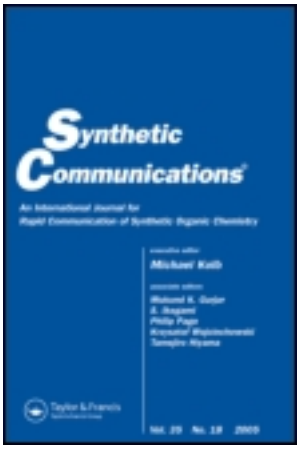

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Reaction of 3-Arylmethylidene-3H-furan-2-ones with 3-Amino-1,2,4-triazole as a Convenient Technique to Synthesize Condensed Diazepinones

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REACTION OF 3-ARYLMETHYLIDENE-3H-FURAN-2-ONES WITH 3-AMINO-1,2,4-TRIAZOLE AS A CONVENIENT TECHNIQUE TO SYNTHESIZE CONDENSED DIAZEPINONES

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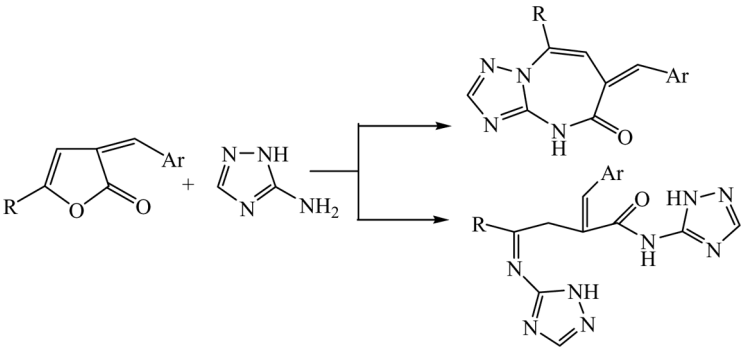
GRAPHICAL ABSTRACT



Abstract *The interaction of the arylmethylidene derivatives of 3H-furan-2-ones with 3-amino-1,2,4-triazole was studied. The structure of the final products depends on reaction conditions and reagent ratio.*

Keywords 3-Amino-1,2,4-triazole; diazepin-5-one; 3H-furan-2-ones

INTRODUCTION

The arylmethylidene derivatives of 3H-furan-2-ones are interesting mainly as intermediate compounds combining the properties of internal esters and α,β-unsaturated carbonylic compounds. They are capable of reacting with substances having mobile hydrogen atoms.

The structure of the compounds determines the possibility of their interaction with various binucleophilic reagents, which can proceed with opening of the lactonic

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cycle, formation of amides and hydrazides of substituted 4-oxoalkane acids, their cyclic amides, and other recyclization products.

Michael's condensation,[1] and interactions with electrophilic[2] and nucleophilic reagents[3] were studied in the 3-arylmethylene-3H-furan-2-on series earlier.

The compounds, which incorporate a triazole ring, have a wide range of practical applications.[4] Introduction of this fragment into the structure of synthesized compounds considerably expands the application areas of the compounds for the first time.

RESULTS AND DISCUSSION

The interaction of furanones with triazole was carried out at an equimolar reagent ratio, while boiling in a solution of ethanol. Aminotriazole was introduced into the reaction gradually.

The ratio of interaction reagents, by the use of the equimolar ratio of reagents, led to the formation of structures, which, according to elementary analysis, infrared (IR), and NMR spectroscopy, were identified as triazolodiazepinones **2a–e**.

The absorption band of a multiple C=C bond conjugated with a carbonylic group within 1630–1590 cm^{-1}, the absorption band of a C=C bond within 1668–1660 cm^{-1}, the absorption band of a C=O bond within 1680–1670 cm^{-1}, valent oscillation of the NH group located within 3100–3080 cm^{-1}, and oscillations of an aromatic ring noted within 1525–1485 cm^{-1} are observed in the IR spectra of compounds **2a–e**.

The ^{1}H NMR spectra of compounds **2a–e** contain a set of signals to completely confirm the hypothesized structure; namely, the singlet of a proton at C_6 of the diazepinone ring is located within 6.74–6.86 ppm, the singlet of a proton of a exocyclic sp^2-hybridized carbon atom is noted within 7.31–7.54 ppm, the proton of the NH group is observed within 8.46–8.86 ppm, and the protons of aromatic rings lay within 6.92–8.24 ppm.

Additional evidence of the structure has been made on the basis of the ^{13}C NMR spectra. In the spectra of compounds **2a–e** noted are the signal of the carbon atom of a carbonylic group within 168.4–169.4 ppm, the signal of a sp^2-hybridized carbon atom of a diazepinone ring within 99.1–99.8 ppm, and the signal of a sp^2-hybridized carbon atom of the triazole ring within 159.1–161.6 ppm. The carbon atoms of the aromatic fragments are shown by a series of signals within 105.7–149.7 ppm.

Probably at the first stage, the most basic center of aminotriazole is attacked by the carbon atom of the carbonylic group, which results in opening of the lactone ring. Stabilization of the intermediate formed is possible by several directions, including by attacking the unshared electronic pair of the nitrogen atom by the carbon atom of the carbonylic group with subsequent heterocyclization, which led to formation of diazepinone structures **2a–e**. Other possible ways of heterocyclization [(attacking the amide nitrogen atom by the carbonylic group to form substituted pyrrol-2-ones (structure **A**) and attacking the nitrogen atom of the triazole ring by the multiple C=C bond to form structure **B**)] are not realized.

We did not exclude initial addition of the triazol ring by the multiple C=C bond and subsequent heterocyclization resulting in formation of structure **C**; however, this direction of the reaction is not realized as well.

Furanones were introduced into the reaction with excessive triazole. The interaction was carried out at room temperature by mixing the components in an alcohol solution for 1 h.

As a result, the products obtained were characterized according to IR and ^{1}H NMR spectroscopy as butanamide **3a, f–i**.

In the IR spectra of compounds **3a, f–i,** the absorption bands within 3418–3318 cm^{-1} characteristic of NH group oscillations, 3229–3226 cm^{-1} of imino group oscillations, 1655–1643 cm^{-1} of C=O group oscillations ("amide I"), and 1564–1539 cm^{-1} ("amide II") are noted.

The ^{1}H NMR spectra of compounds **3a, f–i** contain the singlet of the protons of the methylene link located within 1.98–2.13 ppm, the singlet of the NH group of the amide fragment noted within 8.53–8.97 ppm, two singlets of the NH groups of the triazole rings within 7.85–8.31 ppm, the singlet of the arylmethylene fragment located within 6.75–6.93 ppm, and a series of signals of aromatic protons within 6.92–7.54 ppm.

The ^{13}C NMR spectra contain a signal of the sp^3-hybridized carbon atom of the CH_2 group within 19.8–25.7 ppm, the sp^2-hybridized carbon atom of the imino group located within 167.1–168.4 ppm, an sp^2-hybridized amide carbon atom noted within 168.5–170.1 ppm, the signal of sp^2-hybridized carbon atoms of triazole rings within 159.3–163.5 ppm, and a series of signals of sp^2-hybridized carbon atoms of aromatic rings within 99.8–155.3 ppm.

Probably, opening of the lactone ring and addition of a second triazole molecule by the free keto group proceed simultaneously and led to formation of compounds **3a, f–i**.

The reaction stops at the stage of formation of compounds **3a, f–i,** Owing to the low reactivity of the functional groups and steric hindrances, none of the possible cyclization directions is realized.

Thus, the interaction of furanones with triazole was studied. The structure of the products depends on reaction conditions and reagent ratio.

EXPERIMENTAL

IR spectra were registered on a Specord (Germany) device, the spectral range being 400–4000 cm^{-1} (in a KBr tablet). ^{1}H NMR spectra were recorded on a Varian 400 spectrometer (400 MHz) in $CDCl_3$, with tetramethylsilane (TMS) as the internal standard. ^{13}C NMR spectra were recorded on a Varian 400 spectrometer (100 MHz) in $CDCl_3$, with TMS as the internal standard.

5-Aryl-3-arylmethylidene-3H-furan-2-ones were obtained according to the known technique.[5]

Synthesis of 6-Arylmethylene-8-R-4*H*-[1,2,4]triazolo-[1,5-*a*][1,3]diazepin-5(6*H*)-one (2)

5-Aryl-3-arylmethylidene-3H-furan-2-one (0.01 mol) in ethanol (15 mL) is placed into a 50-mL flat-bottomed flask supplied with a dropping funnel. The reaction mixture is mixed and heated at direct introduction (through the dropping funnel) of an ethenol solution of 3-amino-1,2,4-triazol. The reaction is stopped when 5-aryl-3-arylmethylene-3H-furan-2-one stain on thin-layer chromatography (TLC)

vanishes. The excessive solvent is evaporated. The crystals obtained are recrystallized from isopropyl alcohol.

6-[(3,4-Dimethoxyphenyl)methylidene]-8-(4-methylphenyl)-4*H*-[1,2,4]triazolo[1,5-*a*][1,3]diazepin-5(6*H*)-one (2a)

Yield: 83%, mp 158–160 °C. Anal. calcd. for $C_{22}H_{20}N_4O_3$: C, 68.03; H, 5.19; N, 14.42. Found: C, 67.81; H, 5.59; N, 14.35. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 3.86 (s, 6H), 6.74 (s, 1H), 6.95–7.26 (m, 7H), 7.31 (s, 1H), 8.64 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$,): δ 26.0, 56.3, 56.4, 99.3, 105.7, 108.7, 114.9, 121.3, 121.4, 125.8, 125.9, 129.1, 131.5, 133.9, 134.8, 136.4, 148.6, 149.7, 161.6, 169.4.

6-(4-Methylphenyl)-8-[(2-nitrophenyl)methylidene]-4*H*-[1,2,4]triazolo[1,5-*a*][1,3]diazepin-5(6*H*)-one (2b)

Yield: 76%, mp 143–145 °C. Anal. calcd. for $C_{20}H_{15}N_5O_3$: C, 64.34; H, 4.05; N, 18.76. Found: C, 64.12; H, 4.44; N, 18.69. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 3H), 6.86 (s, 1H), 7.26–8.24 (m, 8H), 7.36 (s, 1H), 8.46 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 99.8, 120.3, 121.8, 122.5, 123.7, 126.9, 127.2, 128.4, 129.1, 129.5, 131.7, 132.7, 138.4, 140.7, 148.7, 159.1, 168.8.

6-[(4-Hydroxy-3-methoxyphenyl)methylidene]-8-(4-methylphenyl)-4*H*-[1,2,4]triazolo[1,5-*a*][1,3]diazepin-5(6*H*)-one (2c)

Yield: 86%, mp 149–151 °C. Anal. calcd. for $C_{21}H_{18}N_4O_3$: C, 67.37; H, 4.85; N, 14.96. Found: C, 67.51; H, 4.59; N, 14.75. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 3.89 (s, 3H), 5.12 (s, 1H), 6.83 (s, 1H), 6.96–7.34 (m, 8H), 7.40 (s, 1H), 8.54 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.0, 58.6, 99.1, 109.4, 115.5, 123.7, 125.8, 127.9, 129.3, 130.3, 132.6, 133.7, 135.7, 136,8, 138.9, 143.8, 148.7, 159.3, 168.4.

6-[(2-Nitrophenyl)methylidene]-8-phenyl-4*H*-[1,2,4]triazolo-[1,5-*a*][1,3]diazepin-5(6*H*)-one (2d)

Yield: 84%, mp 143–145 °C. Anal. calcd. for $C_{19}H_{13}N_5O_3$: C, 63.51; H, 3.65; N, 19.49. Found: C, 63.35; H, 3.43; N, 19.85. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.78 (s, 1H), 6.92–7.24 (m, 9H), 7.52 (s, 1H), 8.68 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 99.5, 108.6, 113.7, 113.8, 127.5, 127.6, 128.1, 128.9, 129.9, 131.6, 133.7, 134.8, 136.2, 138,9, 142.4, 145.8, 149.7, 160.7, 168.9.

6-[(2-Chlorophenyl)methylidene]-8-phenyl-4*H*-[1,2,4]triazolo-[1,5-*a*][1,3]diazepin-5(6*H*)-one (2e)

Yield: 86%, mp 145–147 °C. Anal. calcd. for $C_{19}H_{13}ClN_4O$: C, 65.43; H, 3.76; N, 16.06. Found: C, 65.74; H, 3.65; N, 15.95. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.75 (s, 1H), 7.03–7.25 (m, 9H), 7.54 (s, 1H), 8.86 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 99.7, 107.5, 116.6, 116.7, 126.3, 126.4, 126.8, 127.6, 128.9, 131.5, 132.0, 134.4, 136.4, 136.9, 140.5, 142.3, 147.3, 161.5, 168.5.

Synthesis of 2-Arylmethylene-*N*-1*H*-1,2,4-triazol-5-yl-4-R-4-(1*H*-1,2,4-triazol-5-ylimino)butanamide (3)

5-Aryl-3-arylmethylidene-3H-furan-2-one (0.01 mol) and 3-amino-1,2,4-triazole (0.02 mol) are placed into a 50-mL flat-bottomed flask. The reaction mixture is mixed in 15 mL of ethanol at room temperature for 2 h. The precipitated crystals are filtered and recrystallized from ethanol.

2-[(3,4-Dimethoxyphenyl)methylidene]-*N*-1*H*-1,2,4-triazol-5-yl-4-(4-methylphenyl)-4-(1*H*-1,2,4-triazol-5-ylimino)butanamide (3a)

Yield: 89%, mp 138–140 °C. Anal. calcd. for $C_{24}H_{24}N_8O_3$: C, 61.01; H, 5.12; N, 23.72. Found: C, 61.24; H, 4.89; N, 24.0 5. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02 (s, 2H), 2.35 (s, 3H), 3.76 (s, 6H), 6.83 (s, 1H), 6.92–7.54 (m, 9H), 8.17 (s, 1H), 8.30 (s, 1H), 8.31 (s, 1H), 8.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 24.3, 50.4, 50.5, 105.8, 106.1, 115.8, 118.5, 119.5, 120.9, 122.4, 123.8, 128.5, 132.1, 135.6, 138.1, 146.0, 146.8, 155.3, 159.3, 167.1, 168.5.

2-[(2-Nitrophenyl)methylidene]-*N*-1*H*-1,2,4-triazol-5-yl-4-[(4-methoxyphenyl)-4-(1*H*-1,2,4-triazol-5-ylimino)butanamide (3f)

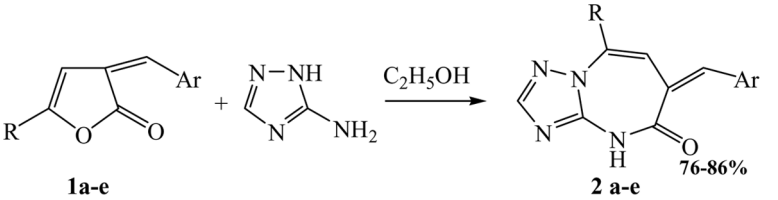
Yield: 93%, mp 178–180 °C. Anal. calcd. for $C_{22}H_{19}N_9O_4$: C, 55.81; H, 4.05; N, 26.63. Found: C, 56.12; H, 4.50; N, 26.15. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.98 (s, 2H), 3.82 (s, 3H), 6.93 (s, 1H), 7.02–7.34 (m, 10H), 7.62 (s, 1H), 7.85 (s, 1H), 7.86 (s, 1H), 8.53 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.3, 53.4, 102.3, 104.5, 105.6, 114.1, 115.3, 117.5, 122.1, 125.3, 127.5, 131.2, 134.5, 138.5, 144.9, 145.3, 153.5, 162.3, 168.4, 170.1.

2-[(3,4-Dimethoxyphenyl)methylidene]-*N*-1*H*-1,2,4-triazol-5-yl-4-phenyl-4-(1*H*-1,2,4-triazol-5-ylimino)butanamide (3g)

Yield: 79%, mp 152–154 °C. Anal. calcd. for $C_{23}H_{22}N_8O_3$: C, 60.25; H, 4.84; N, 24.44. Found: C, 60.49; H, 4.56; N, 24.65. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 2H), 3.76 (s, 6H), 6.86 (s, 1H), 6.97–7.50 (m, 10H), 8.06 (s, 1H), 8.23 (s, 1H), 8.24 (s, 1H), 8.95 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 55.1, 55.2, 99.8, 101.3, 101.4, 105.3, 110.7, 110.8, 113.9, 116.8, 120.9, 122.3, 125.7, 128.3, 132.2, 135.5, 142.9, 143.7, 153.7, 163.5, 167.3, 169.9.

2-[(2-Nitrophenyl)methylidene]-*N*-1*H*-1,2,4-triazol-5-yl-4-phenyl-4-(1*H*-1,2,4-triazol-5-ylimino)butanamide (3h)

Yield: 91%, mp 164–166 °C. Anal. calcd. for $C_{21}H_{17}N_9O_3$: C, 56.88; H, 3.86; N, 28.43. Found: C, 56.44; H, 3.25; N, 28.57. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.05 (s, 2H), 6.75 (s, 1H), 6.98–7.48 (m, 11H), 8.13 (s, 1H), 8.15 (s, 1H), 8.28 (s, 1H), 8.90 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$,): δ 25.7, 102.7, 102.8, 104.6, 105.7, 107.3, 111.7, 112.6, 115.3, 118.4, 126.9, 130.5, 131.4, 138.6, 140.5, 143.8, 147.5, 156.3, 160.5, 167.4, 168.6.

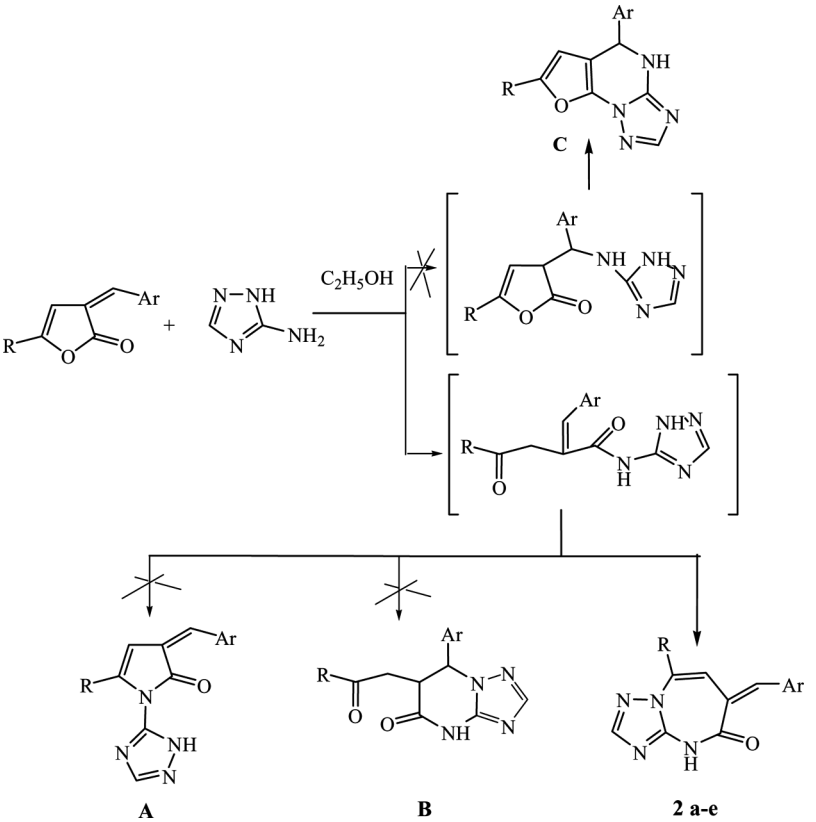


1a-e 2 a-e

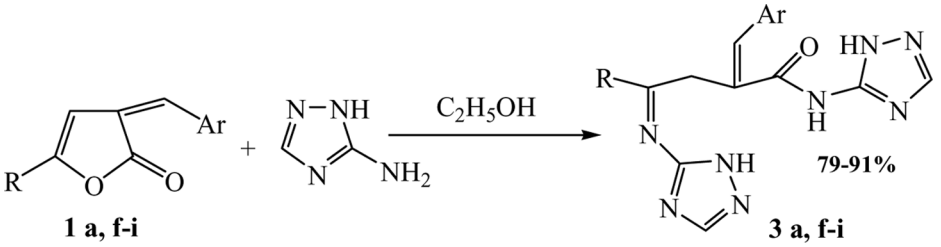
Scheme 1. (a) $R = C_6H_4\text{-}CH_3\text{-}4$, $Ar = C_6H_3\text{-}OCH_3\text{-}3,4$; **(b)** $R = C_6H_4\text{-}CH_3\text{-}4$, $Ar = C_6H_4\text{-}NO_2\text{-}2$; **(c)** $R = C_6H_4\text{-}CH_3\text{-}4$, $Ar = C_6H_3\text{-}OH,OCH_3\text{-}3,4$; **(d)** $R = C_6H_5$, $Ar = C_6H\text{-}NO_2\text{-}2$; **(i)** $R = C_6H_5$, $Ar = C_6H_4\text{-}Cl\text{-}2$.

2-[(2-Chlorophenyl)methylidene]-*N*-1*H*-1,2,4-triazol-5-yl-4-phenyl-4-(1*H*-1,2,4-triazol-5-ylimino)butanamide (3i)

Yield: 87%, mp 169–171 °C. Anal. calcd. for $C_{21}H_{17}ClN_8O_3$: C, 58.27; H, 3.96; N, 25.89. Found: C, 58.38; H, 3.54; N, 25.62. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 2H), 6.82 (s, 1H), 6.94–7.53 (m, 11H), 8.24 (s, 1H), 8.25 (s, 1H), 8.31 (s, 1H), 8.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$,): δ 23.6, 100.3, 102.6, 104.8, 104.9, 106.5, 108.5,



Scheme 2. The possible directions of the heterocyclization.



Scheme 3. (a) $R = C_6H_4$-CH_3-4, $Ar = C_6H_3$-OCH_3-3,4; **(f)** $R = C_6H_4$-OCH_3-4, $Ar = C_6H_4$-NO_2-2; **(g)** $R = C_6H_5$, $Ar = C_6H_3$-OCH_3-3,4; **(h)** $R = C_6H_5$, $Ar = C_6H_4$-NO_2-2; **(i)** $R = C_6H_5$, $Ar = C_6H_4$-Cl-2.

111.3, 114.4, 117.1, 122.6, 129.4, 130.6, 136.3, 139.5, 144.7, 148.8, 154.7,162.9, 167.4, 169.6.

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