

SYNTHESIS OF SUBSTITUTED BENZYL-1H-1,2,3-TRIAZOLO [4,5-d] PYRIDAZIDINE-4,7-DIONES

S. T. Abu-Orabi¹, R. Al-Hamday, S. Shahateet and K. Abu-Shandi
Department of Chemistry, Yarmouk University, IRBID, JORDAN

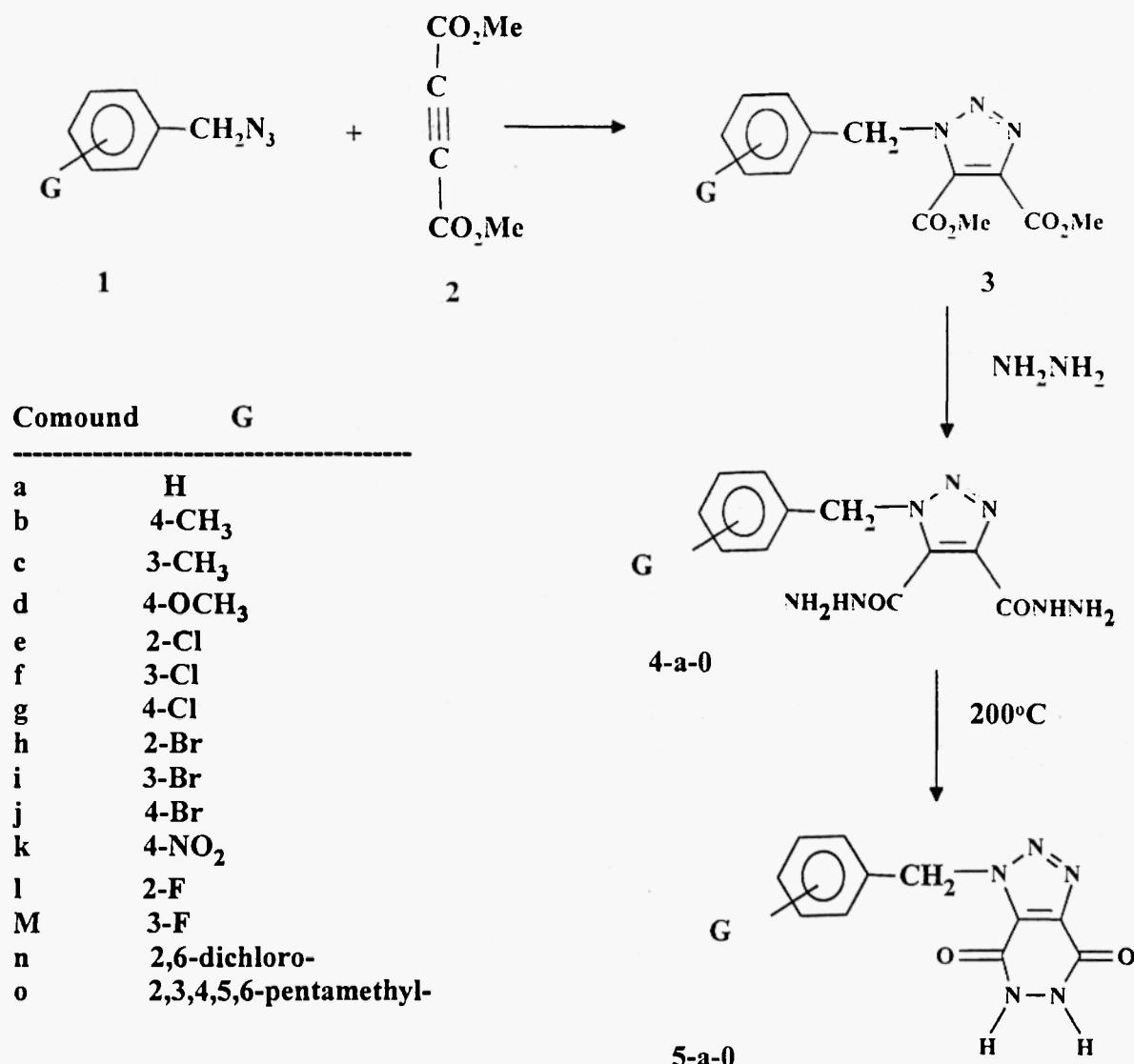
Abstract : A series of substituted benzyl-1H-1,2,3-triazolo[4,5-d]pyridazidine 4,7-diones 5 were prepared via heating the corresponding 1-substituted benzyl-4,5-bis (hydrazinocarbonyl)-1,2,3-triazoles 4. All new compounds were characterized by spectroscopic tools and gave satisfactory elemental analysis.

Introduction : Many derivatives of 1,2,3-triazole have been reported to possess very useful industrial and biological applications¹⁻⁷. Our interest in the title compounds was generated by the pharmacological investigation of triazole and pyridazidine derivatives. It is known that 1,3-dipolar cycloaddition reaction of azide with substituted acetylenes⁸⁻¹² is the most common method for preparing triazole derivatives. Recently we reported the synthesis of triazolopyridazine derivatives¹³, in continuation of our interest in this area we here report in our new results on the synthesis of compounds which posses fused 1,2,3-triazole to pyridazinedione moieties.

Results and discussion : Dipolar cycloaddition reaction of substituted benzyl azides 1a-o with dimethyl acetylenedicarboxylate 2 afforded the expected dimethyl-1-substituted benzyl-1,2,3-triazolo-4,5-dicarboxylates 3a-o. Reactions of 3 with excess hydrazine hydrate under reflux conditions

gave the corresponding bis (hydrazinocarbonyl) derivatives **4a-o**. The ¹H-NMR spectra of compounds **4a-o** shows a singlet at 6.00-6.23 ppm assigned for the benzylic protons, two broad peaks exchange with D₂O at 8.63-10.66 and 11.75-12.07 ppm due to the 2NH protons, broad peak exchange with D₂O at 4.11-4.80 ppm assigned for the 2NH₂ protons. On the other hand the aromatic protons resonate at 6.80-7.92 ppm. The I.R. spectra of these compounds show mainly three absorptions at 3300-3250, 3250-3200 and 1670-1660 cm⁻¹ and were assigned for NH₂, NH and CO stretching frequencies respectively. ¹H-NMR data of compounds **4a-o** are given in Table 2. Heating compounds **4a-o** at 200 °C without solvent for about 4-5 hrs were found to be a convenient method for the synthesis of the title heterocycles; 1-substituted benzyl-1H-1,2,3-triazolo[4,5-d] pyridazidine-4,7-diones **5a-o**. The structure of these compounds were illucidated by spectroscopic tools, in addition to elemental analysis. The I.R. spectra of these compounds showed two broad bands centered at 3300 and 3200 cm⁻¹ and a strong band at 1660-1670 cm⁻¹ assigned for NH and CO stretching frequencies respectively. The broadness in the NH band can be attributed to the strong intermolecular hydrogen bonding between the triazolopyridazidines. The ¹H-NMR spectra of compounds **5a-o** showed a multiplet in the range 6.91-8.25 ppm due to the aromatic protons, a singlet in the range of 5.97-6.23 ppm due to the benzylic protons, the NH protons appeared as a broad peak, exchange with D₂O in the range of 3.29-3.75 ppm. In the mass spectrometry, fragmentation of compounds **5a-o** were in agreement with that expected for substituted triazolo-pyridazidine-4,7-diones. Beside the molecular ion peak M⁺, these compounds gave peaks correspond to [M-C₇H₄G]⁺, [M-N₂]⁺. U.V spectroscopy of these compounds exhibit strong absorption in the range of 262-298 nm. The spectral data of compounds **5a-o** are given in Table 4. The suggested mechanism of the fromation of compounds **5** can only be explained via nucleophilic adddition of NH₂ group in one of the hydrazide on the carbonyl group of the second followed by elimination of hyrazine molecule.

Experimental : Benzyl and substituted benzyl azides **1** were prepared according to the published methods^{14,15}. Melting points were measured on electron thermal digital melting point apperatus and were uncorrected. Infrared spectra were recorded on a PY-Unicam SP 300 spectrometer as KBr discs. ¹H-NMR were recorded on a Brucker WP 80-SY spectrometer using d₆-



DMSO containing TMS as an internal standard. UV spectra were recorded in ethanol on Carry 2390 spectrophotometer. Mass spectra were recorded on a sector with DDP-II minicomputer for control on acquisition. Elemental analysis were performed at MHW Laboratories, Phoenix, Arizona, USA.

General procedure for the synthesis of 1-(substituted benzyl)-4,5-bis(hydrazinocarbonyl)1,2,3-triazoles 4a-o

To an ethanolic solution of triazole 3a-o (0.05 mol) in 50 ml ethanol, 0.5 ml (0.015 mol) of hydrazine hydrate was added. The mixture was heated under reflux for 0.5 hr. Removal of the solvent under reduced pressure afforded a solid which was recrystallized from ethanol yielding of compounds 4a-o. Physical, elemental analysis and spectroscopic data are given in Tables 1 and 2.

General procedure for the synthesis of 1-(substituted benzyl)-1H-1,2,3-triazolo[4,5-d] pyridazidine-4,7-diones 5a-o

0.05 Mol of 1-substituted benzyl-4,5-bis(hydrazinocarbonyl)-1,2,3-triazole 4a-o was inserted in a small test tube, then immersed in a sand bath and was placed in a heating mantle, covered with a sheet of aluminum foil. The compounds were heated at 200 °C for 5 hrs. The completion of the reaction was monitored using litmus paper to detect the evolved hydrazine. The resulting solid was well crushed then washed with ethanol and dimethyl ether, then was recrystallized from ethanol-ethyl acetate mixture. The produced powder was suspended in CCl₄, then 10-15 drops of conc. HNO₃ were added with heating until the all the powder was dissolved. Finally 25 ml of 10% HNO₃ was added. The organic layer was separated and dried over anhydrous Na₂SO₄. Evaporating the solvent afforded the desired products. Melting points, yields, ¹H-NMR, UV and elemental analysis are given in Tables 3 and 4.

Acknowledgment : The authors thank Yarmouk University for financial support of this work. We also thank Miss Fadwa Bani Hani for the preparation of this manuscript.

Table 1 : Physical data of compounds 4a-o.

Compd	G	Molecular formula	yield %	m.p. °C	Elemental analysis found (calculated)		
					C	H	N
4a	H	C ₁₁ H ₁₃ N ₇ O ₂	83	180-2	47.86(47.99)	4.88(4.76)	35.66(35.62)
4b	4-CH ₃	C ₁₂ H ₁₅ N ₇ O ₂	80	208-9	49.63(49.82)	5.09(5.19)	33.82(33.91)
4c	3-CH ₃	C ₁₂ H ₁₅ N ₇ O ₂	81	185-6	49.71(49.82)	5.12(5.19)	33.76(33.91)
4d	4-OCH ₃	C ₁₂ H ₁₅ N ₇ O ₃	85	197-8	47.36(47.21)	4.85(4.91)	32.20(32.13)
4e	2-Cl	C ₁₁ H ₁₂ N ₇ O ₂ Cl	80	190-1	42.46(42.58)	4.22(4.19)	31.58(31.61)
4f	3-Cl	C ₁₁ H ₁₂ N ₇ O ₂ Cl	82	194-5	42.31(42.58)	4.06(4.19)	31.36(31.61)
4g	4-Cl	C ₁₁ H ₁₂ N ₇ O ₂ Cl	84	188-9	42.41(42.58)	4.18(4.19)	31.52(31.61)
4h	2-Br	C ₁₁ H ₁₂ N ₇ O ₂ Br	85	194-6	37.26(37.18)	3.55(3.66)	27.54(27.60)
4i	3-Br	C ₁₁ H ₁₂ N ₇ O ₂ Br	80	196-8	37.01(37.18)	3.52(3.66)	27.36(27.60)
4j	4-Br	C ₁₁ H ₁₂ N ₇ O ₂ Br	90	194-6	37.0(37.18)	3.61(3.66)	27.56(27.60)
4k	4-NO ₂	C ₁₁ H ₁₂ N ₈ O ₄	88	187-9	41.45(41.25)	3.59(3.75)	34.89(35.00)
4l	2-F	C ₁₁ H ₁₂ N ₇ O ₂ F	78	185-6	44.96(45.05)	4.00(4.09)	33.40(33.44)
4m	3-F	C ₁₁ H ₁₂ N ₇ O ₂ F	82	178-8	45.03(45.05)	3.98(4.09)	33.36(33.44)
4n	2,6-dichloro	C ₁₁ H ₁₁ N ₇ O ₂ Cl ₂	88	226-8	38.38(38.37)	3.30(3.20)	28.45(28.49)
4o	2,3,4,5,6-pentamethyl	C ₁₆ H ₂₃ N ₇ O ₂	92	262-4	55.79(55.65)	6.85(6.67)	28.19(28.41)

Table 2 : ¹H-NMR data for compounds 4a-o in d₆-DMSO, (TMS), δ ppm J(Hz).

Compd	G	2NH (b,s)	Ar-H	CH ₂ (s)	2NH ₂ (b)	Others
4a	H	11.85 , 10.40	7.52-7.3 (m)	6.10	4.65	
4b	4-CH ₃	11.96, 8.63	7.92, (d, J = 8 Hz) 7.34, (d, J = 8 Hz)	6.10	4.11	2.31 (s,3H)
4c	3-CH ₃	11.87, 10.44	7.24-6.95 (m)	6.02	4.77	2.26 (s,3H)
4d	4-OCH ₃	11.89, 10.42	7.51 (d, J = 8.8 Hz) 6.55 (d, J = 8.8 Hz)	6.20	4.74	3.73 (s,3H)
4e	2-Cl	11.95, 10.48	7.58-6.7 (m)	6.20	4.79	—
4f	3-Cl	11.95, 10.46	7.41-7.2 (m)	6.10	4.8	—
4g	4-Cl	11.88, 10.44	7.48 (d, J = 7.8 Hz) 7.22 (d, J = 7.8 Hz)	6.10	4.77	—
4h	2-Br	12.06, 10.11	7.74-6.74 (m)	6.13	4.76	—
4i	3-Br	12.03, 10.08	7.71-6.91 (m)	6.12	4.76	—
4j	4-Br	11.87, 10.46	7.6, (d, J = 8.4 Hz) 7.41, (d, J = 8.4 Hz)	6.03	4.57	—
4k	4-NO ₂	12.07, 10.56	8.2, (d, J = 8.0 Hz) 6.22, (d, J = 8.0 Hz)	6.22	4.7	—
4l	2-F	11.94, 10.52	7.03-7.37 (m)	6.13	4.81	—
4m	3-F	11.86, 10.47	7.46-7.23 (m)	6.10	4.78	—
4n	2,6-dichloro	11.75, 10.66	7.90-7.10 (m)	6.23	4.70	—
4o	2,3,4,5,6-pentamethyl	11.81,10.24	—	6.01	4.79	2.15 (s,15H)

Table 3 : Physical data of compounds 5a-o.

Compd	G	Molecular formula	yield %	m.p. °C	Elemental analysis found (calculated)		
					C	H	N
5a	H	C ₁₁ H ₉ N ₅ O ₂	60	231-234	55.06(54.32)	3.62(3.70)	28.72(28.80)
5b	4-CH ₃	C ₁₂ H ₁₁ N ₅ O ₂	57	287d	56.08(56.03)	4.46(4.31)	27.43(27.22)
5c	3-CH ₃	C ₁₂ H ₁₁ N ₅ O ₂	55	277-80	55.88(56.03)	4.4(4.31)	26.98(27.22)
5d	4-OCH ₃	C ₁₂ H ₁₁ N ₅ O ₃	52	282d	52.61(52.74)	4.03(4.02)	25.58(25.64)
5e	2-Cl	C ₁₁ H ₈ N ₅ O ₂ Cl	56	270d	47.40(47.56)	2.91(2.88)	25.18(25.25)
5f	3-Cl	C ₁₁ H ₈ N ₅ O ₂ Cl	51	285d	47.80(47.56)	3.00(2.88)	25.38(25.25)
5g	4-Cl	C ₁₁ H ₈ N ₅ O ₂ Cl	55	280d	47.48(47.56)	2.92(2.88)	25.30(25.25)
5h	2-Br	C ₁₁ H ₈ N ₅ O ₂ Br	56	255-7	40.63(40.99)	2.43(2.48)	21.76(21.73)
5i	3-Br	C ₁₁ H ₈ N ₅ O ₂ Br	53	260-7	40.76(40.99)	2.45(2.48)	21.56(21.73)
5j	4-Br	C ₁₁ H ₈ N ₅ O ₂ Br	52	267-70	40.83(40.99)	2.38(2.48)	21.63(21.73)
5k	4-NO ₂	C ₁₁ H ₈ N ₅ O ₄	49	270d	46.0(45.83)	2.66(2.77)	29.15(29.16)
5l	2-F	C ₁₁ H ₈ N ₅ O ₂ F	47	262d	50.52(50.57)	3.27(3.07)	26.69(26.80)
5m	3-F	C ₁₁ H ₈ N ₅ O ₂ F	53	292d	50.39(50.57)	3.10(3.07)	26.66(26.80)
5n	2,6-dichloro	C ₁₁ H ₇ N ₅ O ₂ Cl ₂	48	284-287	42.16(42.30)	2.21(2.24)	22.41(22.43)
5o	2,3,4,5,6-pentamethyl	C ₁₆ H ₁₉ N ₅ O ₂	52	287d	61.31(61.34)	6.00(6.07)	22.28(22.36)

Table 4 : ¹H-NMR and UV spectral data for compounds 5a-o.

Compd	G	Ar-H	CH ₂ (s)	2NH (bs)	Others	UV nm
5a	H	7.37 (s)	6.01	3.55	—	—
5b	4-CH ₃	7.16-7.22 (m)	5.93	3.30	2.26 (s, 3H)	263
5c	3-CH ₃	7.19-7.22 (m)	5.93	3.30	2.26 (s, 3H)	263
5d	4-OCH ₃	6.91-7.45 (m)	5.98	3.29	3.27 (s, 3H)	272
5e	2-Cl	7.16-7.20 (m)	6.04	3.35	—	272
5f	3-Cl	7.36-7.49 (m)	6.06	3.45	—	274
5g	4-Cl	7.25-7.35 (m)	6.07	3.38	—	274
5h	2-Br	7.67-7.68 (m)	6.07	3.33	—	268
5i	3-Br	7.33-7.42 (m)	6.03	3.36	—	269
5j	4-Br	7.57, (d, J = 8.0 Hz) 7.31, (d, J = 8.0 Hz)	5.97	3.33	—	269
5k	4-NO ₂	7.55, (d, J = 8.2 Hz) 8.25, (d, J = 8.2 Hz)	6.21	3.35	—	262
5l	2-F	7.24-7.35 (m)	6.06	3.50	—	—
5m	3-F	7.42-7.35 (m)	6.02	3.34	—	—
5n	2,6-dichloro	7.57 (s)	6.23	3.75	—	—
5o	2,3,4,5,6-pentamethyl	—	6.13	3.40	2.17 (s, 15H)	—

References :

1. G. Holmewood, K. H. Buechel, P. Reinecke, G. Haenssler: German Patent 3, 510, 411 (1986). *Chem. Abst.* **106**, 1471e (1987).
2. E. Imai, T. Ikeda, H. Fukomoto; Japanese Patent 61, 138, 260 (1986). *Chem. Abst.* **106**, 25783c (1987).
3. S. A. Inke. Spanish Patent 548, 092 (1986). *Chem. Abst.* **106**, 67321f (1987).
4. I. Lalezari, L. A. Gomez, M. Khorshid, *J. Heterocycl. Chem.* **27**, 687, (1990).
5. M. M. Al-Abdallah and S. T. Abu-Orabi, *Korrosion*, **22**, 150 (1991).
6. A. M. S. Abdennabi, A. I. Abdulhadi, S. T. Abu-Orabi and H. Saricimen, *Corrosion Science*, **38**, 1791 (1996).
7. A. M. S. Abdennabi, A. I. Abdulhadi and S. T. Abu-Orabi, *Anti-Corrosion Methods and Materials*, **45**, 103 (1998).
8. S. Patai "The Chemistry of Azido Group", Interscience Publisher, New York NY, 1971, PP 331-388.
9. P. Purvis, R. K. Smalley, H. Suschitzky and M. A. Alkhader. *J. Chem. Soc. Perkin. Trans. I*, **249**, (1984).
10. S. T. Abu-Orabi, M. A. Atfah, I. Jibril, F. M. Marii and A. A. -S. Ali. *J. Heterocyclic Chem.* **26**, 1461 (1989).
11. S. T. Abu-Orabi, M. A. Atfah, I. Jibril, F. Marii and A. A. -S. Ali, *Gazzetta Chimica Italiana*, **121**, 397 (1991).
12. S. T. Abu-Orabi, M. A. Atfah, I. Jibril, A. A. -S. Ali and F. Marii, *Gazzetta Chimica Italiana*, **122**, 29 (1992).
13. S. T. Abu-Orabi, R. Al-Hamdany, M. A. Atfah, A. A. -S. Ali and K. Abu-Shandi. *Asian Journal of Chemistry*, **11**, 774, (1999).
14. H. Henkel and F. Weygand, *Chem. Ber.*, **76**, 812 (1943).
15. A. A. -S. Ali, M. Sc. Thesis, Yarmouk University, Jordan (1990).

Received on July 12, 2000

