, hexachloroethane and triethylamine in good yield (Scheme 1).

Scheme 1

Iminophosphorane 3 reacted with aromatic isocyanates at 0-5 °C to give carbodiimides 4, which were allowed to react with secondary amines to provide guanidine intermediates 5. In the presence of catalytic amount of sodium ethoxide, the intermediates 5 were converted easily to 2-dialkylamino furo[2,3-d]pyrimidin-4(3H)-ones 6a-h in satisfactory yields at room temperature (Scheme 2). The reaction of carbodiimide 4 with phenols in the presence of a catalytic amount of anhydrous potassium carbonate produces 2-aryloxyfuro[2,3-d]pyrimidin-4(3H)-ones 6i-o in good yields at 50-60°C. No matter whether the substituents on the phenols are electron-withdrawing or electron-releasing groups, the cyclization can be completed smoothly under mild conditions. The results are listed in Table 1.
Table 1. Synthesis of Compounds 6

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<th>Compd</th>
<th>Ar</th>
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<th>Yield (%)^a</th>
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<td>2-naphthaloxy</td>
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^aIsolated yields based on iminophosphorane 3.

The structures of compound 6 were established based on their NMR, MS, IR and elementary analysis. For example the ¹H NMR spectral data of 6a show the signals of -OCH₂ or -NCH₂ at 4.36 or 3.13 ppm as quartets, signals of CH₃ at 2.62, 1.37 or 0.86 ppm as singlet or triplets. The phenyl signals appeared at 7.46-7.28 ppm. In the IR spectrum of compound 6a, the strong stretching vibration peak of two C=O appears at 1707 cm⁻¹. The MS spectrum of 6a shows molecule ion peak (M⁺) at m/z 369 with 100% abundance.

In conclusion, we have developed an efficient synthesis of various substituted furo[2,3-d]pyrimidin-4(3H)-ones in good yield via aza-Wittig reaction of an iminophosphorane. Due to the easily accessible and versatile starting material, this method has the potential in synthesis of many biologically and pharmaceutically active furopyrimidinone derivatives.

Experimental Section

General Procedures. Melting points are uncorrected. MS were measured on a Finnigan Trace MS spectrometer. IR spectra were recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in cm⁻¹. NMR spectra were recorded in CDCl₃ on a Varian Mercury 400 spectrometer and resonances are given in ppm (δ) relative to TMS. Elementary analyses were taken on a Vario EL III elementary analysis instrument.
Preparation of diethyl 2-amino-5-methylfuran-3,4-dicarboxylate (2). To a mixture of ethyl cyanooacetate (3.39 g, 30 mmol) and NEt3 (8 mL, 56 mmol) in EtOH (15 mL) was added dropwise ethyl 2-chloroacetoacetate 1 (4.93 g, 30 mmol) at room temperature. After stirring for 1 h, the solvent was removed under reduced pressure and the residue was recrystallized from EtOH/H2O (1:1) to give diethyl 2-amino-5-methylfuran-3,4-dicarboxylate 2. White solid (6.34 g, yield 88%), m.p. 85-86 °C, lit.22 m.p. 81.5-82.5 °C.

Preparation of N-(3,4-diethoxycarbonyl-5-methylfuran-2-yl)iminotriphenylphosphorane (3). To a mixture of diethyl 2-amino-5-methylfuran-3,4-dicarboxylate 2 (2.41 g, 10 mmol), PPh3 (3.93 g, 15 mmol) and C2Cl6 (3.56 g, 15 mmol) in dry CH3CN (30 mL), was added dropwise NEt3 (4.2 mL, 30 mmol) at room temperature. After stirred for 1-2 h, the solvent was removed under reduced pressure and the residue was recrystallized from EtOH to give iminophosphorane 3 as white solid (4.06 g, yield 81%), m.p. 169-170 °C. 1H NMR (CDCl3, 400 MHz): δ 7.82-7.45 (m, 15H, Ar-H), 4.28-4.20 (m, 4H, 2OCH2), 2.62 (s, 3H, CH3), 1.28 (t, J = 7.2 Hz, 6H, 2CH3).

IR (KBr): 1727 (C=O), 1681, 1562, 1109 cm−1. MS m/z (%): 501 (100, M +), 456 (66), 260 (98), 182 (98), 107 (92), 77 (69). Anal. Calcd for C29H28NO5P (501.5): C, 69.45; H, 5.63; N, 2.79. Found: C, 69.22, H, 5.73; N, 2.95.

General preparation of 2-dialkylaminofuro[2,3-d]pyrimidines 6a-6h
To a solution of iminophosphorane 3 (1.0 g, 2 mmol) in dry methylene chloride (15 mL) was added aromatic isocyanate (2 mmol) under nitrogen at room temperature. After the reaction mixture was stood for 8-12 hours at 0-5 °C, the solvent was removed off under reduced pressure and ether/petroleum ether (1:2, 20 mL) was added to precipitate triphenylphosphine oxide. After filtration the solvent was removed to give carbodiimide 4, which was used directly without further purification. To the solution of 4 prepared above in methylene chloride (15 ml) was added dialkylamine (2 mmol). After the reaction mixture was allowed to stand for 0.5-6 h, the solution was condensed and anhyd. EtOH (8 mL) with EtONa (0.3 mmol, 10% equiv) in EtOH was added. The mixture was stirred for 4-6 h at r. t. The solution was condensed and the residue was recrystallized from EtOH to give 6a-6h.

2-(Diethylamino)-5-ethoxycarbonyl-6-methyl-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6a). White crystals (yield 0.63 g, 85%), m.p. 160-161 °C. IR (KBr): 1707 (C=O), 1589, 1538, 1233 cm−1. 1H NMR (400 MHz, CDCl3): δ 7.46-7.28 (m, 5H, Ar-H), 4.36 (q, J = 7.2 Hz, 2H, OCH2), 3.13 (q, J = 7.2 Hz, 4H, 2×NCH2), 2.62 (s, 3H, CH3), 1.37 (t, J = 7.2 Hz, 3H, CH3), 0.86 (t, J = 7.2 Hz, 6H, 2×CH3). MS (m/z, %): 369 (M+, 100), 323 (27), 295 (26), 175 (72), 118 (47), 105 (56). Anal. Calcd for C20H23N3O4 (369.4): C, 65.03; H, 6.28; N, 11.37. Found: C, 65.20, H, 6.53; N, 11.34.

5-Ethoxycarbonyl-6-methyl-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6b). White crystals (yield 0.67 g, 88%), m.p. 153-155 °C. IR (KBr): 1705 (C=O), 1534, 1250 cm−1. 1H NMR (400 MHz, CDCl3): δ 7.47-7.31 (m, 5H, Ar-H), 4.36 (q, J = 7.2 Hz, 2H, OCH2), 3.12 (q, J = 5.2 Hz, 4H, 2×NCH2), 2.62 (s, 3H, CH3), 1.37 (t, J = 7.2 Hz, 3H, CH3), 1.34-
5-Ethoxycarbonyl-6-methyl-2-(morpholin-4-yl)-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6c). White crystals (yield 0.66 g, 86%), m.p. 174-175 °C. IR (KBr): 1714 (C=O), 1589, 1541, 1114 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.51-7.27 (m, 5H, Ar-H), 4.38 (q, J = 7.2 Hz, 2H, OCH₂), 3.14 (t, J = 7.2 Hz, 6H, 3×CH₂). MS (m/z, %): 381 (M⁺, 100), 335 (36), 307 (27), 187 (52), 159 (11). Anal. Calcd for C₂₁H₂₃N₃O₄ (381.4): C, 66.13; H, 6.08; N, 11.02. Found: C, 66.17, H, 6.23; N, 10.74.

5-Ethoxycarbonyl-6-methyl-3-(3-methylphenyl)-2-(piperidin-1-yl)furo[2,3-d]pyrimidin-4(3H)-one (6d). White crystals (yield 0.71 g, 90%), m.p. 158-159 °C. IR (KBr): 1705 (C=O), 1591, 1534, 1372, 1099 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.36-7.10 (m, 4H, Ar-H), 4.38 (q, J = 7.2 Hz, 2H, OCH₂), 3.13 (t, J = 4.8 Hz, 4H, 2×NCH₂), 2.64 (s, 3H, CH₃), 1.46-1.22 (m, 6H, 3×CH₂), 1.38 (t, J = 7.2 Hz, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 13.6, 14.3, 21.2, 23.9, 24.8, 49.8, 60.7, 98.1, 111.0, 125.8, 128.6, 128.7, 129.4, 137.8, 138.6, 155.9, 157.4, 158.2, 163.1, 163.7. MS (m/z, %): 395 (M⁺, 48), 350 (11), 320 (15), 201 (100), 174 (51), 145 (34), 91 (68). Anal. Calcd for C₂₂H₂₅N₃O₄ (395.5): C, 66.82; H, 6.37; N, 10.63. Found: C, 66.85, H, 6.40; N, 10.50.

5-Ethoxycarbonyl-6-methyl-3-(4-chlorophenyl)-2-(diethylamino)-furo[2,3-d]pyrimidin-4(3H)-one (6e). White crystals (yield 0.66 g, 82%), m.p. 170-172 °C. IR (KBr): 1712 (C=O), 1589, 1532, 1114 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.46-7.23 (m, 4H, Ar-H), 4.38 (q, J = 7.2 Hz, 2H, OCH₂), 3.13 (q, J = 7.2 Hz, 4H, 2×NCH₂), 2.62 (s, 3H, CH₃), 1.38 (t, J = 7.2 Hz, 3H, CH₃), 0.90 (t, J = 7.2 Hz, 6H, 2×CH₃). MS (m/z, %): 403 (M⁺, 42), 357 (20), 329 (17), 209 (100), 179 (32), 153 (25), 138 (44), 111 (32). Anal. Calcd for C₂₀H₂₂ClN₃O₄ (403.9): C, 59.48; H, 5.49; N, 10.40. Found: C, 59.54, H, 5.73; N, 10.24.

3-(4-Chlorophenyl)-5-ethoxycarbonyl-6-methyl-2-(morpholin-4-yl)furo[2,3-d]pyrimidin-4(3H)-one (6f). White crystals (yield 0.73 g, 87%), m.p. 158-160 °C. IR (KBr): 1705 (C=O), 1689, 1538, 1245 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.48-7.27 (m, 4H, Ar-H), 4.38 (q, J = 7.2 Hz, 2H, OCH₂), 3.50 (t, J = 4.8 Hz, 4H, 2×OCH₂), 3.15 (t, J = 4.8 Hz, 6H, 2×CH₂), 2.64 (s, 3H, CH₃), 1.38 (t, J = 7.2 Hz, 3H, CH₃). MS (m/z, %): 417 (M⁺, 100), 371 (58), 343 (41), 297 (32), 223 (63), 179 (15), 167 (10). Anal. Calcd for C₂₀H₂₀ClN₃O₅ (417.8): C, 57.49; H, 4.82; N, 10.06. Found: C, 57.64, H, 4.63; N, 10.11.

2-(Diethylamino)-5-ethoxycarbonyl-3-(4-fluorophenyl)-6-methylfuro[2,3-d]pyrimidin-4(3H)-one (6g). White crystals (yield 0.66 g, 85%), m.p. 131-132 °C. IR (KBr): 1704 (C=O), 1689, 1545, 1233 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.29-7.14 (m, 4H, Ar-H), 4.38 (q, J = 7.2 Hz, 2H, OCH₂), 3.90 (t, J = 7.2 Hz, 6H, 2×CH₂), 2.63 (s, 3H, CH₃), 1.38 (t, J = 7.2 Hz, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 12.4, 13.7, 14.3, 45.2, 60.8, 110.9, 115.9, 116.2, 130.7, 130.8, 133.9, 156.1, 157.0, 158.4, 163.1, 163.9. MS (m/z, %): 387 (M⁺, 62), 341 (21), 313 (19), 287 (16), 193 (100), 168 (68), 137 (76), 123 (75). Anal. Calcd for C₂₀H₂₂FN₃O₄ (387.4): C, 62.01; H, 5.72; N, 10.85. Found: C, 62.25, H, 5.66; N, 10.82.
5-Ethoxycarbonyl-3-(4-fluorophenyl)-6-methyl-2-(morpholin-4-yl)furo[2,3-d]pyrimidin-4(3H)-one (6h). White crystals (yield 0.67 g, 85%), m.p. 169-170 °C. IR (KBr): 1714 (C=O), 1580, 1541, 1216 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.34-7.16 (m, 4H, Ar-H), 4.38 (q, \(J = 7.2\) Hz, 2H, OCH\(_2\)), 3.48 (t, \(J = 4.8\) Hz, 4H, 2×OCH\(_2\)), 3.14 (t, \(J = 4.8\) Hz, 4H, 2×NCH\(_2\)), 2.63 (s, 3H, CH\(_3\)), 1.38 (t, \(J = 7.2\) Hz, 3H, CH\(_3\)). MS (m/z, %): 401 (M\(^+\), 96), 355 (69), 327 (64), 207 (100), 163 (74), 134 (40), 122 (33). Anal. Calcd for C\(_{20}\)H\(_{20}\)FN\(_3\)O\(_5\) (401.4): C, 59.85; H, 5.02; N, 10.47. Found: C, 59.68, H, 5.26; N, 10.33.

General Preparation of 2-aryloxy furo[2,3-d]pyrimidines 6i-6o

To the solution of carbodiimide 4 (ca. 3 mmol) prepared above in CH\(_3\)CN (15 mL) was added K\(_2\)CO\(_3\) (0.03 g, 0.2 mmol) and ArOH (3 mmol) in anhydrous CH\(_3\)CN (10 mL). The mixture was stirred for 6-8 h at 50-60 °C. The solution was concentrated under reduced pressure and the residual was recrystallized from ethanol/dichloromethane (1:2, v/v) to give 6i-6o.

5-Ethoxycarbonyl-2-(4-methoxyphenoxy)-6-methyl-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6i). White crystals (yield 0.75 g, 89%), m.p. 159-161 °C. IR (KBr): 1732 (C=O), 1687, 1554, 1200 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.53-6.86 (m, 9H, Ar-H), 4.33 (q, \(J = 7.2\) Hz, 2H, OCH\(_2\)), 3.78 (s, 3H, OCH\(_3\)), 2.59 (s, 3H, CH\(_3\)), 1.34 (t, \(J = 7.2\) Hz, 3H, CH\(_3\)). MS (m/z, %): 420 (M\(^+\), 100), 374 (28), 297 (91), 268 (58), 155 (21), 145 (41). Anal. Calcd for C\(_{23}\)H\(_{20}\)N\(_2\)O\(_6\) (420.4): C, 65.71; H, 4.79; N, 6.66. Found: C, 65.85, H, 4.83; N, 6.38.

5-Ethoxycarbonyl-6-methyl-2-(3-methylphenoxy)-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6j). White crystals (yield 0.70 g, 87%), m.p. 181-183 °C. IR (KBr): 1732 (C=O), 1688, 1554, 1205 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.54-6.96 (m, 9H, Ar-H), 4.37 (q, \(J = 7.2\) Hz, 2H, OCH\(_2\)), 2.60 (s, 3H, CH\(_3\)), 2.34 (s, 3H, CH\(_3\)), 1.38 (t, \(J = 7.2\) Hz, 3H, CH\(_3\)). MS (m/z, %): 404 (M\(^+\), 96), 358 (80), 297 (100), 268 (58), 198 (33), 145 (76). Anal. Calcd for C\(_{23}\)H\(_{20}\)N\(_2\)O\(_5\) (404.4): C, 68.31; H, 4.98; N, 6.93. Found: C, 68.27, H, 5.12; N, 6.68.

5-Ethoxycarbonyl-6-methyl-2-(2-methylphenoxy)-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6k). White crystals (yield 0.70 g, 87%), m.p. 196-198 °C. IR (KBr): 1732 (C=O), 1689, 1554, 1205 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.57-7.05 (m, 9H, Ar-H), 4.39 (q, \(J = 7.2\) Hz, 2H, OCH\(_2\)), 2.60 (s, 3H, CH\(_3\)), 2.10 (s, 3H, CH\(_3\)), 1.38 (t, \(J = 7.2\) Hz, 3H, CH\(_3\)). MS (m/z, %): 404 (M\(^+\), 23), 358 (19), 297 (100), 269 (91), 198 (33), 145 (83). Anal. Calcd for C\(_{23}\)H\(_{20}\)N\(_2\)O\(_5\) (404.4): C, 68.31; H, 4.98; N, 6.93. Found: C, 68.27, H, 5.12; N, 6.68.

5-Ethoxycarbonyl-6-methyl-2-(3-nitrophenoxy)-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6l). White crystals (yield 0.75 g, 86%), m.p. 204-206 °C. IR (KBr): 1734 (C=O), 1695 (C=O), 1554, 1238 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.16-7.36 (m, 9H, Ar-H), 4.39 (q, \(J = 7.2\) Hz, 2H, OCH\(_2\)), 2.63 (s, 3H, CH\(_3\)), 1.38 (t, \(J = 7.2\) Hz, 3H, CH\(_3\)). MS (m/z, %): 435 (M\(^+\), 17), 389 (30), 297 (58), 269 (100), 241 (83), 198 (22), 145 (76), 118 (34). Anal. Calcd for C\(_{22}\)H\(_{17}\)N\(_3\)O\(_7\) (435.4): C, 60.69; H, 3.94; N, 9.65. Found: C, 60.41, H, 3.79; N, 9.78.

2-(2,4-Dichlorophenoxy)-5-ethoxycarbonyl-6-methyl-3-phenylfuro[2,3-d]pyrimidin-4(3H)-one (6m). White crystals (yield 0.77 g, 84%), m.p. 161-162 °C. IR (KBr): 1727 (C=O), 1699 (C=O), 1555, 1295 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.57-7.12 (m, 8H, Ar-H), 4.38 (q, \(J = 7.2\) Hz, 2H, OCH\(_2\)), 3.78 (s, 3H, OCH\(_3\)), 2.63 (s, 3H, CH\(_3\)), 1.38 (t, \(J = 7.2\) Hz, 3H, CH\(_3\)). MS (m/z, %): 449 (M\(^+\), 17), 389 (30), 297 (58), 269 (100), 241 (83), 198 (22), 145 (76), 118 (34). Anal. Calcd for C\(_{22}\)H\(_{17}\)N\(_3\)O\(_7\) (449.4): C, 60.69; H, 3.94; N, 9.65. Found: C, 60.41, H, 3.79; N, 9.78.
7.2 Hz, 2H, OCH_2), 2.64 (s, 3H, CH_3), 1.38 (t, J = 7.2 Hz, 3H, CH_3). \^13C NMR (100 MHz, CDCl_3): δ 13.6, 14.3, 60.9, 100.6, 111.1, 124.5, 127.6, 128.2, 129.3, 129.5, 130.3, 132.6, 134.4, 145.9, 154.1, 156.7, 157.5, 162.1, 162.7. MS (m/z, %): 458 (M^+, 44), 414 (37), 297 (100), 269 (73), 194 (25), 145 (68), 118 (24). Anal. Calcd for C_{22}H_{16}Cl_2N_2O_5 (459.3): C, 57.53; H, 3.51; N, 6.10. Found: C, 57.47, H, 3.48; N, 6.32.

5-Ethoxycarbonyl-6-methyl-3-(3-methylphenyl)-2-(3-nitrophenoxy)furo[2,3-d]pyrimidin-4(3H)-one (6n). White crystals (yield 0.78 g, 87%), m.p. 201-202 °C. IR (KBr): 1732 (C=O), 1700, 1552, 1296 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl_3): δ 8.16-7.16 (m, 8H, Ar-H), 4.33 (q, J = 7.2 Hz, 2H, CH_2), 2.62 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 1.35 (t, J = 7.2 Hz, 3H, CH_3). \(^13C NMR (100 MHz, CDCl_3): δ 13.6, 14.2, 21.3, 60.9, 100.7, 111.1, 117.4, 121.4, 124.9, 128.0, 128.5, 129.4, 130.2, 130.3, 134.2, 139.7, 148.7, 151.3, 154.4, 156.7, 157.6, 161.8, 162.6. MS (m/z, %): 449 (M^+, 15), 403 (28), 311 (17), 283 (19), 159 (27), 133 (45), 91 (100). Anal. Calcd for C_{23}H_{19}N_3O_7 (449.4): C, 61.47; H, 4.26; N, 9.35. Found: C, 61.65, H, 4.33; N, 9.25.

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References