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Double 1,3-dipolar cycloadditions of 2,4-diphenyl-3-methyloxazolium 5-oxide and 3-phenylsydnone to two molecules of *N*-substituted maleimide afforded one or two isomeric 4,8-iminobenzof[1,2-*c*:4,5-*c'*]dipyrrole-1,3,5,7-tetrone derivatives owing to the types of heterocycles as well as *N*-substituents of maleimides.

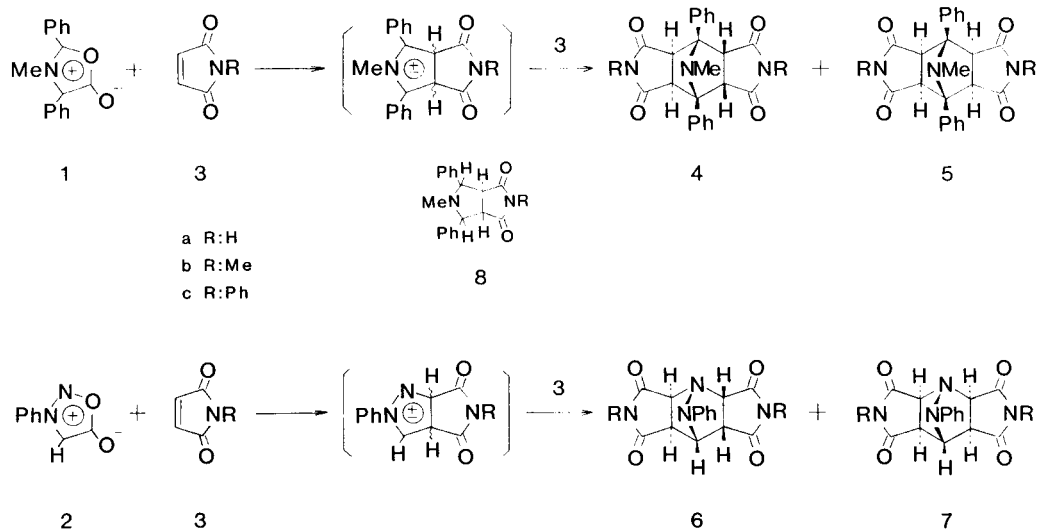
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In previous communication [1] we described that the double 1,3-dipolar cycloadditions of 2,4-diphenyl-3-methyloxazolium 5-oxide (**1**) and 3-phenylsydnone (**2**) with *N*-phenylmaleimide (**3c**) occurred in a stereoselective manner. However, the reactions of **1** with *N*-methylmaleimide (**3b**) or maleimide (**3a**) and **2** with **3a** [2] produced *endo,exo*- and *exo,exo*-isomers of the corresponding 1:2 cycloadducts. In addition, these reactions were carried out in chloroform at room temperature in the presence of triethylamine instead of *N,N*-dimethylformamide at higher temperature.

A mixture of **1** and **3b** with molar ratio of 1:2 in chloroform was allowed to stand at room temperature in the presence of triethylamine for two days to afford two isomeric 1:2 adducts, 2,6,9-trimethyl-4,8-diphenylperhydro-4,8-iminobenzof[*endo*-1,2-*c*:*exo*-4,5-*c'*]dipyrrole-1,3,5,7-tetrone (**4b**) and 2,6,9-trimethyl-4,8-diphenylperhydro-4,8-iminobenzof[*exo*-1,2-*c*:*exo*-4,5-*c'*]dipyrrole-1,3,5,7-tetrone (**5b**) in 50% and 22% yields respectively after the usual work up. The configurations of the two isomeric products were determined by the nmr spectrum: the *two singlet* signals at δ 4.07 and δ 2.95 ppm assignable to each of the two hydrogens at the 3a- and 8a-positions as well as

at the 4a- and 7a-positions exhibit that the *endo,exo*-configuration of **4b**, whereas a *singlet* signal at δ 3.42 ppm for four hydrogens show that all four bridgehead hydrogen atoms, 3a, 4a, 7a and 8a are on the same side (*exo,exo*-configuration) of **5b**. Furthermore, two sets of signals in the ^{13}C nmr spectrum of **4b** at 50.66 and 53.79 ppm assignable to each of the two carbons are compatible with the two groups of carbons, namely at the 3a- and 8a- positions as well as at the 4a- and 7a-positions bonding to *alpha*- and *beta*-hydrogens. A signal at 53.38 ppm in the ^{13}C nmr spectrum of **5b** is also compatible with the four carbons at the 3a, 4a, 7a and 8a-positions being in magnetic equivalence.

The reactions of **2** with **3** in chloroform in the presence of triethylamine proceeded slowly and therefore this method had no practical use. The cycloaddition of **2** to **3b** in refluxing benzene afforded exclusively 8-aza-2,6-dimethyl-9-phenylperhydro-4,8-iminobenzof[*exo*-1,2-*c*:*exo*-4,5-*c'*]dipyrrole-1,3,5,7-tetrone (**7b**) in 95% yield. This configuration was concluded by the ^1H and ^{13}C nmr spectra in comparison with those of **7c** [1]. By refluxing the mixture of **2** and **3a** in benzene or toluene with triethylamine for 15-30 hours two isomeric 1:2 cycloadducts, 8-aza-9-phenyl-



Table

Compound	R	Yield (%)	Reaction Temperature (°C)	Mp (°C) (Recrystallized from)	Molecular Formula	Mass (M ⁺)	Elemental Analyses (%) Found/(Calcd.)		
							C	H	N
4a	H	44	rt	342-344 (hygroscopic) Benzene-ethyl acetate	C ₂₃ H ₁₉ N ₃ O ₄ (401.4)	401	68.70 (68.82)	4.88 (4.77)	10.31 (10.47)
5a	H	22	rt	330-333 (hygroscopic) Methanol	C ₂₃ H ₁₉ N ₃ O ₄ (401.4)	401	68.61 (68.82)	4.93 (4.77)	10.26 (10.47)
4b	Me	50	rt	315-316 Methanol	C ₂₅ H ₂₃ N ₃ O ₄ (429.5)	429	69.88 (69.92)	5.48 (5.40)	9.89 (9.78)
5b	Me	22	rt	323-324 Methanol	C ₂₅ H ₂₃ N ₃ O ₄ (429.5)	429	69.79 (69.92)	5.53 (5.40)	9.67 (9.78)
4c	Ph	75 76	140 [1] rt	204-206 205-207 Benzene	C ₃₅ H ₂₇ N ₃ O ₄ (553.6)	553	75.63 (75.93)	4.96 (4.92)	7.47 (7.59)
8	Ph	2	140	269-270 Benzene	C ₂₅ H ₂₂ N ₂ O ₂ (382.5)	382	78.29 (78.51)	6.02 (5.80)	7.11 (7.32)
6a	H	20	110	192-194 (hygroscopic) Benzene	C ₁₅ H ₁₂ N ₄ O ₄ (312.3)	312	57.60 (57.69)	3.94 (3.87)	17.71 (17.94)
7a	H	68	110	207-210 (hygroscopic) Benzene	C ₁₅ H ₁₂ N ₄ O ₄ (312.3)	312	57.58 (57.69)	4.09 (3.87)	17.66 (17.94)
7b	Me	95 28	80 rt [c]	244-245 Benzene	C ₁₇ H ₁₆ N ₄ O ₄ (340.3)	340	60.21 (59.99)	4.73 (4.74)	16.19 (16.46)
7c	Ph	89 [a] 79 [b]	80 140	190-192 Benzene	C ₂₇ H ₂₀ N ₄ O ₄ (464.5)	464	70.13 (69.82)	4.25 (4.34)	11.95 (12.06)

[a] The reaction mixture with a molar ratio of **2** and **3** of 1:2 was refluxed for 30 hours in the presence of triethylamine. [b] Molar ratio of **2** and **3** of 1:1 was used in [1]. [c] The mixture was allowed to stand for 30 days.

perhydro-4,8-iminobenzo[*endo*-1,2-*c:exo*-4,5-*c'*]dipyrrole-1,3,5,7-tetrone (**6a**) and 8-aza-9-phenylperhydro-4,8-iminobenzo[*exo*-1,2-*c:exo*-4,5-*c'*]dipyrrole-1,3,5,7-tetrone (**7a**) were obtained in 20% and 68% yields respectively. The ¹H nmr spectrum of the minor isomer, **6a** showed a 5.7 Hz coupling of the bridgehead proton at the 4-position in the *beta*-configuration with the *beta*-proton at the 3a-position, but no coupling with the *alpha*-proton at the 4a-position being in reasonable agreement with the Karplus' correlation [3]. And in the ¹³C nmr spectrum of **6a** five signals appeared for corresponding five carbons at the 3a, 4, 4a, 7a and 8a-positions.

From the reaction mixture of **1** and **3c** 5-methyl-2,4,6-triphenylperhydropyrrolo[3,4-*c*]pyrrole-1,3-dione (**8**), 1:1 adduct was isolated as a by-product in 2% yield. The further reaction of **8** with **3c** formed no **4c** or **5c** showing that **8** is no intermediate compound of **4c** or **5c**.

The double cycloaddition of **1** or **2** to **3** produces one or isomeric two 1:2 bisadducts being based on *N*-substituents of maleimide **3** and on the types of meso-ionic heterocycles owing presumably to the substituent effects.

The physical and analytical data for the compounds obtained in these cycloadditions are listed in the Table.

EXPERIMENTAL

Melting points were determined on a Yanaco micromelting point apparatus and are uncorrected. The infrared spectra were

taken on a JASCO A-102 spectrometer using potassium bromide pellets. The ¹H and ¹³C nmr spectra were measured on a Varian XL-200 or Hitachi R-90 spectrometer using tetramethylsilane as the internal standard. Mass spectra were obtained with M-2000 or ESCO EMD-05B spectrometer. For column chromatography, silica gel (Kieselgel 60, Merck, 70-230 mesh ASTM) and for preparative layer chromatography, silica gel pre-coated plates (Kieselgel 60, Merck) were used. Elemental analyses were performed at Elemental Analysis Center in Kyoto University.

General Procedure for the 1,3-Dipolar Cycloaddition of 2,4-Diphenyl-3-methyloxazolium 5-Oxide **1** with Maleimide **3**.

A mixture of 1 mmole of **1** [4], 2 mmoles of **3** and 0.1 ml of triethylamine in 10 ml of chloroform was allowed to stand under stirring at room temperature for 2-5 days. After evaporating the chloroform under reduced pressure, the residue was chromatographed on silica gel column using benzene-ethyl acetate (9:1 and 1:1) or silica gel pre-coated plate using benzene-ethyl acetate (1:1). From the first fraction of the 1:1 eluent *endo,exo*-bisadduct **4** was obtained as the main product and the second fraction *exo,exo*-bisadduct **5** was isolated.

From the benzene-ethyl acetate (9:1) eluent of the mixture of **1** and **3c** 5-methyl-2,4,6-triphenylperhydropyrrolo[3,4-*c*]pyrrole-1,3-dione (**8**) was isolated in 2% yield.

Compound **4a** had ir (cm⁻¹): 3430, 1345 and 1198 (NH), 1763 and 1710 (CO); ¹H nmr (acetone-*d*₆): δ 10.32 (br, 1H, NH), 10.05 (br, 1H, NH), 7.86 (m, 4H, arom), 7.41 (m, 6H, arom), 4.26 (s, 2H, H-3a and 8a), 3.21 (s, 2H, H-4a and 7a), 1.96 (s, 3H, NMe); ¹³C nmr (deuteriodimethyl sulfoxide): 176.76 and 174.33 (CO), 134.67, 128.50 and 126.38 (2Ph), 75.48 (PhC), 53.83 and 50.71 (C-4a and 7a and C-3a and 8a), 28.93 (NMe).

Compound **5a** had ir (cm⁻¹): 3425, 1340 and 1195 (NH), 1763 and 1705 (CO); ¹H nmr (acetone-d₆): δ 9.27 (br, 2H, 2NH), 7.66 (m, 4H, arom), 7.35 (m, 6H, arom), 3.72 (s, 4H, H-3a, 4a, 7a and 8a), 2.49 (s, 3H, NMe); ¹³C nmr (DMSO-d₆): 175.96 (CO), 133.98 and 126.96 (2Ph), 79.54 (PhC), 54.74 (C-3a, 4a, 7a and 8a), 33.81 (NMe).

Compound **4b** had ir: 1762, 1708 and 1685 (CO) cm⁻¹; ¹H nmr (deuteriochloroform): δ 7.87-7.76 (m, 4H, arom), 7.47-7.39 (m, 6H, arom), 4.07 (s, 2H, H-3a and 8a), 3.12 (s, 3H, 2-NMe), 2.95 (s, 5H, 6-NMe and H-4a and 7a), 2.00 (s, 3H, 9-NMe); ¹³C nmr (DMSO-d₆): 176.38 and 174.04 (CO), 135.50, 129.65 and 127.70 (2Ph), 76.70 (PhC), 53.79 and 50.66 (C-4a and 7a and C-3a and 8a), 30.14 (9-NMe), 25.27 and 24.80 (2-NMe and 6-NMe).

Compound **5b** had ir: 1762 and 1690 (CO) cm⁻¹; ¹H nmr (deuteriochloroform): δ 7.46 (m, 10H, arom), 3.42 (s, 4H, H-3a, 4a, 7a and 8a), 2.76 (s, 6H, 2- and 6-NMe), 2.32 (s, 3H, 9-NMe); ¹³C nmr (DMSO-d₆): 174.47 (CO), 133.80 and 127.01 (2Ph), 79.53 (PhC), 53.38 (C-3a, 4a, 7a and 8a), 33.20 (9-NMe), 24.48 (2- and 6-NMe).

Cycloaddition of 3-Phenylsydnone **2** with Maleimide **3**. Method A.

A chloroform solution of 1 mmole of **2** [5], 2 mmoles of **3b** and 0.1 ml of triethylamine was treated for 30 days by the same way described above. By the column chromatography on silica gel *exo,exo*-bisadduct **7b** in 28% yield and starting material **2** were obtained. The reaction with **3a** or **3c** proceeded more slowly, and after 30 days **7a** or **7c** was observed on the thin layer chromatogram.

Method B.

A mixture of **2** (1 mmole), **3b** (2.1 mmoles) and triethylamine (0.1 ml) in benzene (10 ml) was refluxed for 15 hours and was concentrated under reduced pressure. The resulting solid was purified by recrystallization from benzene and by the column chromatography of the mother liquor on silica gel using benzene and benzene-ethyl acetate (1:1) as the eluent. The obtained crystals in 95% yield were exclusively 8-aza-2,6-dimethyl-9-phenylperhydro-4,8-iminobenzof[*exo*-1,2-*c:exo*-4,5-*c'*]dipyrrole-1,3,5,7-tetrone **7b**.

Compound **7b** had ir: 1773, 1720 and 1690 (CO) cm⁻¹; ¹H nmr (deuteriochloroform): δ 7.20-6.68 (m, 5H, arom), 5.45 (s, 1H, H-4), 4.00 (d, J = 6.5 Hz, 2H, H-7a and 8a), 3.08 (d, J = 6.5 Hz, 2H, H-3a and 4a), 2.56 (s, 6H, 2NMe); ¹³C nmr (DMSO-d₆): 175.13 and

173.71 (CO), 143.81, 128.68, 128.36 and 121.00 (Ph), 67.82 (C-7a and 8a or C-3a and 4a), 62.48 (C-4), 48.78 (C-3a and 4a or C-7a and 8a), 24.16 (Me).

The mixture of **2** and **3a** in toluene was refluxed for 48 hours as described in Method B. The resulting solid was chromatographed on the silica gel column using benzene-acetone (2:1) as the eluent. From the first pale yellow fraction *endo,exo*-bisadduct **6a** in 20% yield and the second pale yellow fraction *exo,exo*-bisadduct **7a** in 68% yield were obtained.

Compound **6a** had ir (cm⁻¹): 3450, 3210, 1345 and 1190 (NH), 1775 and 1720 (CO); ¹H nmr (acetone-d₆): δ 10.29 (br, 2H, 2NH), 7.28-6.87 (m, 5H, arom), 5.29 (d, J = 5.7 Hz, 1H, H-4), 4.51 (d, J = 8.8 Hz, 1H, H-8a), 4.16 (d, J = 6.6 Hz, 1H, H-7a), 3.59 (dd, J = 5.7 and 8.8 Hz, 1H, H-3a), 3.20 (d, J = 6.6 Hz, 1H, H-4a); ¹³C nmr (DMSO-d₆): 176.76, 175.47, 175.39 and 173.74 (CO), 143.80, 129.46, 122.46 and 116.60 (Ph), 69.34, 65.46, 63.95, 50.00 and 48.43 (C-8a, 7a, 4, 3a and 4a).

Compound **7a** had ir (cm⁻¹): 3450, 3220, 1340 and 1198 (NH), 1765 and 1710 (CO); ¹H nmr (acetone-d₆): δ 9.89 (br, 2H, 2NH), 7.08-6.88 (m, 5H, arom), 5.39 (s, 1H, H-4), 4.22 (d, J = 6.8 Hz, 2H, H-7a and 8a), 3.34 (d, J = 6.8 Hz, 2H, H-3a and 4a); ¹³C nmr (DMSO-d₆): 176.63 and 175.20 (CO), 144.11, 128.69, 128.38 and 121.05 (Ph), 69.27 (C-7a and 8a), 61.96 (C-4), 50.19 (C-3a and 4a).

Compound **8** had ir (cm⁻¹): 1780 and 1712 (CO); ¹H nmr (deuteriochloroform): δ 7.67-7.25 (m, 15H, arom), 3.63 (m, 2H) and 3.39 (m, 2H) (H-3a, 4, 6 and 6a), 2.05 (s, 3H, NMe).

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