

TETRAHEDRON LETTERS

(E)-AND (Z)-3-(4-CHLORO-5H-DITHIAZOL-5-YLIDENE)-1,1,1-TRIFLUOROPENTANE-2,4-DIONES AND THEIR ANALOGS: STEREOCHEMISTRY AND THEIR MECHANISMS OF FORMATION

Hyi-Seung Lee and Kyongtae Kim*

Department of Chemistry, Seoul National University, Seoul 151-742. Korea

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Abstract: The reactions of Appel's salt with active methylene compounds such as 1, 1, 1, 5, 5, 5-hexafluoro-2,4-pentanedione, 1, 1, 1-trifluoro-2,4-pentanedione, ethyl 4, 4, 4-trifluoro-3-oxobutanoate, 4, 4, 4-trifluoro-1-phenyl-1,3-butanedione, and 4, 4, 4-trifluoro-1-(2-naphthyl)-1,3-butanedione in the presence of pyridine in CH₂Cl₂ at room temperature afforded the corresponding 5-alkyliden-1,2,3-dithiazoles. The ratios of each stereoisomer were determined by ¹⁹F NMR spectroscopy. (© 1998 Elsevier Science Ltd. All rights reserved.

Appel had previously shown that methyl and ethyl cyanoacetates reacted with 4,5-dichloro-1,2,3-dithiazolium chloride (Appel's salt) (1) to give methyl and ethyl (4-chloro-5H-1,2,3-dithiazol-5-ylidene)cyanoacetates (2a) in 68 and 76% yields, respectively.¹ The stereochemistry around the carbon-carbon double bond of 2a has not been clearly established although the ester carbonyl group and S-1 of dithiazole



moiety are suggested to be *cis* presumably due to the driving force for the strong interaction with an electrondeficient S-1 atom.² Recently Rees et al. reported the preparation of dithiazol-5-ylidene derivatives 2b, 3 and 4 from 4-chloro-1,2,3-dithiazole-5-thione 5 and active methylene compounds such as malonitrile, barbituric acid, and Meldrum's acid, respectively.³ In addition, treatment of diphenyldiazomethane with 5 in benzene or dichloromethane at room temperature was reported to give the alkene 2c.³ All of the dithiazol-5-ylidene derivatives 2b-c, 3, and 4 have identical groups at one of the carbons of the carbon-carbon double bond. Consequently the stereoelectronic effects involved in the formation of the carbon-carbon double bond cannot be analyzed with these olefins having two identical groups, in spite of the observation that the ¹H NMR spectrum of 2c appeared to show that each peak is doubled, indicating that the two phenyl groups of 2c are in different environments.

In order to understand the stereoelectronic effects involved in the formation of dithiazol-5-ylidene derivatives, we prepared new, unsymmetrically substituted dithiazol-5-ylidene derivatives and determined the ratios of each stereoisomers. We wish to communicate the results herein.

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After some trial, it was found that the reactions of 1 with 1,3-dicarbonyl compounds 6 having at least one trifluoromethyl group bonded to a carbonyl carbon proceeded smoothly to give new 5-alkyliden-1,2,3dithiazoles 7-9, albeit in low yields (Scheme 1).⁴ When 1,1,1,5,5,5-hexafluoro-2,4-pentanedione (**6a**) (R = CF₃) was used, 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,1,1,5,5,5-hexafluoro-2,4-pentanedione (7) (R = CF₃) and 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,1,1-trifluoro-2-propanone (**9**) were isolated in 18 and 44% yields, respectively. With 1,1,1-trifluoro-2,4-pentanedione (**6b**) (R = Me), a mixture of stereoisomers 7**b** and **8b** (21%; **7b:8b** = 85:15), which was inseparable by either column chromatography (silica gel, 230-400 mesh ASTM) or HPLC (µPorasil, 10 µm, 7.8 × 300 mm i.d., CH₂Cl₂, flow rate = 0.8 mL/min) was isolated. With ethyl 4,4,4-trifluoro-3-oxo-butanoate (**6c**) (R = EtO), a mixture of 7**c** and 8**c** (52%; 7**c**:8**c** = 10:90) was isolated. Interestingly, the reactions with aroyl trifluoroacetylmethanes **6d** (R = Ph) and **6e** (R = 2-naphthyl) under the same reaction conditions gave only single stereoisomers **8d** (34%) and **8e** (18%), respectively.

The ratios of each stereoisomer were determined by ¹⁹F NMR spectroscopy. Their ¹⁹F NMR chemical shifts are shown below:



The ¹⁹F NMR spectrum of **7a** exhibited two quartets at -69.2 (J = 5.5 Hz) ppm and -76.2 (J = 5.5 Hz) ppm. The quartets may be attributable to fluorine-fluorine long range coupling through three sp² hybridized carbon atoms (2 C=O and 1 C=C) between two CF₃ groups. Since the carbonyl oxygen close to S-1 would be expected to interact with S-1,^{2, 3} the carbonyl carbon would be more electron deficient than the other carbonyl carbon. Consequently, the ¹⁹F NMR signals of CF₃ bonded to the electron deficient carbonyl carbon would appear more down field (-69.2 ppm). Based on this ¹⁹F NMR spectral data, one could determine the ratios of each stereoisomer of other compounds. The structural assignment based on the ¹⁹F NMR spectroscopic data was further confirmed by X-ray crystallography of **8d**, whose ORTEP drawing is shown in Fig. 1.⁵

Fig. 1 shows that the carbonyl oxygen of the CF₃C=O group is indeed close to the S-1 atom, whereas the carbonyl oxygen of the PhC=O group is oriented toward the opposite direction to that of the CF₃C=O group. The benzoyl phenyl group is oriented to avoid possible repulsive interactions arising from the close proximity between the ortho hydrogens of the phenyl group and the chlorine atom at C-4. On the other hand, if the phenyl group is swapped with a CF₃ group, a severe electronic repulsion as well as unfavorable steric interactions between two electonegative fluorine and chlorine atoms would be expected. Consequently, only **8d** is formed. Compound **8e** was not stable enough to purify by recrystallization. However, ¹³C NMR spectrum of crude product indicated the formation of the only single isomer **8e**. The



Figure 1. ORTEP drawing of 8d

stereochemistry of **8e** can be rationalized on the same grounds as for **8d**. The predominant formation of **8c** may be attributable to a less electronic repulsion between the chlorine atom at C-4 and the carboethoxy oxygen which may be an electron deficient center due to delocalization of nonbonding electrons into the ester carbonyl group. In the case of a mixture of **7b** and **8b**, **7b** would be a major isomer if the steric and electronic repulsion effects foregoing were important. However, this is not the case. The electron-donating effect of a methyl group increases the electron density on the oxygen atom of the acetyl group, which results in the strong interaction between S-1 and the acetyl oxygen atoms to give **7b** as a major product.

Compound 7a is not likely a precursor of 9 in view of the quantitative recovery of 7a from the reaction of 7a with hydrogen chloride gas which is evolved during the reaction in CH_2Cl_2 at room temperature.

The mechanisms for the formation of compounds 7-9 may be rationalized by nucleophilic attack of the enolic carbon of 6 to C-5 of 1 to give an intermediate 10, which then extrudes a chlorine atom to give a new dithiazolium ion 11. Deprotonation, followed by electron migration (path a), gives compounds 7 and/or 8. Alternatively, nucleophilic attack of a chloride to the carbonyl carbon, which would be more electron-deficient than the alternative one because of the interaction with electron deficient S-1 (path b), followed by elimination gives rise to compound 9 (Scheme 2), in which a trifluoroacethyl group and chlorine atom are syn.



Scheme 2

In conclusion, the stereochemistry of dithiazol-5-ylidene derivatives formed from the reactions of Appel's salt with 1,3-dicarbonyl compounds having at least one trifluoromethyl group bonded to a carbonyl carbon is determined by the extent of the attractive interaction between the carbonyl oxygen and an electron-

deficient S-1 atom as well as an electronic and steric repulsion arising from a trifluoromethyl group and a chlorine atom at C-4 of the dithiazole moiety.

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- Typical procedure: To a suspension of 1 (6.70 g, 32.1 mmol) in CH₂Cl₂ (150 mL) was added a solution of 1,1,1,5,5,5-4. hexafluoro-2,4-pentanedione (6.62 g, 31.8 mmol) in CH₂Cl₂ (20 mL), followed by dropwise addition of pyridine (74.2 mmol) in CH₂Cl₂ (30 mL) for 1h. The mixture was stirred for 30 min at room temperature. After removal of the solvent in vacuo, the residue was chromatographed on a silica gel (3 x 17 cm, 230-400 mesh) column. Elution with n-hexane gave a small amount of 5. Elution with a mixture of n-hexane and CH₂Cl₂ (3:1) gave 3-(4-chloro-5H-1,2,3-dithiazol-5-ylidene)-1,1,1-trifluoro-2propanone (9) (3.45 g, 44%): mp 75-77 °C (n-hexane-CH₂Cl₂); ¹H NMR (CDCl₃, 300 MHz) δ 7.57 (s, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 107.4, 117.7 (q, J_{CF} = 286.5 Hz, CF₃), 144.7 (C-4), 161.6 (C-5), 176.8 (q, J_{CCF} = 37.0 Hz, C=O); ¹⁹F NMR (CDCl₃, 188 MHz) δ -75.5; IR (KBr) 1600, 1494, 1434, 1356, 1258, 1190, 1149, 1091, 925, and 797 cm⁻¹; MS m/z 247 (M², 69), 254 (73), 212 (6.3), 178 (100), 85 (64). Anal. Calcd for C3HClF3NOS2: C, 24.25; H, 0.41; N, 5.66; S.25.89. Found: C, 24.17; H. 0.39; N. 5.61; S. 25.73. Elution next with the same solvent mixture (2:1) gave 3-(4-chloro-5H-1,2,3-dithiazol-5ylidene)-1,1,1,5,5,5-hexafluoro-2,4-pentanedione (7a) (1.96 g, 18%): mp 77-79 °C (*n*-hexane-CH₂Cl₂); ¹³C NMR (CDCl₃, 75 MHz) 8 114.8, 115.8 (q, J_{CF} = 292.1 Hz, CF₃), 117.6 (q, J_{CF} = 286.6 Hz, CF₃), 146.2 (C-4), 164.3 (C-5) 172.4 (q, J_{CCF} = 37.5 Hz, C=O), 182.2 (q, J_{CCF} = 38.5 Hz, C=O); ¹⁹F NMR (CDCl₃, 188 MHz) δ -69.2 (q, J = 5.5 Hz), -76.2 (q, J = 5.5 Hz): IR (KBr) 1731, 1586, 1398, 1285, 1211, 1179, 1152, 1048, and 850 cm⁻¹: MS m/z 343 (M⁺, 32), 274 (100), 224 (60). Anal. Calcd for C₇F₆NO₂S₂: C, 24.47; N, 4.08; S, 18.66. Found: C, 24.42; N, 4.01; S, 18.55.
- 5. Crystal data for 8d: C₁₂H₅ClF₃NO₂S₂, M = 351.74, T = 293(2) K, Colorless crystal, 0.3 x 0.4 x 0.4 mm, Monoclinic, Space group P₂₁/C (No. 14), a = 12.064(2), b = 5.752(4), c = 19.586(3) Å, α = 90.00(2), β = 93.87(2), γ = 90.00(2) °. U = 1355.9(10) Å³, Z = 4, D_c = 1.723 gcm⁻³, F(000) = 704, μ = 0.626 mm⁻¹, R = 0.0793, WR² = 0.2153 (190 parameters). The data were collected on an Enraf-Nomius CAD 4 diffractometer using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å). Refinements were carried out by full least-squares techniques. Atomic scattering factors were taken from International Tables for X-ray crystallography, Vol IV, 1974. All calculations and drawings were performed using a Micro VAX II computer with the SPD system.

Selected Bond lengths [Å] and angles [deg] for 8d: S(1)-C(4) 1.731 (6), S(1)-S(2) 2.063 (2), S(2)-N(1) 1.618 (7), N(1)-C(5) 1.304 (9), C(4)-C(5) 1.458 (8), C(3)-C(4) 1.383 (8), C(2)-C(3) 1.432 (8), C(3)-C(6) 1.531 (8), O(1)-C(2) 1.232 (7), O(2)-C(6) 1.214 (8), C(4)-S(1)-S(2) 93.9 (2), N(1)-S(2)-S(1) 97.7 (2), C(5)-N(1)-S(2) 116.5 (5), N(1)-C(5)-C(4) 120.9 (6), C(5)-C(4)-S(1) 110.6 (4), C(3)-C(4)-S(1) 120.5 (4), C(4)-C(3)-C(2) 116.2 (5), C(4)-C(3)-C(6) 123.5 (5), O(1)-C(2)-C(3) 121.9 (5), O(2)-C(6)-C(3) 117.2 (5).