

Note

Claisen rearrangement of 3-(prop-2-ynylsulfanyl)-1,2,4-triazinone: A convenient route to 2-methylthiazolo[3,2-*b*][1,2,4]triazinone

M M Heravi*, M M Mojtahedi & S M Bolourtchian

Chemistry and Chemical Engineering Research Center of Iran,
P.O.Box: 14335-186, Tehran-Iran, Fax (21)8037185

Received 4 August 1997; accepted (revised) 24 March 1998

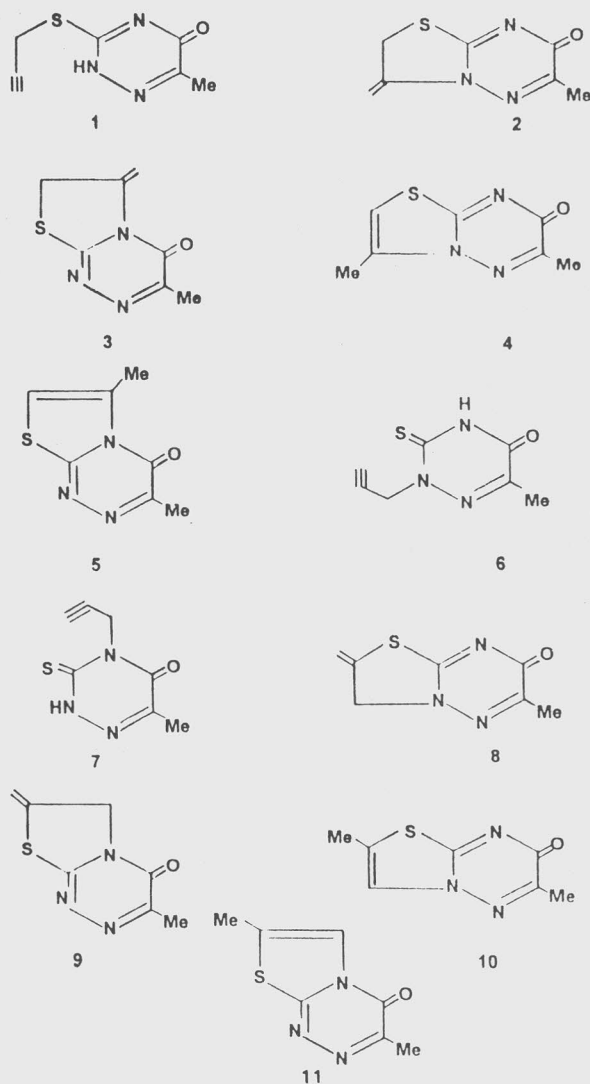
6-Methyl-3-(prop-2-ynylsulfanyl)-1,2,4-triazin-5(2*H*)-one **1** on refluxing with hexamethyl phosphoric triamide (HMPT), in the presence of catalytic amount of $\text{PdCl}_2(\text{PhCN})_2$ affords 2,6-dimethylthiazolo [3,2-*b*][1,2,4] triazin-7-one **10** via an interesting Claisen rearrangement. This structure has been confirmed by unambiguous synthesis of **10**.

Palladium catalyzed S→N allylic rearrangement of allylsulfanyl pyrimidinone and allylsulfanyl-1,2,4-triazinone have been studied extensively owing to their synthetic utility^{1,2}. However examples of S→N propynylic rearrangements are very scarce. The S→N propynylic rearrangement of 2-(prop-2-ynylsulfanyl) benzimidazole is typical example^{3,4}.

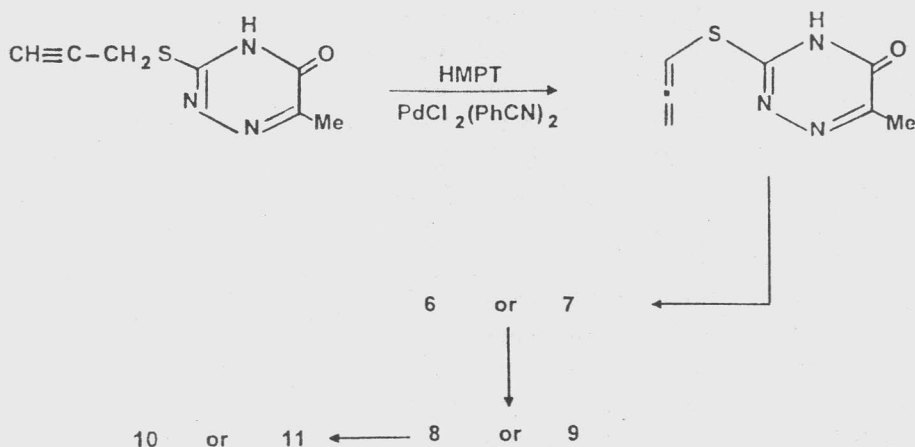
Recently we have demonstrated that base⁵ and Pd-salt^{6,7} very effectively catalyze the cyclization of prop-2-ynylsulfanyl-1,2,4-triazinone to corresponding 3-substituted thiazolo [1,2,4] triazinone. In this pattern of cyclization and aromatization and other methods^{8,9} to synthesize thiazolotriazine, only 3-substituted thiazolo [1,2,4] triazinone can be obtained. Here we wish to report two independent routes to synthesis 2,6-dimethylthiazolo [3,2-*b*][1,2,4] triazin-7-one **10**.

6-Methyl-3-(prop-2-ynylsulfanyl)-1,2,4-triazin-5-one **1** was refluxed in HMPT with catalytic amount of $\text{Pd Cl}_2(\text{PhCN})_2$ for 32 hrs. After evaporation of solvent under reduced pressure, the crude material was subjected directly to column chromatography to obtain a crystalline compound as a major product.

Taking into consideration the problem of regiochemistry, first we thought of alkylation at the N-2 vs. N-4, by direct nucleophilic addition of amide to



acetylenic moiety and subsequent isomerization of either intermediate **2** or **3** to either **4** or **5** respectively. This pattern of cyclization and isomerization by base has been noticed previously⁶. Comparison of spectroscopic data of obtained compound with those known **4**⁵ and **5**⁷ showed considerable differences. Therefore we considered thermal and catalyzed [3,3] sigmatropic rearrangement of **1** to either **6** or **7** with the subsequent cyclization to either **8** or **9** followed by isomerization to either **10** or **11** respectively. (Scheme I).

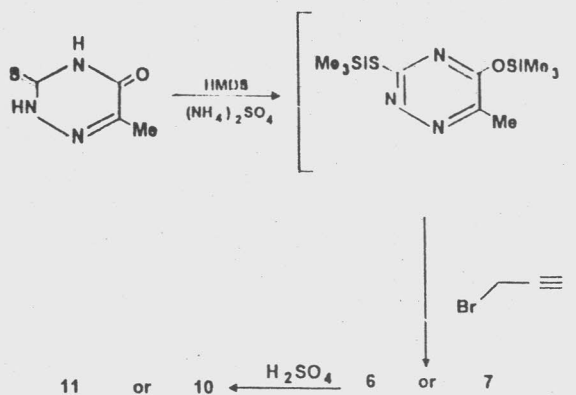


Scheme I

To prove this pattern of one pot [3,3] sigmatropic shift, cyclization and isomerization we decided to synthesize 2-substituted thiazolotriazinone **10** or **11** unambiguously.

6-Methyl-3-thioxo-1,2,4-triazin-5-one **12** was refluxed with excess of hexamethyl disilazane (HMDS) and a catalytic amount of $(\text{NH}_4)_2\text{SO}_4$ ¹⁰ and thereafter propynylbromide was added. After usual work-up a single (TLC) compound was isolated in fairly good yield which could be either **6** or **7**.

The corresponding *N*-propynyl compound **6** or **7** was cyclized and isomerized by acid catalysis¹¹: to afford the identical compound which was obtained by refluxing **1** with HMPT (**10** or **11**) (Scheme II). The structure **10** or **11** was carefully discriminated by the comparison of its UV spectrum with those of well established **4** (λ_{max} 280 nm)⁵ and **5** (λ_{max} 298 nm)⁷. 3,4-Disubstituted-1,2,4-triazin-5 ones are known to show the absorption maxima at the longer wavelengths compared to 2,3-disubstituted compounds⁹ **5** also showed the absorption maxima at the longer wavelength compared to **4**. The UV spectrum of compounds **10** or **11**, was quite similar to that of **4**. Therefore we concluded that in S→N propynylic rearrangement in HMPT, the propynylic group migrates to N-2 of 1,2,4-triazine regioselectively to afford **6** which subsequently cyclizes and isomerizes to **10**. *N*-Alkylation of 1,2,4-triazine **12** in the presence of HMDS also occurs on N-2 selectively, leading to 2-propynyl derivative **6**. Acid catalyzed cyclization and isomerization of the latter led to **10**.



Scheme II

Experimental Section

Melting points were obtained on a Buchi 530 and are uncorrected. ¹HNMR spectra were recorded in δ ppm a Bruker Ac 80 spectrometer in dimethyl sulfoxide as solvent using TMS as internal standard. IR spectra were recorded on a Perkin-Elmer model 883 using KBr disk and mass spectra on a Varian CH-7.

2,6-Dimethyl thiazolo [3,2-*b*][1,2,4] triazin-7-one 10—Compound **1** (1g, 5.5 mmoles) and $\text{PdCl}_2(\text{PhCN})_2$ (0.1g) were refluxed in HMPT (20 mL) for 32 hr. The solvent was evaporated off *in vacuo*. The crude mixture was washed with water and extracted with chloroform. This solution was dried over anhyd. Na_2SO_4 and evaporated off. The

residue obtained was subjected to column chromatography using CHCl_3 : MeOH, 90:10 to afford the title compound. Yield 0.38g, (38%), m.p. 168-69°; $^1\text{HNMR}$ (CDCl_3): δ 2.38(s,6H,2Me), 6.43(s,1H,CH of thiazole ring). IR: (KBr): 3420, 2928, 1640 (amide carbonyl), 1489 and 1372 cm^{-1} ; UV (CHCl_3): (λ max 282 nm. M.S: m/z, M^+ , 181(25), 180(55), 156(18), 139(100), 72, 40(95).

6-Methyl-2N-Propynyl-3-thioxo-1,2,4-triazin-5-one 6. **6-Methyl-3-thioxo-1,2,4-triazin-5-one 12**—(0.36g, 2.5 mmoles), was refluxed with hexamethyldisilazane (HMDS) (0.7 mL, excess) and a catalytic amount of $(\text{NH}_4)_2\text{SO}_4$ (12.5 mg) until a clear solution was obtained. Excess HMDS was removed by distillation *in vacuo*. The catalytic amount of I_2 and propynyl bromide (0.18g, 1 mmole) in CH_3CN (5 mL) was added and the reaction mixture was refluxed for further 4 hr. After evaporation of solvent *in vacuo*, the residue was treated with water to afford the spectroscopic pure product. Yield (0.4 g, 93%), m.p. 98-99°; $^1\text{HNMR}$ (DMSO-d_6): δ 2.1(s,3H,Me), 3.1(t,1H,-C-CH, $J=2.1\text{Hz}$), 3.95 (d, 2H, CH_2 , $J=2.1\text{Hz}$); IR: (KBr): 3417, 3258, 2928, 1640, 1590, 1459, 1033 cm^{-1} ; M.S: m/z, M^+ , 181(22), 143(18), 140(85), 72(100), 71(75), 80(90), 55(65).

Acid catalyzed cyclization of 6 to 10—Compound 6 (0.25g, 1.38 mmole) was dissolved in conc H_2SO_4 . The reaction mixture was kept at 50 C for 5 hrs. It then poured onto crushed ice and the solution was neutralized by adding NaOH. The precipitated solid was crystallized from EtOH to afford spectroscopic pure 10. Yield 0.175g, (70%), mp 168-69.

References

- 1 Mizutani M, Sanemitsu Y, Tamaru Y & Yoshida Z, *J.Org.Chem*, 48, 1983, 4585.
- 2 Mizutani M, Sanemitsu Y, Tamaru & Yoshida Z, *Tetrahedron*, 1984, 5289.
- 3 Balasubramanian K K & Venligopalan B. *Tetrahedron lett*, 1974, 2643.
- 4 Balasubramanian K K & Venligopalan B. *Tetrahedron lett*, 1974, 2645.
- 5 Heravi M M, *Iran.J.Chem & Chem Eng*, 11(2),1992, 8. *Chemical Abstract*, 120-323500d.
- 6 Heravi M M & Bakavoli M., *J.Chem.Res*, 11,1995, 480.
- 7 Heravi M M, Bakavoli M, Shafaie M, Sadeghi M M & Khoshdast A, *Indian. J.Chem.*, 35,1996,1260.
- 8 Nyitrai J, Bekassy S & Lempert K. *Acta Chem Acad Sci.Hurg*, 53,1967, 309.
- 9 Dawnis J, Guindio Y, Jacquier R & Viallefont P, *Bull.Soc.Chim.Fr*, 1972, 1511.
- 10 Muller C E, *Tetrahedron Lett*, 32(45), 1991, 6539.
- 11 Heravi M M, Aghapoor K & Nooshabadi M H to *synth commun*, 28(2), 1998 in Press.