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A New Method of Dimroth Rearrangement in Fused Triazolo[1,5-d]-1,2,4-triazine

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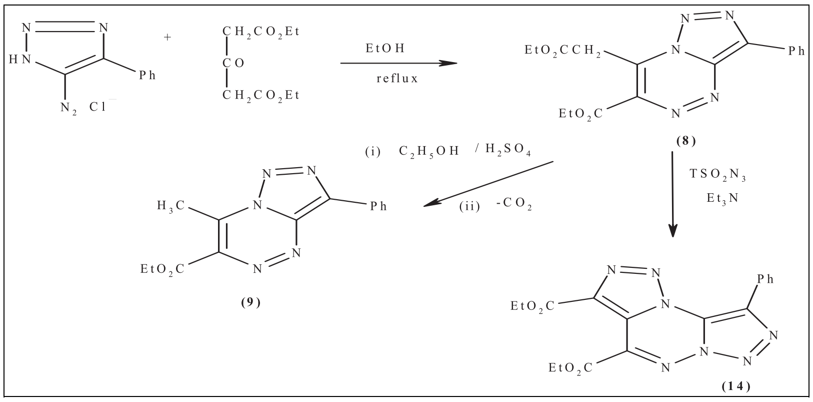

Ethyl 7-(2-ethoxy-2-oxoethyl)-3-phenyl-[1–3]triazolo[5,1-c][1,2,4]triazine-6-carboxylate (the parent compound) was synthesized by reaction of 4-phenyl–1H-1,2,3-triazole-5-diazonium chloride with diethyl-2-oxopropane-1,3-dicarboxylate at cooling for 2 h. During the reaction of the parent compound with p-toluenesulphonyl azide in triethylamine, the Dimroth rearrangement occurred to give the tricyclic compound.

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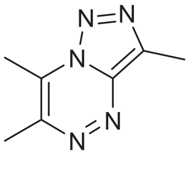
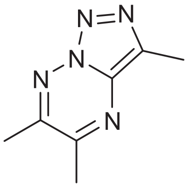
INTRODUCTION

The isomerisation of heterocycles in which the endocyclic or exocyclic heteroatoms and their attached substituents are translocated through ring-opening-ring-closure is known as Dimroth rearrangement. The first of observation of this type of rearrangement was made on triazine derivative, but no rationalization was provided to explain the findings [1] until 1909, when Dimroth proposed the correct mechanism for the rearrangement of triazole derivative [2]. The generality of this process was first recognized in pyrimidine series [3,4] and was shown to occur in many nitrogen-containing heterocycle [5]. The 1,2,3-triazoles are important heterocyclic compounds that have been studied by many researchers as a result of their extensive pharmacological activities, synthetic utilities, and theoretical interest [6–10]. There are only four bridgehead-fused *1,2,3-triazolo-1,2,3-triazines* having a single nitrogen atom common to both rings – namely, the [5,1-c] (**1**), [1,5-b] (**2**), [1,5-d] (**3**), and [5,1-f] (**5**) ring system [11]. The first two ring systems are known [12], while little is known about rings (**3**) and (**5**), respectively [13,14].



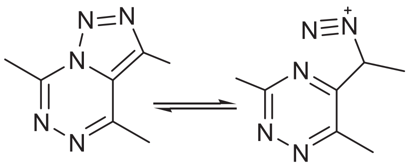
[5, 1-c]

(1)



[1, 5-c]

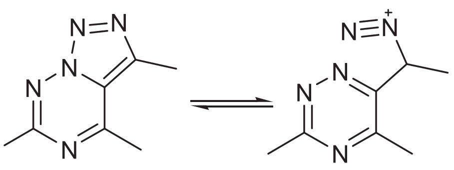
(2)



[1, 5-d]

(3)

(4)



[5, 1-f]

(5)

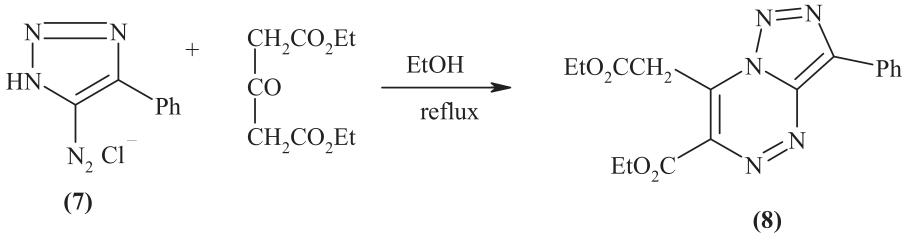
(6)

The [1,5-d] **3** and [5,1-f] **5** ring structures are capable of diazoalkylideneamine-1,2,3-triazole ring-chain tautomerism [(**3**)⇌(**4**)] and [(**5**)⇌(**6**)], but Dimroth rearrangement of the type [(**1**)⇌(**2**)] has not been demonstrated for them. In this paper, the [1,5-d] ring structure **3** was synthesized, and Dimroth rearrangement demonstrated for it.

RESULTS AND DISCUSSION

The coupling reaction of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (**7**) with diethyl-2-oxopropane-1,3-dicarboxylate at cooling gave a mixture of the new triazolotriazine (**8**) and the known compound (**9**) identical in all respects to an authentic sample [15] (Scheme 1).

A repetition of the coupling reaction of **7** and diethyl-2-oxopropane-1,3-dicarboxylate under reflux gave only the triazolotriazine **8**, which gave analytical data and showed spectral properties consistent with its assigned structure **8**. However, its IR spectrum showed only one carbonyl band, indicating that the two ester groups are superimposed because the 6-ethoxycarbonyl group attached to the electron – withdrawing triazine ring absorbs at a higher frequency than would have been expected. The ^{1}H NMR spectrum of **8** in ($CDCl_3$) exhibited signals at δ 8.29 (2H, d, Ar-H), 7.66–7.56 (3H, m, Ar-H), 4.50 (2H, q, CH_2), 4.37 (2H, q, CH_2), 3.71 (2H, s, CH_2), 1.48 (3H, t, CH_3) and 1.28 (3H, t, CH_3). ^{13}C-NMR gave further evidence of the structure by exhibiting signals at ppm: 178.102, 173.045 corresponding to 2C=O groups of the esters, 138.214 (C-1 of phenyl-), 129.104, 128.712, and 127.086 (5C of phenyl-), 60.610 and 60.504 ($2CH_2$) and 15.416 assigned to ($2CH_3$).



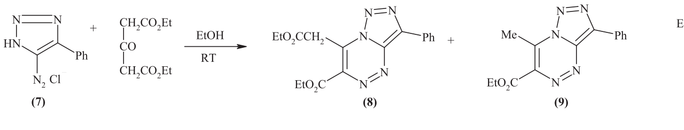
In an effort to further establish the structure of the triazolotriazine **8**, it was heated under reflux with aqueous ethanolic sulphuric acid. The triazolotriazine **8** underwent decarboxylation to give the known compound **9**. This transformation of [8,9] must have involved the initial hydrolysis to the carboxylic acid (**10**), which, on further heating, lost carbon dioxide to give **9** (Scheme 2).

Treating the methylene compound **8** with p-toluenesulphonyl azide in the "diazo-transfer reaction" afforded sulphanamide (**11**) and a tricyclic diester (**14**) (Scheme 3) whose structure was based on the following evidence [structures (**12**) and (**13**) are ring-chain tautomers of (**11**)].

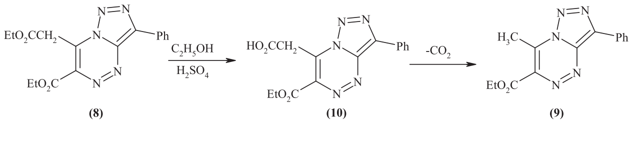
Compound **14** gave analytical data and spectral properties consistent with the molecular formula $C_{12}H_{15}N_7O_4$. Its IR spectrum showed a single carbonyl band at 1740 cm^{-1} indicating the close similarity of the two ester groups. This similar environment of the two ester functions in (**14**) was further borne out by its ^{1}H NMR spectrum, which showed superposition of the four methylene hydrogen and the six methyl hydrogen at δ 4.52 (4H, q) and 1.44 (6H, t), respectively, and also δ 8.32 (2H, d, Ar-H), 7.44–7.52 (3H, m, Ar-H), respectively. The ^{13}C-NMR gave further evidence exhibiting signals at ppm 176.012, 172.102 corresponding to the 2C=O groups, ppm 58.214, 58.014 assigned to $2CH_2$ and ppm 15.312, 15.106 for $2CH_3$ groups of the diester. The diester **14** was further characterized by its hydrolysis to the diacid (**15**). The IR spectrum of **15** contained broad hydroxyl absorption at 3550–3370 cm^{-1} and two carbonyl bands at 1740 and 1725 cm^{-1}. ^{1}H-NMR showed signals at δ 9.40 (2H, br, 2COOH), 8.40 (5H, s, Ar-H); the ^{13}C-NMR gave further evidence by exhibiting signals at ppm 178.412, 174.302 corresponding to the 2C=O groups

The formation of this tricyclic diester [1,5-d]-[1,5-c] **14** can be explained in terms of the proposed mechanism in what follows (Scheme 4). First, the diazo-transfer reaction occurred to afford the diazo intermediate **11**, whose ring opens and suffers Dimroth rearrangement [(**11**)⇌(**12**)] to the bis-diazo intermediate **13**, which on subsequent ring closure gave the diester **14**.

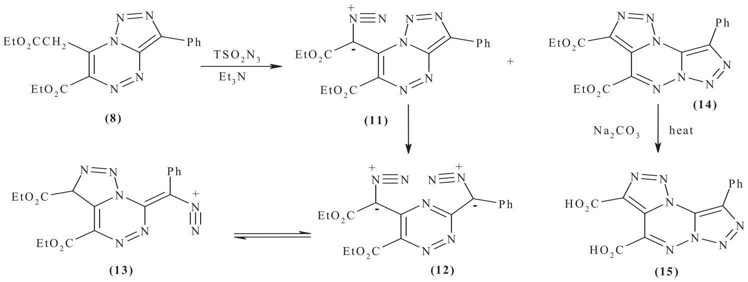
Scheme 1



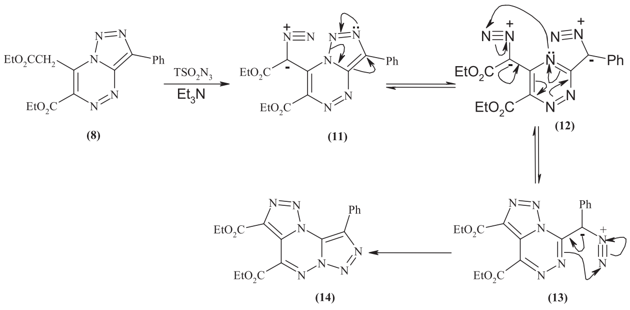
Scheme 2



Scheme 3



Scheme 4



EXPERIMENTAL

Melting points (uncorrected) of all analytical samples were determined on a Kofler block. U.V. spectra were recorded for ethanol solutions on a Pye-Unicam S.P. 800 spectrophotometer using matched 1 cm^3 quartz cells. The absorption maxima were always given in nanometers: the figures in parenthesis are $\log^a$ values. Infrared spectra were obtained for Nujol suspensions on a Perkin-Elmer 157G Infrared spectrophotomer. ^1H and ^{13}C NMR spectra were measured at 200 MHz using a Varian instrument. Chemical shifts are reported on the δ scale relative to TMS as an internal standard. The letters s, d, t, q, and m are used to indicate singlet, doublet, triplet, quartet, and multiplet, respectively. Elemental analysis was performed on CHN-O rapid analyzer. The mass spectra were measured at 800 kv on an A.E.I. M.S 902 instrument.

Ethyl 7-(2-ethoxy-2-oxoethyl)-3-phenyl-[1,2,3]triazole[5,1-c][1,2,4]triazine-6-carboxylate (8). Solutions of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride 4.90 g (0.012 mole) (7), in 60 mL of water and 60 mL of ethanol, diethyl-2-oxopropane-1,3-dicarboxylate 4.90 g (0.012 mole), and sodium acetate 3.20 g in 16 mL of water and 940 mL of ethanol, were mixed, cooled in an ice salt-bath and stirred for 2 h. The ethanol was removed under reduced pressure, and the aqueous mother liquor was extracted with chloroform to give an oil in which on trituration with ethanol yielded Ethyl 7-(2-ethoxy-2-oxoethyl)-3-phenyl-[1,2,3]triazolo[5,1-c][1,2,4]triazine-6-carboxylate (**8**) 0.6 g, mp 174° (from ethanol), identical (m.p and IR spectrum) with an authentic sample.

The ethanol mother liquor was heated under reflux for 10 min and concentrated to give the triazolotriazine (8) as orange needles (2.86 g), mp 104° (from benzene-light petroleum); uv spectrum λ max. 210 (4.44), 228 (4.30), 281 (4.12), 3.41 (3.57); max, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) 8.29 (2H,d, Ar-H), 7.66–7.56 (3H, m, Ar-H), 4.50 (2H, q, CH_2), 4.39 (2H, q, CH_2) 3.17 (2H, s, CH_2), 1.48 (3H, t, CH_3) and 1.28 (2H, t, CH_3);. ^{13}C-NMR ($CDCl_3$) ppm: 178.102, 173.045 (2C=O), 140.046 (1C), 138.214 (1C), 136.516 (1C), 131.120 (2C), 129.104, 128.712, 127.086, 60.610, 60.504, 15.416 [M^+, 355]. *Anal.* Found: C, 57.5; H, 4.8; N, 20.7%, Calcd. for $C_{17}H_{17}N_5O_4$; C, 57,5; H, 4.8; N. 19.7%.

5,6-Diethoxycarbonyl-l-phenyl-1,2,3-triazolo[1,5-d][1,5-c]-1,2,3-triazine (14). A solution of the methylene triazolotriazine (**8**) 1.40 g, (0.04 mole) in 200 mL of absolute ethanol was stirred at 0° (ice-salt bath) and treated in one portion with triethylamine 0.81 g, (0.08 mole) and then dropwise with a solution of p-toluenesulphonyl azide 0.80 g; (0.0 4 mole) in 20 mL of absolute ethanol. The mixture was stirred for 2 h and filtered to give 0.50 g of the unreacted diester (8); mp 90°, which was identical (mp and IR spectrum) with an authentic sample.

The ethanol filtrate was evaporated and the resulting oil was triturated with ethanol-water to give the tricyclic diester (14) as yellow needles (0.41 g), mp 171° (dimethylformamide-ethanol), λ max 211 (4.44), 221 (4.40) and 281 (4.34), υ max 1740 cm^{-1}, ($CDCl_3$) 8.32 (2H, d, Ar-H), 7.44–7.52 (3H, m, Ar-H), 4.52 (4H, q, $2CH_2$), and 1.44 (6H, t, $3CH_3$), ^{13}C-NMR ($CDCl_3$) ppm: 176.012, 172.102 (2C=O), 164.046 (1C), 138.214 (1C), 136.016 (1C), 134.502 (1C), 132.120 (2C), 129.104 (2C), 128.712 (1C), 127.086 (2C), 58.214, 58.014 ($2CH_2$), 15.312, 15.106 ($2CH_3$) [M^+, 381]. *Anal.* Found: C, 53.3; H, 4.0; N, 26.0%, Calcd. for $C_{17}H_{17}N_5O_4$; C, 53.5; H, 3.9; N, 25.8%.

l-Phenyl-1,2,3,-triazolo[1,5,-d][1,5-c]-1,2,4-triazin-5,6-dicarboxylic acid (15). A solution of the tricyclic diester (**14**) 0.38 g (0.01 mole), in 25 mL of ethanol, was heated under reflux with aqueous solution of 2 mL of 2 M sodium carbonate for 3 h. The mixture on evaporation left a residue, which was dissolved in water and extracted with chloroform. Evaporation of the chloroform extract gave oil, which in contact with methanol-light petroleum, gave the diacid (15) as a pale pink solid 0.70 g, mp 121° (from benzene), λ max 213 (94.43), 271 (4.40), 275 (4.44) and 284 (4.41); υ max 3520, 1940, 1740, and 1725 cm^{-1}; ($CDCl_3$) 9.40 (2H, br, 2COOH), 8.40 (5H,s, Ar-H); ^{13}C-NMR ($CDCl_3$) ppm: 178.102, 174.302 (2C=O), 164.046 (1C), 138.214 (1C), 136.016 (1C), 134.502 (1C), 132.120 (2C), 129.104 (2C), 128.712 (1C), 127.086 (2C) [M^+325]. *Anal.* Found: C. 48.1; H, 2.3; N, 29.9%, Calcd. for $C_{13}H_7O_4$ C, 48.0; H, 2.2; N, 30.1%.

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