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1,3-DIPHENYLTHIAZOLO[3,4-a]BENZIMIDAZOLE, A NEW RING-FUSED TETRAVALENT SULFUR THIAZOLE SYSTEM[1)]

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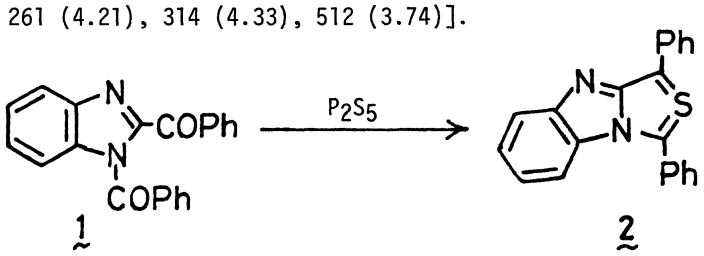
1,3-Diphenylthiazolo[3,4-a]benzimidazole, a new 10π-electron heterocycle containing tetravalent sulfur, was prepared by the reaction of 1,2-dibenzoylbenzimidazole with phosphorus pentasulfide in refluxing toluene. Its cycloadditions with alkenes and alkynes occurred across the thiocarbonyl ylide dipole in highly stereoselective and/or regiospecific fashions.

Recently, several 10π-electron fused thiophenes containing tetravalent sulfur have been prepared and subjected to cycloadditions.[2-8)] Examples have included fuan[3)], pyrrole[3,4)], pyrazole[5)], isothiazole[6)], 1,2,5-thiadiazole[7)], and 1,2,5-oxadiazole[8)] ring systems fused to a thiophene nucleus, all of which functioned as the thiocarbonyl ylide dipole in cycloaddition reactions. However, no information concerning regiochemistry in cycloadditions of tetravalent sulfur compounds has so far been obtained. As 10π-electron fused heterocycles incorporated tetravalent sulfur other than fused thiophenes thiazolo[3,4-b]indazole[9)] and thiazolo[3,4-b]isoindole[10)] systems have also been reported: the former functioned as the thiocarbonyl ylide or azomethine imine dipole toward N-phenylmaleimide or dimethyl acetylenedicarboxylate respectively, whereas the latter was found to react as the azomethine ylide dipole with electron-deficient alkenes.

Thus, our interest has been directed toward a new thiazolo[3,4-a]benzimidazole system containing tetravalent sulfur which would be expected to function as the thiocarbonyl ylide dipole alone, offering useful information concerning regiochemistry in cycloaddition reactions. In this communication we wish to report the synthesis of such a system, 1,3-diphenylthiazolo[3,4-a]benzimidazole, and its cycloadditions with alkenes and alkynes.

Synthesis of 1,3-Diphenylthiazolo[3,4-a]benzimidazole. One of the most usual synthetic routes to the tetravalent sulfur system is the reaction of appropriate dicarbonyl compounds with phosphorus pentasulfide (P_2S_5). Thus, the reaction of 1,2-dibenzoylbenzimidazole (1)[11)] with P_2S_5 has been investgated under various conditions, and it has eventually been found that the treatment of 1 with 3 molar amounts of P_2S_5 in refluxing toluene, under nitrogen, for 3 h afforded a 49% yield of 1,3-diphenylthiazolo[3,4-a]benzimidazole (2) as reddish violet needles [mp 165-167°C (dec); NMR ($CDCl_3$) δ 6.85-8.20 (m); UV λ_{max}^{EtOH} nm (log ε) 261 (4.21), 314 (4.33), 512 (3.74)].



1 2

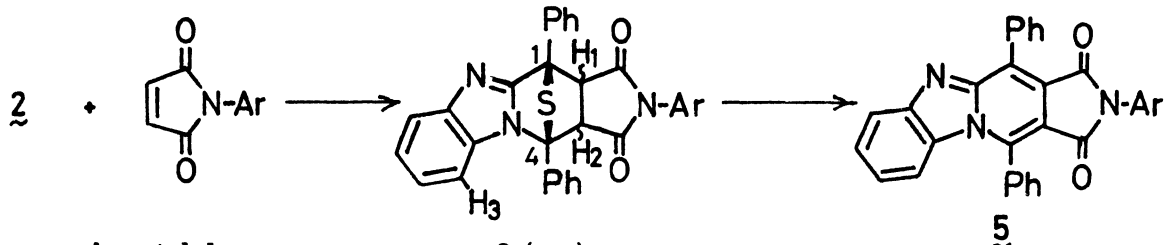
The mass spectrum of 2 showed very intense parent ion at m/e 326 (100%) and doubly charged ion at m/e 163 (7%), reflecting the stability of 2 as was observed with other tetravalent sulfur compounds. Additional evidence in support of structure 2 comes from the formation of cycloadducts described below.

Cycloaddition Reactions of Thiazolobenzimidazole 2. When a mixture of equimolar amounts of 2 and N-(p-tolyl)maleimide in benzene was refluxed under nitrogen for 2.5 h, two 1:1 adducts, 3 and 4, were obtained in 71 and 16% yields respectively. On heating in acetic acid for 1 h, both 3 and 4 afforded the same pyrido[1,2-a]benzimidazole derivative 5 in a quantitative yield respectively.[12] It is thus evident that the maleimide adds across the thiocarbonyl ylide dipole of 2.

3: colorless prisms; mp 216-217°C (dec); IR (KBr) 1720 cm^{-1}; NMR ($CDCl_3$) δ 2.30 (3H, s), 3.92 (1H, d, H_1, J=6.0 Hz), 4.36 (1H, d, H_2, J=6.0 Hz), 5.95 (1H, ddd, H_3, J=8.0, 2.0, 1.5 Hz)[13]; MS m/e 513 (M^+).

4: colorless needles; mp 235-236°C (dec); IR (KBr) 1720 cm^{-1}; NMR ($CDCl_3$) δ 2.19 (3H, s), 4.91 (1H, d, H_1, J=9.0 Hz), 5.16 (1H, d, H_2, J=9.0 Hz), 6.35 (1H, ddd, H_3, J=8.0, 2.0, 1.5 Hz); MS m/e 513 (M^+).

5: yellow needles; mp > 300°C; IR (KBr) 1760, 1720 cm^{-1}; NMR ($CDCl_3$) δ 2.31 (3H, s), 6.36, 7.03 (each 1H, ddd, J=8.0, 2.0, 1.5 and 8.0, 8.0, 2.0 Hz respectively), 7.32-8.0 (16H, m); MS m/e 419 (M^+).



Scheme 1

On the basis of NMR spectra, 3 and 4 were assigned as the exo- and endo-adducts respectively. Thus, the protons H_1 and H_2 in 4 appear at lower field than those in 3, because of the deshielding effect of the sulfur bridge. Analogous effects have been noted for other related exo-endo adducts pairs containing a sulfur bridge.[8,14] An inspection of the Dreiding models indicated that the proton H_3 in 3 is affected by stronger shielding effect of the 4-phenyl group than that in 4. In fact, the proton H_3 in 3 appears at higher field than that in 4.

Next, we have investigated the cycloadditions with acyclic olefins such as dimethyl maleate, fumarate, methyl crotonate, and acrylate under similar conditions. The reaction of 2 with maleate gave the sole cycloadduct 6 in 64% yield, whereas 2 reacted with fumarate or crotonate to give two isomeric cycloadducts 7 and 8, or 9 and 10 in 78 and 13, or 51 and 5% yields respectively. In the reaction with acrylate 2 the cycloadduct 11 was obtained in 76.5% yield. On treatment with silica gel 11 was readily converted into the ring-opening compound 12 (Scheme 2).

6: colorless needles; mp 190.5-191°C (dec); IR (KBr) 1750, 1730 cm^{-1}; NMR ($CDCl_3$) δ 3.33, 3.60 (each 3H, s), 4.08 (1H, d, H_1, J=9.0 Hz), 4.30 (1H, d, H_2, J=9.0 Hz), 6.02 (1H, ddd, H_3, J=8.0, 2.0, 1.5 Hz); MS m/e 470 (M^+).

7: colorless prisms; mp 181.5-183°C (dec); IR (KBr) 1730 cm^{-1}; NMR ($CDCl_3$) δ 3.23, 3.37 (each 3H, s), 3.92 (1H, d, H_1, J=4.0 Hz), 5.14 (1H, d, H_2, J=4.0 Hz), 6.58 (1H, ddd, H_3, J=7.5, 1.5, 1.0 Hz); MS m/e 470 (M^+).

8: colorless needles; mp 191-192°C (dec); IR (KBr) 1760, 1740 cm^{-1}; NMR ($CDCl_3$) δ 3.44, 3.68 (each 3H, s), 4.38, 4.53 (each 1H, H_1, H_2, J=4.0 Hz), 6.05 (1H, ddd, J=7.5, 1.5, 1.0 Hz); MS m/e 470 (M^+).

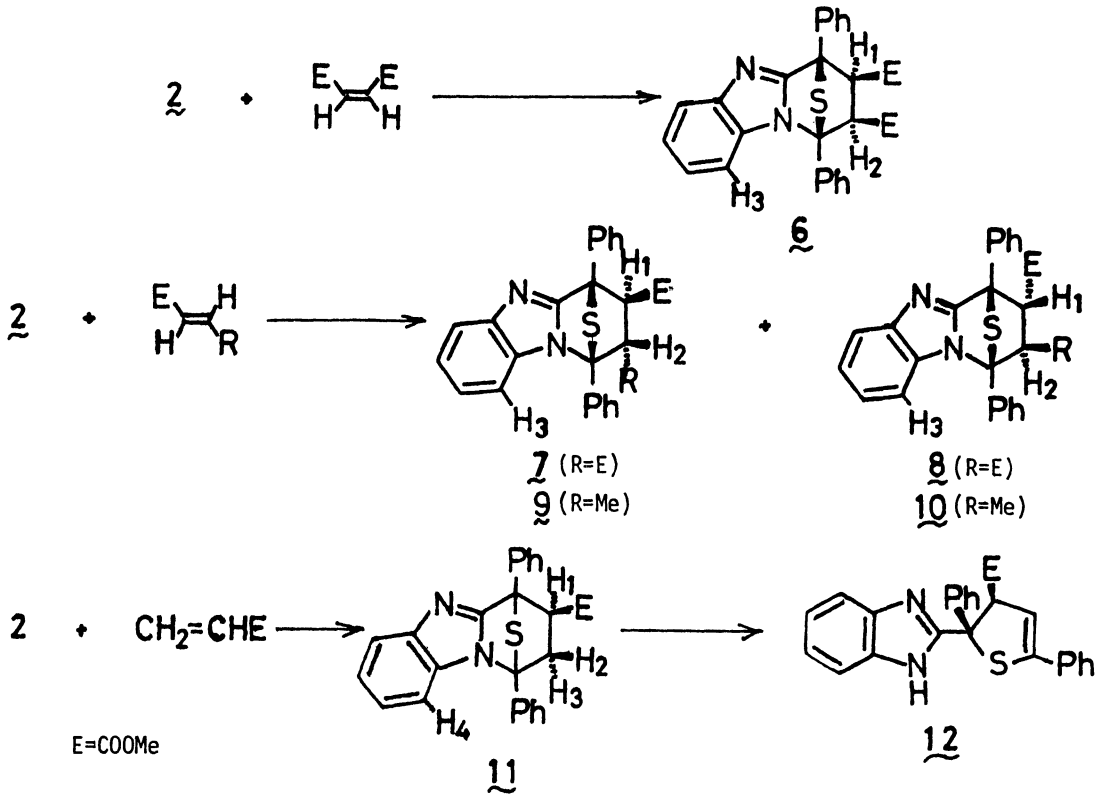
9: pale yellow prisms; mp 134-138°C (dec); IR (KBr) 1730 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (3H, d, CH_3, J=7.0 Hz), 3.07 (1H, d, H_1, J=4.0 Hz), 3.40 (3H, s), 4.25 (1H, dq, H_2, J=7.0, 4.0 Hz), 6.61 (1H, ddd, H_3, J=8.0, 2.0, 1.5 Hz); MS m/e 426 (M^+).

10: colorless prisms; mp 129-132°C (dec); IR (KBr) 1740 cm^{-1}; NMR ($CDCl_3$) δ 1.47 (3H, d, CH_3, J=7.0 Hz), 3.46 (3H, s), 3.60 (1H, dq, H_2, J=7.0, 4.0 Hz), 3.89 (1H, d, H_1, J=4.0 Hz), 6.13 (1H, ddd, H_3, J=

8.0, 2.0, 1.5 Hz); MS m/e 426 (M^+).

11: colorless prisms; mp 169-174°C (dec); IR (KBr) 1740 cm^{-1}; NMR ($CDCl_3$) δ 2.86 (1H, dd, H_3, J=11.0, 7.0 Hz), 3.32 (3H, s), 3.47 (1H, dd, H_1, J=7.0, 4.5 Hz), 3.62 (1H, dd, H_2, J=11.0, 4.5 Hz), 6.12 (1H, ddd, H_4, J=7.5, 1.5, 1.0 Hz); MS m/e 412 (M^+).

12: colorless needles; mp 147-149°C (dec); IR (KBr) 3150, 1720 cm^{-1}; NMR ($CDCl_3$) δ 5.52 (1H, d, CH, J=3.0 Hz), 6.11 (1H, d, =CH, J=3.0 Hz), 7.20-7.62 (14H, m, ArH + NH).[15]



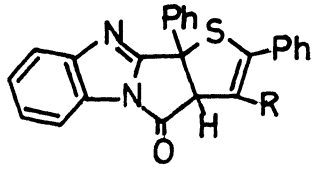
Scheme 2

Structural elucidation of adducts 6 — 11 was accomplished on the basis of spectral data as well as chemical conversions. From the values of coupling constants between H_1 and H_2, it is evident that the starting olefins are retained in cycloadducts 6 — 10.

On heating in acetic acid for 1 h, 9 and 10 were converted into the same thieno[2',3':3,4]tetrahydropyrrolo[1,2-a]benzimidazole compound 13 in 61 and 69% yields respectively. Similarly, 11 afforded an 81% yield of the same type of compound 14, which was also obtained on heating 12 in acetic acid. It is clear that 13 and 14 are formed via the corresponding 2-(2-dihydrothienyl)benzimidazoles like 12 with loss of methanol.[16] It is thus reasonable to conclude that the methoxycarbonyl group is located at 2-position in the respective cycloadducts 9 — 11.

13: pale yellow prisms; mp 176-178°C; IR (KBr) 1760 cm^{-1}; NMR ($CDCl_3$) δ 2.14 (3H, s), 4.73 (1H, s, CH), 7.10-8.14 (14H, m); MS m/e 394 (M^+).

14: colorless needles; mp 185-186°C (dec); IR (KBr) 1760 cm^{-1}; NMR ($CDCl_3$) δ 4.90 (1H, d, CH, J=4.0 Hz), 5.98 (1H, d, =CH, J=4.0 Hz), 7.16-8.0 (14H, m); MS m/e 380 (M^+).



13 (R=Me)
14 (R=H)

We have next investigated the reaction of 2 with dimethyl acetylenedicarboxylate (DMAD) and methyl propiolate. When 2 was allowed to react with 2 molar amounts of DMAD in refluxing toluene for 24 h, the pyrido[1,2-a]benzimidazole derivative

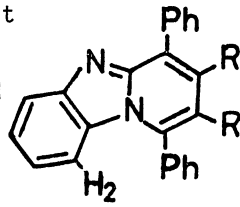
15 was obtained in 42% yield. It is evident that 15 was derived from desulfurization of the expected cycloadduct across the thiocarbonyl ylide dipole of 2. Similarly, 2 reacted with propiolate to afford two isomeric pyrido[1,2-a]benzimidazoles 16 and 17 in 49 and 4% yields respectively.

15: yellow green crystals; mp 204.5-206°C; IR (KBr) 1740, 1720 cm^{-1}; NMR ($CDCl_3$) δ 3.54, 3.59 (each 3H, s), 6.08 (1H, ddd, H_2, J=8.5, 1.5, 1.0 Hz), 6.95, 7.36 (each 1H, ddd, J=8.5, 8.5, 1.5 Hz), 7.40-7.72 (10H, m), 7.90 (1H, ddd, J=8.5, 1.5, 1.0 Hz); MS m/e 436 (M^+).

16: yellow needles; mp 233-234°C; IR (KBr) 1730 cm^{-1}; NMR ($CDCl_3$) δ 3.65 (3H, s), 6.61 (1H, ddd, H_2, J=8.5, 1.5, 1.0 Hz), 7.00 (1H, ddd, J=8.5, 8.5, 1.5 Hz), 7.08 (1H, s, H_1), 7.38 (1H, ddd, J=8.5, 8.5, 1.5 Hz), 7.40-7.65 (10H, m), 7.94 (1H, ddd, J=8.5, 1.5, 1.0 Hz); MS m/e 378 (M^+).

17: pale yellow needles; mp 222-223°C; IR (KBr) 1730 cm^{-1}; NMR ($CDCl_3$) δ 3.69 (3H, s), 5.94 (1H, ddd, H_2, J=8.5, 1.5, 1.0 Hz), 6.91, 7.38 (each 1H, ddd, J=8.5, 8.5, 1.5 Hz), 7.40-7.70 (8H, m), 7.92 (1H, ddd, J=8.5, 1.5, 1.0 Hz), 8.00-8.15 (2H, m), 8.11 (1H, s, H_1); MS m/e 378 (M^+).

Such an addition followed by desulfurization is consistent with that observed previously in other tetravalent sulfur systems.[17] On the basis of NMR spectral data, it was deduced that 16 and 17 would be 2- and 3-methoxycarbonyl derivative respectively. Thus, the proton H_2 in 17 appears at higher field than that in 16, because of shielding effect of 4-phenyl group. In addition, the regiochemistry of 16 was confirmed by the following fact. Treatment of 11 with sodium methoxide in methanol at room temperature for 1 h afforded 16 in 28% yield, along with recovery (52%) of 11.



15 (R^1=R^2=COOMe)
16 (R^1=COOMe, R^2=H_1)
17 (R^1=H_1, R^2=COOMe)

As described above, cycloadditions of olefins and acetylenes occurred across the thiocarbonyl ylide dipole of 2 by highly stereoselective and regiospecific processes.

References and Notes

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10) H. Shimoharada, S. Ikeda, S. Kajigaeshi, and S. Kanamasa, Chem. Lett., 1977, 1237.
11) The compound 1 was prepared by benzoylation of 2-benzoylbenzimidazole with benzoyl chloride in pyridine [mp 103-104°C; IR (KBr) 1720, 1630 cm^{-1}; MS m/e 326 (M^+)]. All new compounds in this communication gave satisfactory elemental analyses.
12) Treatment of 3 and 4 with sodium methoxide in methanol at room temperature for 1 h afforded 5 in 97 and 3% yields respectively.
13) In this communication NMR spectral data of aromatic protons except H_3 (or H_4 in 11) in all cycloadducts of 2 to olefins are omitted.
14) M. P. Cava, N. M. Pollack, O. A. Mamer, and M. J. Mitchell, J. Org. Chem., 36, 3932 (1971); M. P. Cava, N. M. Pollack, and G. A. Dieterle, J. Am. Chem. Soc., 95, 2558 (1973); M. P. Cava, M. Behforonz, G. E. M. Husbands, and M. Srinivasan, ibid., 95, 2561 (1973).
15) ^{13}C NMR (DMSO-d_6) of 12: δ 51.26 (q, $\underline{C}H_3$), 62.03 (d, tert. $\underline{C}$), 66.66 (s, quat. $\underline{C}$), 116.03 (d, =$\underline{C}$H).
16) On heating in acetic acid cycloadducts 6, 7, and 8 afforded the same thieno[2',3':3,4]tetrahydropyrrolo[1,2-a]benzimidazole (R=COOMe) [mp 191-192°C (dec); IR (KBr) 1750, 1700 cm^{-1}; NMR (DMSO-d_6) δ 3.62 (3H, s), 5.65 (1H, s), 7.34-8.00 (14H, m); MS m/e 438 (M^+)].
17) For example, O. Tsuge and T. Takata, J. Org. Chem., 45 (1980) in press.

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