

DIELS-ALDER TYPE REACTIONS OF 2-PHENYL-1-AZASPIRO[2.2]PENT-1-ENE

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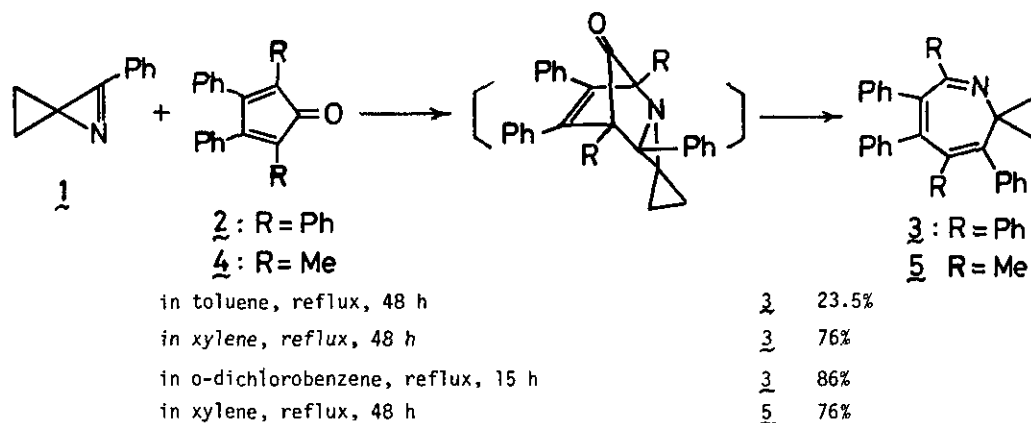
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Abstract — Highly strained 2-phenyl-1-azaspiro[2.2]pent-1-ene reacted with cyclopentadienones to give the corresponding 2H-azepine-2-spiro-cyclopropanes directly, with loss of carbon monoxide. However, the reaction of the azaspiropentene with 1,3-diphenylisobenzofuran afforded the exo-Diels-Alder adduct. The azaspiropentene reacted with thiobenzoyl isocyanates to give 3-aryl-5-oxo-2,4,6-thiadiazabicyclo[5.2.0]nona-3,6-dienes arising from the rearrangement of initial [4 + 2] cycloadducts.

In contrast to a trisubstituted 1-azirine such as 3,3-dimethyl-2-phenyl-1-azirine¹, 2-phenyl-1-azaspiro[2.2]pent-1-ene **1**², whose structure is a trisubstituted 1-azirine, exhibited high reactivity toward 1,3-dipoles^{3,4}. The high reactivity of **1** may be attributable to its highly strained structure. We have now found that **1** was also reactive for Diels-Alder reactions. In this paper we wish to report on the cycloaddition reactions of **1** with cyclopentadienones, 1,3-diphenylisobenzofuran, and thiobenzoyl isocyanates.

Reaction of 1 with Cyclopentadienones. It is known that the reaction of monosubstituted and 2,3-disubstituted 1-azirines with cyclopentadienones proceeds via initial formation of Diels-Alder adducts, followed by loss of carbon monoxide to give primarily 2H-azepines which in many cases rearranged to the more stable 3H-azepines⁵. However, 3,3-dimethyl-2-phenyl-1-azirine did not react with tetracyclone even on being refluxed in xylene for 13 days^{5a}. We report here the first example for the cycloaddition of a trisubstituted 1-azirine to cyclopentadienones.

When a solution of **1** in toluene was refluxed for a long time with an equimolar amount of tetracyclone **2** under nitrogen, a 2H-azepine, pentaphenyl-2H-azepine-2-spiro-cyclopropane **3**, was obtained in a low yield. However, the same reaction in higher boiling solvents such as xylene and o-dichlorobenzene gave **3** in good yields respectively. Similarly, **1** reacted with 2,5-dimethyl-3,4-diphenylcyclopentadienone **4** in refluxing xylene to give the corresponding 2H-azepine derivative **5** (Scheme 1).



Scheme 1

Structural elucidation of $\underline{3}$ and $\underline{5}$ was accomplished on the basis of spectral data⁶. The ^1H and ^{13}C NMR spectra indicated the presence of cyclopropyl ring, and mass spectrum exhibited the major fragment ion $[\text{M}^+ - \text{RCN}]$ besides molecular ion $[\text{M}^+]$.

$\underline{3}$: mp 188-189 $^{\circ}$; colorless prisms; ^1H NMR (CDCl_3) δ 0.90-1.40 (4H, m), 6.50-7.58 (25H, m); ^{13}C NMR (CDCl_3) δ 14.0, 17.1 (each CH_2), 47.1 (quat. C), 171.5 ($\text{C}=\text{N}$); $\text{UV}\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ) 236 (4.23), 280 (3.92); MS m/e (rel. intensity %) 499 (M^+ , 100), 396 ($\text{M}^+ - \text{PhCN}$, 90), 321 ($\text{M}^+ - \text{Ph-C}\equiv\text{C-Ph}$, 92).

$\underline{5}$: mp 172-173 $^{\circ}$; colorless prisms; ^1H NMR (CDCl_3) δ 0.60-1.45 (4H, m), 1.61, 2.07 (each 3H, s), 6.97-7.45 (15H, m); ^{13}C NMR (CDCl_3) δ 14.0, 17.2 (each CH_2), 19.0, 27.8 (each CH_3), 46.1 (quat. C), 169.6 ($\text{C}=\text{N}$); $\text{UV}\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ) 225 (4.17), 256 (3.95), 307 (3.29); MS m/e (rel. intensity %) 375 (M^+ , 100), 360 ($\text{M}^+ - \text{Me}$, 35), 334 ($\text{M}^+ - \text{MeCN}$, 26).

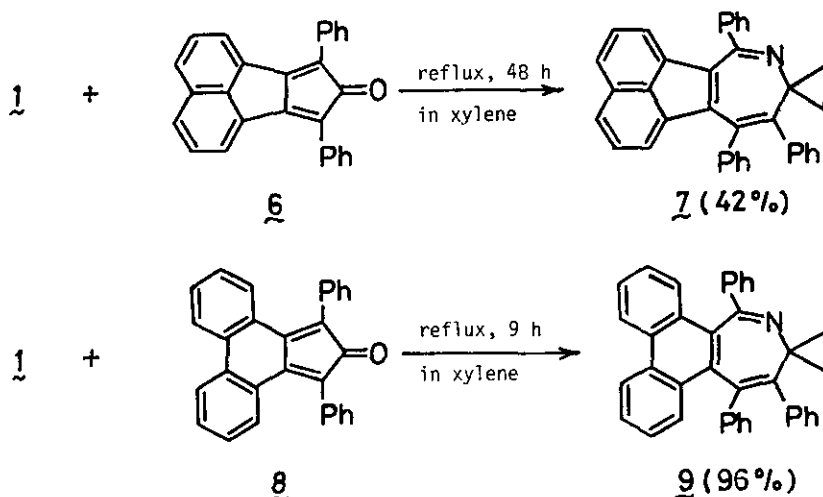
It is thus clear that in analogy with the reactions of 1-azirines with cyclopentadienones⁵, $\underline{1}$ adds to cyclopentadienones $\underline{2}$ and $\underline{4}$ to yield Diels-Alder adducts. This is followed by the elimination of carbon monoxide to give 2H-azepines $\underline{3}$ and $\underline{5}$ which are stabilized by the conjugation with spirocyclopropyl ring.

Azaspiropentene $\underline{1}$ reacted with diphenylacecyclopropane $\underline{6}$ and diphenylphencyclopentene $\underline{8}$ in refluxing xylene to give the corresponding 2H-azepines $\underline{7}$ and $\underline{9}$ (Scheme 2). The spectral data for $\underline{7}$ and $\underline{9}$ are in agreement with the assigned structures, respectively.

$\underline{7}$: mp 235-236 $^{\circ}$; orange prisms; ^1H NMR (CDCl_3) δ 0.50-0.82, 1.05-1.50 (each 2H, m), 6.60-7.80 (21H, m); ^{13}C NMR (CDCl_3) δ 14.3, 16.4 (each CH_2), 47.9 (quat. C), 168.5 ($\text{C}=\text{N}$); $\text{UV}\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ) 237 (4.30), 273 (3.85), 320 (3.74), 336 (3.78); MS m/e (rel. intensity %) 471 (M^+ , 100), 394 ($\text{M}^+ - \text{Ph}$, 58), 368 ($\text{M}^+ - \text{PhCN}$, 15).

$\underline{9}$: mp > 300 $^{\circ}$; colorless prisms; ^1H NMR (CDCl_3) δ 0.20-0.68, 0.90-1.45 (each 2H, m), 6.80-8.75 (23H, m); ^{13}C NMR (CDCl_3) δ 12.7, 14.8 (each CH_2), 48.4 (quat. C), 170.6 ($\text{C}=\text{N}$); $\text{UV}\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ) 227

(4.94), 251 (4.63), 265 (4.68), 280 (4.54); MS m/e (rel. intensity %) 497 (M^+ , 100), 420 ($M^+ - Ph$, 23), 394 ($M^+ - PhCN$, 11).



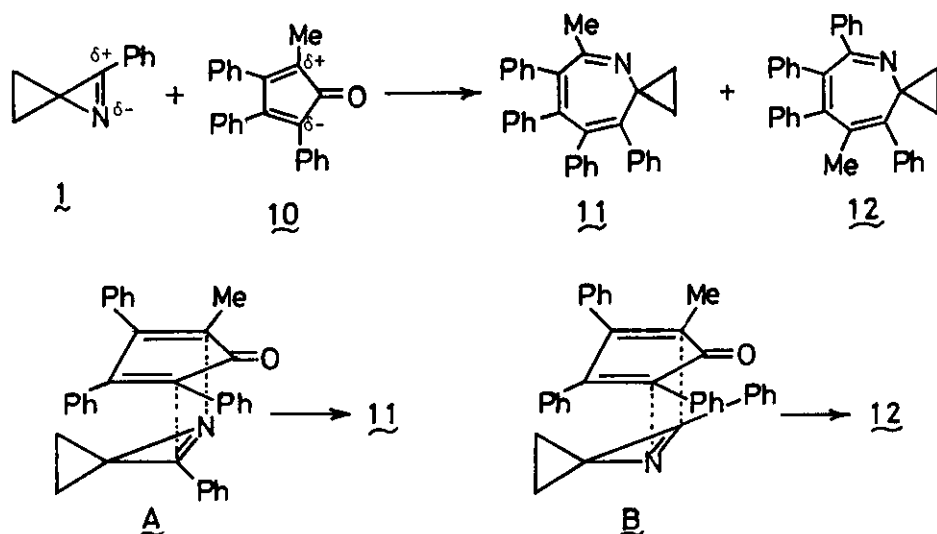
Scheme 2

The regiochemistry of the cycloaddition reaction of **1** was next examined, using unsymmetrical cyclopentadienone **10**. Azaspiropentene **1** reacted with **10** in refluxing xylene for 26 h to give 7-methyl-2H-azepine **11** and 4-methyl-2H-azepine **12** in 62 and 37% yields, respectively. Structural elucidation of **11** and **12** was accomplished on the basis of spectral data.

11: mp 108–111°; colorless prisms; 1H NMR ($CDCl_3$) δ 0.70–1.35 (4H, m), 2.07 (3H, s), 6.50–7.30 (20H, m); ^{13}C NMR ($CDCl_3$) δ 14.0, 17.4 (each CH_2), 24.9 (CH_3), 46.6 (quat. C), 170.4 (C=N); $UV\lambda_{max}^{EtOH}$ nm (log ϵ) 255 (3.85), 310 (3.24); MS m/e (rel. intensity %) 437 (M^+ , 100), 422 ($M^+ - Me$, 24), 396 ($M^+ - MeCN$, 91), 360 ($M^+ - Ph$, 30).

12: mp 169–171°; colorless prisms; 1H NMR ($CDCl_3$) δ 0.65–1.40 (4H, m), 1.77 (3H, s), 6.97–7.70 (20H, m); ^{13}C NMR ($CDCl_3$) δ 14.2, 17.1 (each CH_2), 19.2 (CH_3), 46.8 (quat. C), 171.0 (C=N); $UV\lambda_{max}^{EtOH}$ nm (log ϵ) 220 (4.35), 262 (4.03), 320 (3.20); MS m/e (rel. intensity %) 437 (M^+ , 100), 422 ($M^+ - Me$, 18), 360 ($M^+ - Ph$, 13), 334 ($M^+ - PhCN$, 40).

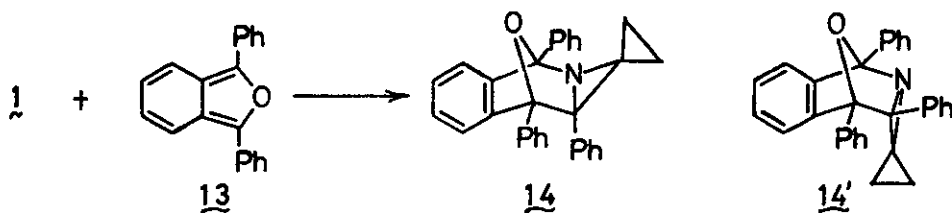
It is noteworthy that 7-methyl-2H-azepine **11** was formed in much larger amount than 4-methyl-2H-azepine **12** from the reaction of **1** with **10**, since it has been reported that 2-phenyl-3-methyl(or phenyl)-1-azirine reacted with **10** to afford the 5-methyl-3H-azepine (arising from the 4-methyl-2H-azepine) as the major product accompanied by the 2-methyl-3H-azepine (arising from the 7-methyl-2H-azepine), whereas a reversal of the product ratios occurred when 2-aryl-1-azirines having no 3-substituents were used^{5c}. Hassner and Anderson^{5c} assumed that the relative amounts of two 3H-azepine isomers depended on the electronic nature of the azirine C=N bond and the steric factors involved in the addition. If the Hassner's hypothesis is applicable to our case, in the reaction of



Scheme 3

1 with **10** it appears that the electronically favorable transition state **A** overcomes the sterically favorable one **B** (Scheme 3).

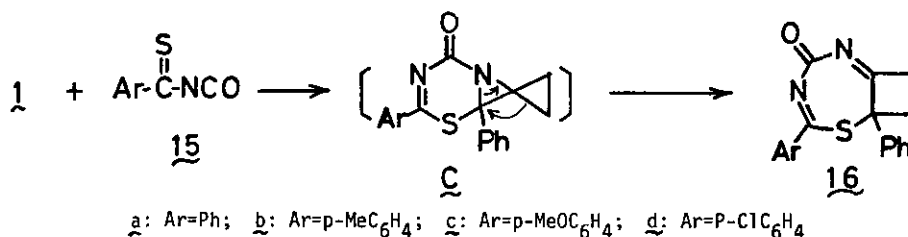
Reaction of 1 with 1,3-Diphenylisobenzofuran. Monosubstituted and 2,3-disubstituted 1-azirines reacted with 1,3-diphenylisobenzofuran **13** to give the corresponding exo-Diels-Alder adducts^{7,8}. However, no reaction of trisubstituted 1-azirines with **13** has so far been reported. When **1** was treated with **13** in refluxing xylene for 7 h, an 1:1 adduct was obtained in 76% yield. On the basis of the spectral evidence and inspection of the Dreiding models, the adduct was assigned as exo-Diels-Alder adduct **14** but not endo-adduct **14'**. The ¹H NMR and ¹³C NMR spectra showed the presence of cyclopropyl ring and four quaternary carbon atoms. Inspection of the Dreiding models indicates



that there is a significant interaction between the cyclopropyl ring and benzene ring in **14'** but not in **14**. It was thus proved that in analogy with monosubstituted and 2,3-disubstituted 1-azirines **1** undergoes the cycloaddition reaction with **13**.

14: mp 178–179°C; colorless prisms; ¹H NMR (CDCl₃) δ 0.50–1.55 (4H, m), 6.70–8.00 (19H, m); ¹³C NMR (CDCl₃) δ 3.7, 5.5 (each CH₂), 49.9, 58.9, 90.1, 101.4 (each quat. C); MS m/e (rel. intensity %) 413 (M⁺, 26), 359 (M⁺ - C₃H₄N, 99), 336 (M⁺ - Ph, 77), 270 (**13**⁺, 100), 143 (**1**⁺, 9).

Reaction of 1 with Thiobenzoyl Isocyanates. Thiobenzoyl isocyanates react with a variety of C=N bonds by a 1,4-cycloaddition process⁹. 2-Phenyl-1-azirine and 2-phenyl-3-phenyl(or methyl)-1-azirine reacted with thiobenzoyl isocyanate at room temperature to give the corresponding bicyclic [4 + 2] cycloadducts, which at higher temperature were transformed into the thiadiazepinones¹⁰. Thus, we have investigated the reaction of 1 with p-substituted thiobenzoyl isocyanates 15. Azaspiropentene 1 did not react with thiobenzoyl isocyanate 15a¹¹, generated in situ from 2-phenylthiazoline-4,5-dione in xylene, at room temperature. When 1 was treated with 15a in xylene at 120° for 1 h, however, 1:1 adduct 16a was obtained in 52% yield. Similarly, 1 reacted with p-methylthiobenzoyl 15b, p-methoxythiobenzoyl 15c, and p-chlorothiobenzoyl isocyanate 15d to give the corresponding 1:1 adducts 16b, 16c, and 16d in 66, 65, and 70% yields, respectively.



On the basis of spectral data, the 1:1 adducts were assigned as the corresponding 3-aryl-5-oxo-2,4,6-thiadiazabicyclo[5.2.0]nona-3,6-dienes arising from the rearrangement of initial [4 + 2] cycloadducts C.

16a: mp 142-143°; colorless prisms; IR (KBr) 1680 cm⁻¹ (C=O); ¹H NMR (CDCl₃) δ 2.38-2.80, 3.18-3.80 (each 2H, m), 7.16-7.60 (8H, m), 7.70-7.95 (2H, m); ¹³C NMR (CDCl₃) δ 32.9, 33.1 (each CH₂), 63.4 (quat. C), 161.7, 166.7 (each C=N), 170.6 (C=O); MS m/e (rel. intensity %) 306 (M⁺, 11), 175 (M⁺ - Ph-N=O, 18), 163 (15a⁺, 12), 143 (M⁺ - 15a, 9), 142 (16), 121 (PhCS⁺, 100), 103 (PhCN⁺, 63).

16b: mp 178-180°; colorless prisms; IR (KBr) 1675 cm⁻¹ (C=O); ¹H NMR (CDCl₃) 2.36 (3H, s), 2.45-2.80, 3.20-3.82 (each 2H, m), 7.10-7.60 (7H, m), 7.70-7.90 (2H, m); ¹³C NMR (CDCl₃) δ 21.3 (CH₃), 32.9, 33.1 (each CH₂), 63.3 (quat. C), 161.8, 166.6 (each C=N), 170.7 (C=O); MS m/e (rel. intensity %) 320 (M⁺, 15), 177 (15b⁺, 4), 175 (M⁺ - Ar-N=O, 25), 143 (M⁺ - 15b, 10), 142 (20), 135 (ArCS⁺, 23), 121 (PhCS⁺, 100), 117 (ArCN⁺, 33).

16c: mp 163-164°; colorless prisms; IR (KBr) 1675 cm⁻¹ (C=O); ¹H NMR (CDCl₃) δ 2.40-2.78, 3.40-3.72 (each 2H, m), 3.81 (3H, s), 6.75-7.05 (2H, m), 7.10-7.60 (5H, m), 7.80-8.0 (2H, m); ¹³C NMR (CDCl₃) δ 32.8, 33.0 (each CH₂), 55.5 (OCH₃), 63.3 (quat. C), 163.6, 165.8 (each C=N), 170.6 (C=O); MS m/e (rel. intensity %) 336 (M⁺, 31), 203 (M⁺ - ArCN, 21), 175 (M⁺ - Ar-N=O, 28), 151 (ArCS⁺, 31), 143 (M⁺ - 15c, 10), 142 (17), 133 (ArCN⁺, 100), 121 (PhCS⁺, 61).

16d: mp 164-165°; colorless prisms; IR (KBr) 1675 cm⁻¹ (C=O); ¹H NMR (CDCl₃) δ 2.45-2.80, 3.25-3.75 (each 2H, m), 7.15-7.60 (7H, m), 7.75-7.95 (2H, m); ¹³C NMR (CDCl₃) δ 33.0, 33.2 (each CH₂),

63.5 (quat. C), 161.5, 165.2 (each C=N), 170.6 (C=O); MS m/e (rel. intensity %) 342 (M^+ , 24), 340 (M^+ , 59), 305 ($M^+ - Cl$), 199 ($15d^+$, 18), 197 ($15d^+$, 49), 175 ($M^+ - Ar-\overset{N}{\text{C}}=O$, 23), 157 ($ArCS^+$, 12), 155 ($ArCS^+$, 30), 143 ($M^+ - 15d$, 14), 142 (26), 139 ($ArCN^+$, 22), 137 ($ArCN^+$, 63), 121 ($PhCS^+$, 100).

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