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1,3-DIPOLAR CYCLOADDITION OF THIAZOLIUM N-PHENYLIMIDES WITH ACRYLONITRILE

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3-Anilinothiazolium salt(1) was synthesized via three steps from ammonium 3-phenyldithiocarbazate, and the cycloaddition reaction of the ylide(2) prepared from 1 with acrylonitrile was carried out in two different solvents, DMF and methanol. The reaction in DMF produced two compounds, derivatives of 2,3,3a,8b-tetrahydro-4H-2,4-ethanothiazolo[4,5-b]indole(3a and 3b), while the similar reaction in methanol unexpectedly gave bis(4,5-dimethyl-2-thiazolyl)cyanomethane (5). The structures of 3a and 3b were established by the ^{1}H-NMR(400 MHz) spectral data and the X-ray analysis.

KEYWORDS——— 1,3-dipolar cycloaddition; thiazolium N-phenylimide; 2,3,3a,8b-tetrahydro-4H-2,4-ethanothiazolo[4,5-b]indole; ^{1}H-NMR(400 MHz); X-ray analysis; sigmatropic rearrangement; bis(4,5-dimethyl-2-thiazolyl)cyanomethane

Although the synthetic methods and the chemical reactions of thiazolium N-imides have been reported by several researchers,[1-3] little attention has been paid to the chemistry of thiazolium N-arylimides until now. Here we describe the reaction of thiazolium N-phenylimide with acrylonitrile as a dipolarophile.

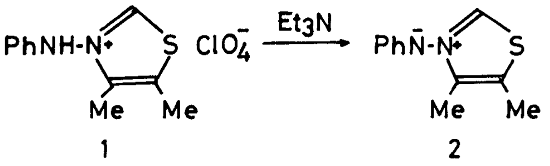


Chart 1

We synthesized 3-anilino-4,5-dimethylthiazolium salt according to the following process. The reaction of ammonium 3-phenyldithiocarbazate with 3-chlorobutan-2-one gave 3-anilino-4-hydroxy-4,5-dimethylthiazolidine-2-thione, and did not produce thiadiazine compound, unlike the similar reaction with 3-unsubstituted dithiocarbazate or its 3-benzoyl derivative.[4] Acid treatment of the above thiazolidine compound readily produced 3-anilino-4,5-dimethylthiazole-2-thione, which was desulfurized by hydrogen peroxide under acidic condition to give 3-anilino-4,5-dimethylthiazolium salt; this product was crystallized as the perchlorate(1), which was converted to the deep purple ylide(2) by elimination of perchloric acid.

In order to examine the 1,3-dipolar cycloaddition of the thiazolium ylide(2) to olefinic dipolarophile, we first attempted the reaction with acrylonitrile in DMF to obtain two compouds, 3a and 3b. Mass spectral data and microanalysis of 3a(mp 233°C, colorless needles, M$^+$ m/e 368) and 3b(mp 198-202°C, colorless needles, M$^+$ m/e 257) agreed with the molecular formulae $C_{19}H_{20}N_4S_2$(Anal. Calcd: C, 61.92; H, 5.47; N, 15.20. Found: C, 62.07; H, 5.34; N, 15.50) and $C_{14}H_{15}N_3S$(Anal. Calcd: C, 65.34; H, 5.87; N, 16.33. Found: C, 65.53; H, 6.01; N, 16.05), respectively, and each of them showed the absorption band attributable to a cyano group at 2250 cm^{-1} (KBr) in the IR spectrum. It was suggested by these observations that 3b should be an equimolar adduct of 2 to acrylonitrile, while 3a might be constituted by participation of a 4,5-dimethylthiazolyl group in a skeleton of 3b. Structures of both compounds, 3a and 3b, were finally established to be derivatives of 2,3,3a,8b-tetrahydro-4H-2,4-ethanothiazolo[4,5-b]indole by the ^{1}H-NMR(400 MHz) spectral data and the X-ray crystallographic analysis.

The ^{1}H-NMR spectral data of 3a and 3b are as follows: 3a(in $CDCl_3$) δ: 1.414, 1.797(each 3H, s, C_{3a}-CH_3, C_{8b}-CH_3), 2.312(3H, d, J=0.7 Hz, $C_{4'}$-CH_3), 2.338(3H, d, J=0.7 Hz, $C_{5'}$-CH_3), 3.334(1H, s, N_3-H), 3.705(1H, d, J=14.3 Hz, C_{10}-H), 3.966(1H, dd, J= 14.3 Hz, 7.0 Hz, C_{10}-H), 4.493(1H, d, J=7.0 Hz, C_9-H). 3b(in $CDCl_3$) δ: 1.359, 1.692(each 3H, s, C_{3a}-CH_3, C_{8b}-CH_3), 2.819(1H, d, J=4.8 Hz, N_3-H), 3.558(1H, d, J=13.9 Hz, C_{10}-H), 3.598(1H, dd, J=7.6 Hz, 6.6 Hz, C_9-H), 3.783(1H, dd, J =13.9 Hz, 6.6 Hz, C_{10}-H), 5.135(1H, dd, J=4.8 Hz, 7.6 Hz, C_2-H).

For X-ray studies of 3a and 3b, a crystal of approx. 0.4 x 0.3 x 0.1mm(3a) or 0.3 x 0.6 x 0.2mm(3b) dimensions was used. Preliminary oscillation and Weissenberg photographs unequivocally showed the crystal of 3a to be monoclinic with space group $P2_1/\underline{c}$, and 3b to be orthorhombic with space group $P2_12_12_1$ from respective systematic absences. Crystal data determined by Rigaku four-circle diffractometer with graphite-monochromated Cu Kα radiation and refined by the least-squares method are as follows: 3a, $\underline{a}$=12.528(3), $\underline{b}$=7.603(2), $\underline{c}$=21.642(5) Å, β=118.87(1)°, D_m=1.352(2) g·cm^{-3}, and $\underline{Z}$=4; 3b, $\underline{a}$=12.365(3), $\underline{b}$=7.625(2), $\underline{c}$=26.812(6) Å, D_m=1.335(3) g·cm^{-3}, and $\underline{Z}$=8. 3065(3a) or 2473(3b) independent intensities less than 2ϑ=130° were measured by the same diffractometer employing ω-2ϑ scan technique with scan speed of 4° min^{-1} and were corrected for Lorentz and polarization factors, but not for absorption effect because of the smallness of the used crystal size. The intensities of four standard reflections, measured at every 100 reflection intervals, indicated no structural deterioration during the data collection. The structures for both crystals were solved by the direct method[program MULTAN5)] and refined by block-diagonal least-squares method with anositropic temperature factors for nonhydrogen atoms and with isotropic ones for hydrogen atoms. The final $\underline{R}(\underline{R}_w)$ value was 0.071(0.070) for 3a and 0.042(0.041) for 3b.

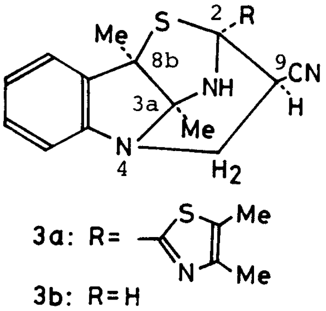
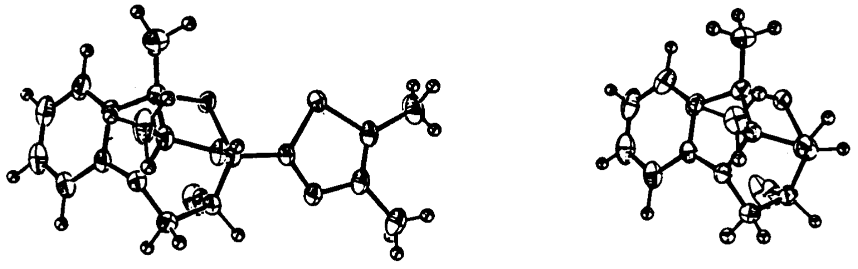


Chart 2

The molecular conformation for 3a and 3b are shown in Fig 1. Although two crystallographically independent molecules existed in crystal of 3b, one of them is shown because these two molecules are nearly stereoisomeric to each other.

Formation of the tetracyclic system B in 3a and 3b(Chart 3b) was believed to arise from rearrangement of an intermediate, tetrahydropyrazolo[5,1-b]thiazole(A), which might be initially formed by the 1,3-cycloaddition of thiazolium N-phenylimide with a dipolarophile; such an aspect can be elucidated by the reaction mechanism including a 3,3-sigmatropic shift followed by a break of the N-N bond, as pointed out by Huisgen6) in the formation of a pentacyclic system compound from



3a 3b

Fig 1

tetrahydropyrazolo[5,1-a]isoquinoline. In the present work, the intermediates, the compounds of type A, were transformed to the compound of type B so fast as to be not isolable.

Formations of 3a and 3b were affected by the procedures for the reaction; when the reaction was carried out by dropwise addition of triethylamine to the mixture of 1 and acrylonitrile in DMF, 3a and 3b were only isolated in 12% and 6% yield, respectively, while when acrylonitrile was added to a solution of the ylide(2) prepared from 1 and triethylamine in DMF, 3a was obtained in 54% yield without formation of 3b. As for the formation of 3a, it has not been sufficiently elucidated how the thiazolyl substituent at the 2-position was introduced. However, from the observations on yields of both products under two different reaction conditions and the fact that an attempt to obtain 3a by the reaction of 3b with 2 was unsuccessful, we posit that dimerization proceeds between two moles of the thiazolium N-

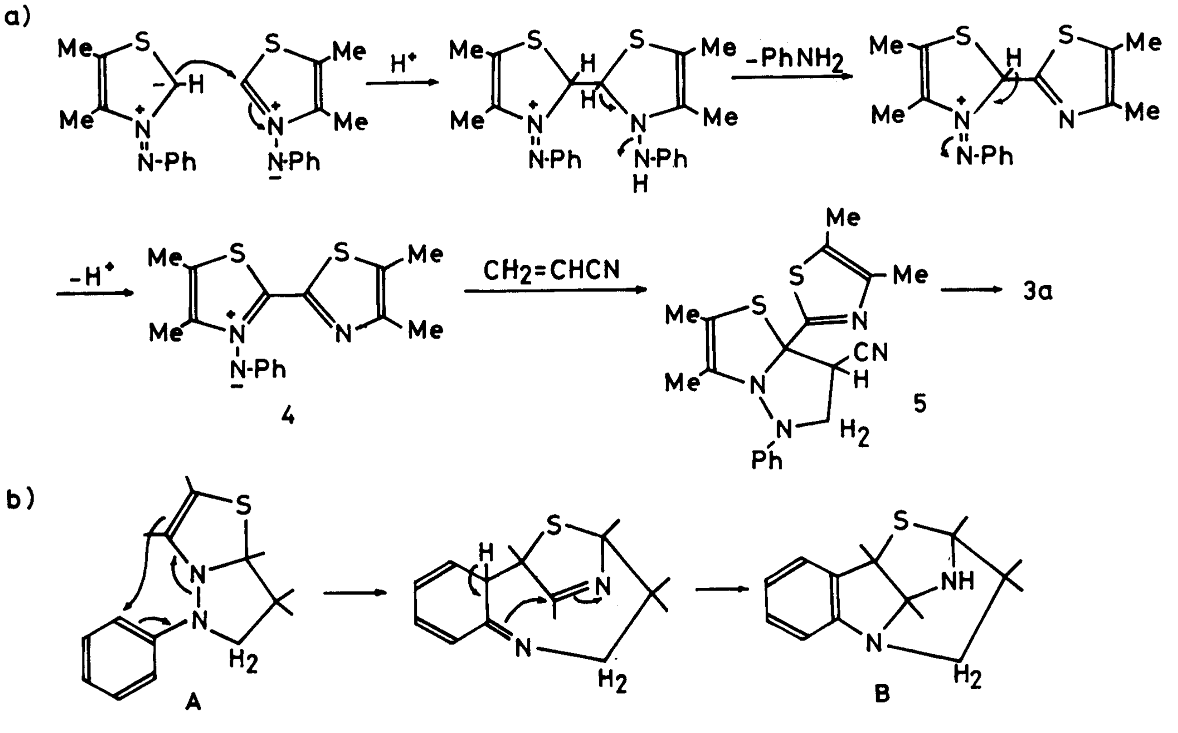


Chart 3

phenylimide(2), giving 2-(2'-thiazolyl)thiazolium N-phenylimide with elimination of aniline, and subsequent 1,3-dipolar cycloaddition of the resulting ylide(4) with acrylonitrile, probably occurs to give 7a-(2'-thiazolyl)-5,6,7,7a-tetrahydropyrazolo[5,1-b]thiazole(5) as shown in Chart 3a.

On the other hand, when the same reaction was carried out in methanol instead of DMF, a new compound 6 as well as 3a was isolated in 15% and 25% yields, respectively. Mass spectral data and microanalysis of 6(mp 234-235°C, yellow needles, M^+ m/e 263) agreed with the molecular formula $C_{12}H_{13}N_3S_2$(Anal. Calcd: C, 54.72; H, 4.97; N, 15.94. Found: C, 54.42; H, 4.90; N, 15.90). The IR spectrum showed the existence of a cyano group by the absorption band at 2180 cm^{-1}; and the ^1H-NMR(90 MHz, in DMSO-d_6) spectrum exhibited an overlapping signal attributable to four methyl groups at δ 2.22(12H, s) and a broad singlet attributable to an imino proton at about δ 9.5-10.2.

Treatment of 6 with 20% sulfuric acid under heating resulted in elimination of a cyano group to give bis(4,5-dimethyl-2-thiazolyl)methane, which was identified with an authentic sample synthesized from malondithioamide and 3-chlorobutan-2-one. From these observations, compound 6 was determined to be bis(4,5-dimethyl-2-thiazolyl)cyanomethane. A molecule of 6 is estimated to take a plane structure like an aromatic tricyclic compound, because the extremely broad signal of the imino proton in ^1H-NMR spectrum suggests that the proton is delocalized between nitrogen atoms on two thiazole rings.

One of possible pathways for formation of 6 from 2 is shown in Chart 4.

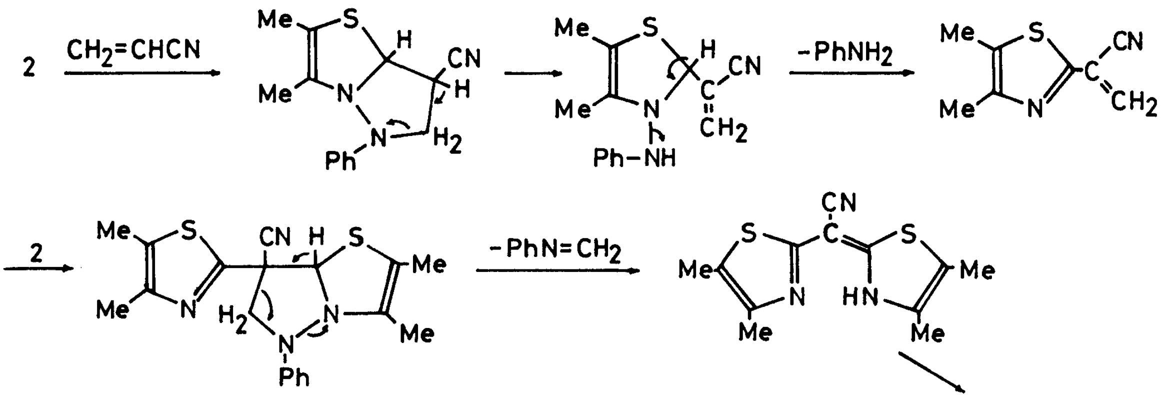
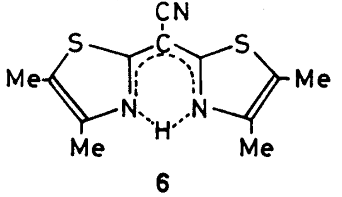


Chart 4



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