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NOVEL CAGE COMPOUNDS FROM THE REACTIONS OF THIAZOLIUM N-METHYLIDES WITH METHYLENECYCLOPROPENES

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Thiazolium N-dicyanomethylide and N-phenacylide reacted with methylenecyclopropenes bearing a carbonyl functional group at the 4-position in THF to give novel cage compounds arising from an intramolecular cyclization of the initially formed endo-[3 + 2] cycloadducts. Although the reaction of the N-dicyanomethylide with a methylenecyclopropene having two cyano groups at the 4-position in THF gave no adduct, the same reaction in an alcohol afforded a cage compound incorporated with the alcohol.

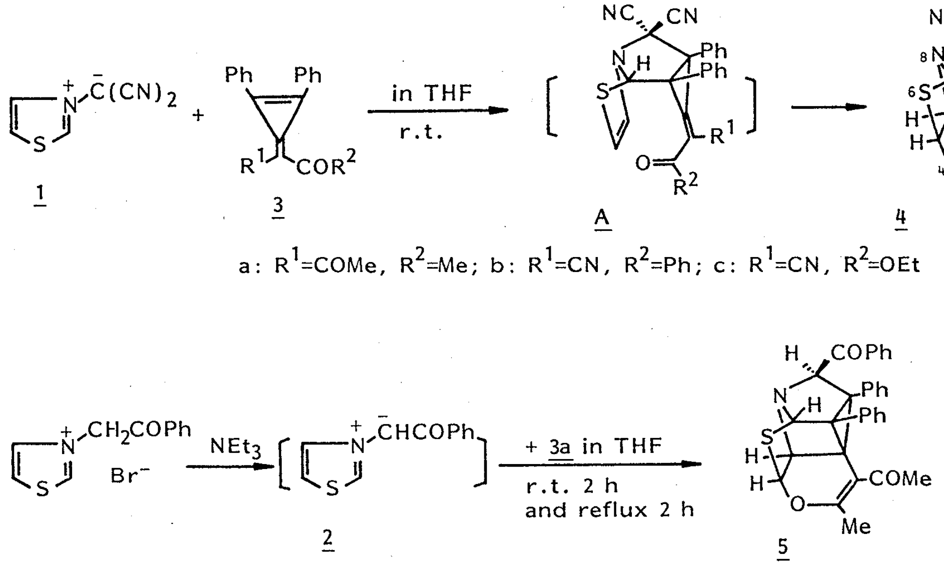
KEYWORDS —— thiazolium N-dicyanomethylide; N-phenacylide; methylenecyclopropenes; cycloaddition reaction; 4,6,8-oxathiazapentacyclo-$[6.3.1.0^{1,10}.0^{5,11}.0^{7,11}]$dodecenes; 4,6-thiazatetracyclo$[6.1.0.0^{2,6}.0^{5,9}]$-nonanes

It is known that methylenecyclopropenes are versatile reagents in organic syntheses.[1] Methylenecyclopropenes undergo cycloaddition reactions with a variety of 1,3-dipoles;[1-3] the modes of these reactions depend not only on the nature of 1,3-dipoles, but also on the subsituents at the 4-position of methylenecyclopropenes.[4] Recently, we have reported unique reactions of benzothiazolium N-phenacylide[5,6] and thiazolium N-methylides[7] with methylenecyclopropenes. It is particularly noteworthy that the reaction of thiazolium N-methylides with a methylenecyclopropene bearing an aryl group at the 4-position gives novel cage compounds arising from an intramolecular Diels-Alder reaction of the initially formed endo-[3 + 2] cycloadducts, followed by a hydrogen shift.[7] To extend this new route for the formation of cage compounds, we planned to investigate the reaction of thiazolium N-methylides with methylenecyclopropenes having substituents at the 4-position other than an aryl group. In the present communication we report the formation of novel cage compounds from the reaction of thiazolium N-dicyanomethylide 1 and N-phenacylide 2 with methylenecyclopropenes bearing a carbonyl functional group and two cyano groups at the 4-position.

A solution of the methylide 1[8] (1.0 mmol) and 3-(2,3-diphenyl-2-cyclopropenylidene)-2,4-pentanedione 3a[9] (1.0 mmol) in dry THF (15 ml) was stirred at room temperature for 4 days until the 3a was completely consumed. The reaction mixture was then evaporated in vacuo to leave a residue, which was purified by chromatography on silica gel, using benzene as an eluent, to give the 1:1 adduct 4a, mp 188-189°C (dec.), in 94% yield. Similarly, the methylide 1 reacted with 2-cyano-(2,3-

diphenyl-2-cyclopropenylidene)acetophenone 3b$^{10)}$ for 6 days and with 2-cyano-(2,3-diphenyl-2-cyclopropenylidene)acetate 3c$^{10)}$ for 6 days to afford the corresponding 1:1 adducts 4b, mp 278-279°C (dec.), and 4c, mp 162-164°C (dec.), in 100 and 96% yields, respectively.

In the reaction of the methylide 2 with 3a a 1:1 adduct was also obtained. To a solution of 3-phenacylthiazolium bromide (1.0 mmol) and 3a (1.0 mmol) in dry THF (50 ml) NEt_3 (1.0 mmol) was added at room temperature with stirring under nitrogen. After the mixture was stirred for 2 h under the same conditions, the precipitated triethylammonium bromide (quantitative) was removed by filtration. The filtrate was refluxed for 2 h, and then evaporated in vacuo to leave a residue, which was chromatographed on silica gel using benzene as an eluent to give the 1:1 adduct 5, mp 203-204°C (dec.), in 93% yield.



a: R^1=COMe, R^2=Me; b: R^1=CN, R^2=Ph; c: R^1=CN, R^2=OEt

Chart 1

On the basis of spectral data,$^{11)}$ the adducts 4 and 5 were identified as the cage compounds, 4,6,8-oxathiazapentacyclo[6.3.1.0^{1,10}.0^{5,12}.0^{7,11}]dodecenes. It is evident that the reaction proceeds via an intramolecular cyclization of initially formed endo-[3 + 2] cycloadducts like A (Chart 1).

As reported previously,$^{5)}$ 2-(2,3-diphenyl-2-cyclopropenylidene)malononitrile 6$^{10)}$ exhibited a behavior toward benzothiazolium N-phenacylide different from other methylenecyclopropenes. Thus we have investigated the reaction of the methylide 1 with 6. Although the reaction in THF gave no adduct,$^{12)}$ it has been found that 1 in reaction with 6 in an alcohol gives a type of cage compound different from 4 or 5. The reaction in refluxing ethanol or methanol for 24 h afforded a product 7, mp 112-113°C (dec.), or 8, mp 194-196°C (dec.), in 85 or 72% yield respectively.

Structural elucidation of the products 7 and 8, 4,6-thiazatetracyclo[6.1.0.0^{2,6}.0^{5,9}]nonanes, was accomplished on the basis of spectral data.$^{13)}$ The protons at the 2- and 3-positions in both 7 and 8 each appeared as singlets in the ^{1}H NMR spectra, indicating that 2-H and 3-H are trans.14)

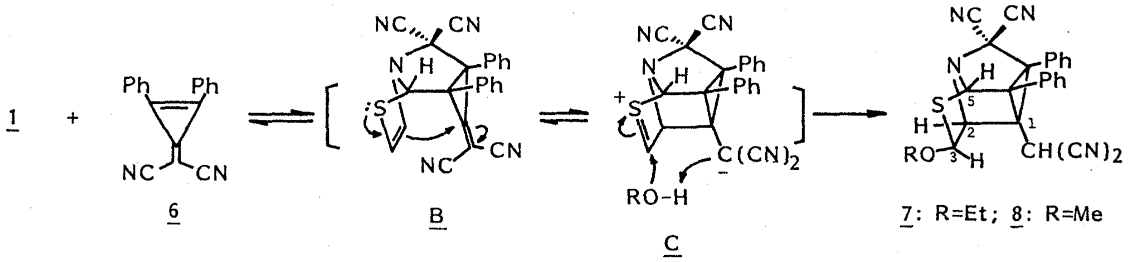


Chart 2

The pathway for the formation of 7 or 8 is illustrated in Chart 2. In a manner similar to 3, 1 adds to 6 to yield the endo-[3 + 2] cycloadduct B. Subsequent ring closure of B generates a betaine C. Although the processes leading to B and C are reversible, since 1 and 6 were recovered quantitatively from the reaction in THF,12) C reacts with ethanol or methanol to give stable cage compounds 7 or 8. It seems to give analogous cage compounds from the reaction of 1 with 6 in the presence of nucleophiles other than alcohol; work along this line is in progress.

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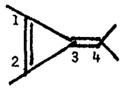
4) The numbering of methylenecyclopropene system is as follows.1)



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11) All new compounds in this paper gave satisfactory elemental analyses.
4a: colorless prisms; IR (KBr) 2240, 1665 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.51, 2.12 (each 3H, s), 4.32 (1H, d, 12-H, J=5.0 Hz), 5.08 (1H, s, 7-H), 6.40 (1H, d, 5-H, J=5.0 Hz), 6.90-7.45 (10H, m); ^{13}C NMR ($CDCl_3$) δ 18.5, 30.6 (each q, CH_3), 29.5, 42.0, 45.6, 63.5 (each s, quat. C), 69.7, 78.9, 83.8 (each d, tert. C); MS m/e 437 (M^+).
4b: colorless prisms; IR (KBr) 2250, 2200, 1600 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 4.92 (1H, d, 12-H, J=5.0 Hz), 6.18 (1H, s, 7-H), 6.91 (1H, d, 5-H, J=5.0 Hz), 6.98-7.65 (15H, m); ^{13}C NMR (DMSO-d_6) δ 27.8, 43.1, 47.0, 66.3 (each s, quat. C), 67.6, 74.6, 85.3 (each d, tert. C); MS m/e 482 (M^+).
4c: colorless prisms; IR (KBr) 2240, 2200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.23 (3H, t),

4.12 (2H, q), 4.38 (1H, d, 12-H, J=5.0 Hz), 5.47 (1H, s, 7-H), 6.53 (1H, d, 5-H, J=5.0 Hz), 6.70-7.80 (10H, m); ^{13}C NMR ($CDCl_3$) δ 14.6 (q, CH_3), 28.5, 41.2, 47.4, 67.1 (each s, quat. C), 66.3 (t, OCH_2), 68.3, 75.3, 86.4 (each d, tert. C); MS m/e 450 (M^+).

5: colorless prisms; IR (KBr) 1680, 1665 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28, 2.08 (each 3H, s), 3.92 (1H, d, 12-H, J=5.0 Hz), 4.64 (1H, s, 9-H), 5.44 (1H, s, 7-H), 6.34 (1H, d, 5-H, J=5.0 Hz), 6.47-8.35 (15H, m); ^{13}C NMR ($CDCl_3$) δ 18.0, 29.8 (each q, CH_3), 30.2, 39.2, 41.8 (each s, quat. C), 71.0, 73.0, 78.9, 84.7 (each d, tert. C); MS m/e 491 (M^+).

12) The starting materials 1 and 6 were quantitatively recovered.

13) 7: colorless needles; IR (KBr) 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.32 (3H, t), 3.32-3.92 (2H, pair of double q), 4.06 (1H, s, $HC(CN)_2$), 4.86 (1H, s, 2-H), 5.33 (1H, s, 5-H), 5.87 (1H, s, 3-H), 6.83-7.70 (10H, m); ^{13}C NMR ($CDCl_3$) δ 14.6 (q, CH_3), 20.0 (d, $HC(CN)_2$), 33.6, 42.2, 48.1, 63.3 (each s, quat. C), 65.4 (t, CH_2), 77.5, 77.9, 84.5 (each d, tert. C); MS m/e 449 (M^+).

8: colorless needles; IR (KBr) 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.45 (3H, s), 4.04 (1H, s, $HC(CN)_2$), 4.87 (1H, s, 2-H), 5.31 (1H, s, 5-H), 5.78 (1H, s, 3-H), 6.84-7.62 (10H, m); MS m/e 435 (M^+).

14) An inspection of the Dreiding models indicates that the dihedral angle between 2-H and 3-H is ca. 90° when 2-H and 3-H are trans.

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