# CYCLOADDITION REACTIONS OF THIAZOLIUM N-DICYANOMETHYLIDE WITH OLEFINIC DIPOLAROPHILES

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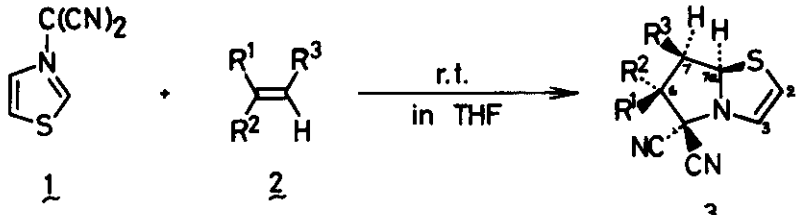
Abstract —— The cycloaddition reaction of a stable N-methylide, thiazolium N-dicyanomethylide, with acyclic olefinic dipolarophiles such as dimethyl fumarate, maleate, and trans-1,2-dibenzoylethylene proceeded in a stereoselective manner to give only the corresponding endo-[3 + 2] cycloadducts, all of which were stable in boiling tetrahydrofurn. In the reaction of the methylide with N-substituted maleimides, however, a mixture of endo- and exo-[3 + 2] cycloadducts, whose relative yields changed with the reaction time, was formed. The endo cycloadduct was found to isomerize into the exo cycloadduct in tetrahydrofuran even at room temperature.

A few cycloaddition reactions of N-methylides in thiazolium system have been investigated. Potts and his co-workers[1] have reported that 4-methylthiazolium N-phenacylide reacted with N-phenylmaleimide to give the cycloadduct whose stereochemistry was not fully established, whereas no identifiable cycloadducts were obtained in the reaction with other olefinic dipolarophiles. We have recently found that benzothiazolium N-phenacylide, generated in situ from 3-phenacylbenzothiazolium bromide and triethylamine, added to a variety of olefinic dipolarophiles with one exception of maleonitrile to give the corresponding endo-cycloadducts in good yields[2]. It has also been demonstrated that an unstable methylide, 4-methylthiazolium N-phenacylide[1], and a stable one, thiazolium N-dicyanomethylide[3], gave a pyrrolo[2,1-c][1,4]thiazine and thiapyrrocoline through an isomerization of the corresponding initial cycloadduct respectively, in the reaction with dimethyl acetylenedicarboxylate.

However, the cycloaddition reaction of a stable thiazolium N-methylide with olefinic dipolarophiles has not been reported so far. In this paper we wish to report the cycloaddition reaction of thiazolium N-dicyanomethylide 1 with acyclic and cyclic olefinic dipolarophiles.

A solution of equimolar amounts of the methylide 1, mp 209°C (lit.[3] mp 202-203°C), prepared from

thiazole and tetracyanoethylene oxide according to the reported method[3], and dimethyl fumarate 2a in dry tetrahydrofuran (THF) was stirred at room temperature for 25 h until 2a disappeared. The reaction mixture was concentrated in vacuo, and the residue was chromatographed on silica gel using chloroform as an eluent to afford a 1:1 adduct 3a as the sole product in 70% yield. Dimethyl maleate 2b and trans-1,2-dibenzoylethylene 2c exhibited rather low reactivity toward the methylide 1. Under similar conditions for 120 or 98 h until the olefin was completely consumed, 1 reacted with the olefin 2b or 2c to afford only the corresponding 1:1 adduct 3b or 3c in 41 and 45% yield, respectively[4] (Scheme 1).




1 + 2 → 3

a : $R^1$=H ; $R^2$=$R^3$= $CO_2Me$

b : $R^1$=$R^3$=$CO_2Me$ ; $R^2$=H

c : $R^1$=H ; $R^2$=$R^3$=COPh

Scheme 1

All the adducts were assigned as endo-[3 + 2] cycloadducts, 3a (6-H,7-H—trans—7-H,7a-H—cis), 3b (6-H,7-H,7a-H—all cis), and 3c (6-H,7-H—trans—7-H,7a-H—cis) on the bais of spectral data[5].

3a: Colorless needles; mp 130-131°C (dec); ir (KBr) 2230, 1740 $cm^{-1}$; $^1H$ nmr (acetone-$d_6$) δ 3.77, 3.89 (each 3H, s), 3.95 (1H, dd, 7-H, J=7.0, 11.0 Hz), 4.47 (1H, d, 6-H, J=11.0 Hz), 5.82 (1H, d, 7a-H, J=7.0 Hz), 6.14, 6.42 (each 1H, d, 2-H, 3-H, J=5.0 Hz); $^{13}C$ nmr ($CDCl_3$) δ 51.1 (tert. C), 53.3, 53.8 (each $CH_3$), 55.6 (tert. C), 58.1 (quat. C), 73.1 (tert. C), 110.3, 112.3 (each C≡N), 117.1, 123.0 (each =CH), 165.4, 168.5 (each C=O); mass spectrum m/e 293 ($M^+$).

3b: Colorless needles; mp 92-93°C (dec); ir (KBr) 2240, 1730 $cm^{-1}$; $^1H$ nmr (acetone-$d_6$) δ 3.75, 3.83 (each 3H, s), 4.18 (1H, dd, 7-H, J=7.0, 7.0 Hz), 4.50 (1H, d, 6-H, J=7.0 Hz), 6.00 (1H, d, 7a-H, J=7.0 Hz), 6.10, 6.30 (each 1H, d, 2-H, 3-H, J=5.0 Hz); $^{13}C$ nmr (acetone-$d_6$) δ 53.7, 53.8 (each $CH_3$), 56.1, 56.4 (each tert. C), 60.1 (quat. C), 73.2 (tert. C), 112.7, 115.3 (each C≡N), 116.1, 124.6 (each =CH), 167.6, 169.0 (each C=O); mass spectrum m/e 293 ($M^+$).

3c: Colorless needles; mp 136-137°C (dec); ir (KBr) 2240, 1670 $cm^{-1}$; $^1H$ nmr ($CD_3CN$) δ 5.16 (1H, dd, 7-H, J=7.0, 11.0 Hz), 5.50 (1H, d, 6-H, J=11.0 Hz), 5.67 (1H, d, 7a-H, J=7.0 Hz), 6.08, 6.30 (each 1H, d, 2-H, 3-H, J=5.0 Hz), 7.30-8.20 (10H, m); $^{13}C$ nmr ($CDCl_3$) δ 54.6, 56.5 (each tert. C), 58.9 (quat. C), 73.9 (tert. C), 73.9 (tert. C), 110.1, 112.8 (each C≡N), 116.3, 127.3 (each =CH), 191.5, 194.5 (each C=O); mass spectrum m/e 385 ($M^+$).

Next, the reaction of the methylide 1 with N-methylmaleimide 4a was investigated under similar conditions (in THF at room temperature). When 1 was allowed to react with 4a for 24 h until 4a was completely consumed, a mixture of two stereoisomeric cycloadducts, endo 5a and exo isomer 6a, was isolated in 78% yield. Although it was very difficult to separate either of them from the mixture, the structures of 5a and 6a were confirmed on the basis of inspection of $^1$H nmr spectrum (acetone-$d_6$) of the mixture; the methine protons in 5a appeared at δ 4.50 (t, 8a-H, J=8.0 Hz), 4.78 (d, 5a-H, J=8.0 Hz) and 6.14 (d, 8b-H, J=8.0 Hz), whereas those in 6a at δ 4.32 (dd, 8a-H, J=2.0, 8.5 Hz), 4.70 (d, 5a-H, J=8.5 Hz) and 5.89 (d, 8b-H, J=2.0 Hz).

As described later, it has become apparent that the endo isomer 5a is predominantly formed in an initial reaction stage. After careful chromatographic purification ($SiO_2$, $CHCl_3$) of the reaction mixture obtained from the reaction for 5 h, we have succeeded in the isolation of pure 5a as colorless prisms, mp 129-130°C (dec), in 31% yield [ir (KBr) 2330, 1700 cm$^{-1}$; $^1$H nmr (acetone-$d_6$) δ 6.14, 6.24 (each d, 2-H, 3-H, J=5.0 Hz) besides signals described above; mass spectrum m/e 260 ($M^+$)].

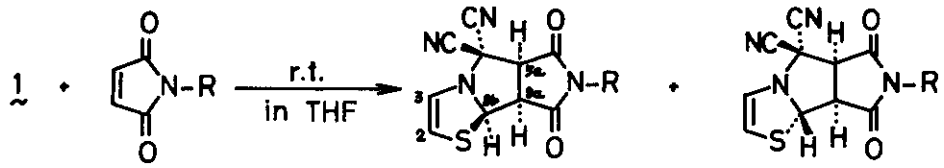
The reaction of 1 with 4a in THF was followed by $^1$H nmr spectroscopic analyses of the reaction mixture. The $^1$H nmr signals of 5a and 6a in THF are as follows: 5a δ 2.93 (s, N-$CH_3$), 4.11 (dd, 8a-H, J=8.5, 9.5 Hz), 4.46 (d, 5a-H, J=9.5 Hz), 5.96 (d, 8b-H, J=8.5 Hz), 6.13, 6.34 (each d, 2-H, 3-H, J=4.5 Hz); 6a δ 2.96 (s, N-$CH_3$), 4.16 (dd, 8a-H, J=2.0, 8.0 Hz), 4.50 (d, 5a-H, J=8.0 Hz), 5.84 (d, 8b-H, J=2.0 Hz), 6.14, 6.61 (each d, 2-H, 3-H, J=4.5 Hz). The quantitative estimation of the reaction mixture was carried out using the key signals at δ 2.88 (s, N-$CH_3$) and 6.73 (s, =CH) for 4a, at δ 2.93 (s) and 5.96 (d) for 5a, and at δ 2.96 (s) and 6.61 (d) for 6a, respectively. The selected results are shown in the following table. They indicate that the endo isomer 5a is

Table. Reaction of 1 with 4a in THF at room temperature

| Reaction time | Unreacted 4a, % | endo 5a % | exo 6a % | 5a/6a |
|---|---|---|---|---|
| 1 h | 60 | 40 | trace | |
| 2 h | 47 | 53 | trace | |
| 3.5 h | 33 | 67 | trace | |
| 24 h | 0 | 75 | 25 | 3/1 |
| 2 d | 0 | 63 | 37 | 5/3 |
| 3d | 0 | 58 | 42 | 3/2 |
| 4 d[a] | 0 | 39 | 61 | 2/3 |

[a]The reaction mixture was contaminated with small amounts of an unidentified decomposed product.

initially formed, and both the isomers increase in yields with the elapse of time until for about 24 h. Subsequently, an increase of 6a and a decrease of 5a are observed although the both are very slow, and at last the ratio, 5a/6a, in the reaction mixture after for 4 d reverses the situation.




a : R=Me ; b : R=Ph ; c : R=p-MeOC$_6$H$_4$

Scheme 2

Under similar conditions, 1 reacted with N-phenyl- 4b or N-(p-methoxyphenyl)maleimide 4c to give a mixture of the corresponding endo and exo isomer, respectively. Thus, the reaction of 1 with 4b for 45 h (until 4b disappeared) gave a mixture of endo 5b and exo isomer 6b (ca. 1:1) in 87% yield. In the reaction for 24 h, however, pure endo isomer 5b, mp 145-146°C (dec), as colorless needles was isolated in 57% yield. The structures of 5b and 6b were confirmed on the basis of $^1$H nmr spectra (acetone-$d_6$): 5b $^1$H nmr δ 4.48 (1H, t, 8a-H, J=8.0 Hz), 4.83 (1H, d, 5a-H, J=8.0 Hz), 6.15 (1H, d, 8b-H, J=8.0 Hz), 6.25, 6.65 (each 1H, d, 2-H, 3-H, J=4.5 Hz); mass spectrum m/e 322 ($M^+$). 6b $^1$H nmr δ 4.43 (dd, 8a-H, J=2.8, 9.0 Hz), 4.77 (d, 5a-H, J=9.0 Hz), 6.07 (d, 8b-H, J=2.8 Hz), 6.19, 6.46 (each d, 2-H, 3-H, J=4.5 Hz). In the reaction of 1 with 4c for 94 h (until 4c disappeared) a mixture of endo 5c and exo isomer 6c (ca. 1:1) was obtained in 56% yield. Although isolation of each isomer in a pure form was also very difficult, the structures were confirmed on the basis of $^1$H nmr spectrum (acetone-$d_6$) showing methine protons at δ 4.52 (dd, 8a-H, J=8.5, 9.3 Hz), 4.84 (d, 5a-H, J=9.3 Hz) and 6.18 (d, 8b-H, J=8.5 Hz) for 5c, and at δ 4.40 (dd, 8a-H, J=2.4, 8.5 Hz), 4.87 (d, 5a-H, J=8.5 Hz) and 6.12 (d, 8b-H, J=2.4 Hz) for 6c.

Although the mechanism for the isomerization of endo isomer 5 into exo one 6 is not evident, it seems to occur via a retro-cycloaddition reaction[6]. However, the endo isomers 3 were unchanged in THF even under reflux.

REFERENCES AND NOTES

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2. O. Tsuge, H. Shimoharada, and M. Noguchi, Heterocycles, 1981, 15, 807.
3. V. Boekelheide and N. A. Fedoruk, J. Am. Chem. Soc., 1968, 90, 3830.
4. Intractable materials were formed in significant amounts.
5. All new compounds isolated here gave satisfactory elemental analyses.
6. We previously found some examples for isomerizations via a retro-cycloaddition reaction of [3 + 2] cycloadducts (Chem. Letters, 1979, 1029; 1980, 1031).

Received, 6th August, 1982