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CYCLOADDITION REACTION OF 5-PHENYLAZOTROPONES WITH CYCLOPROPENE

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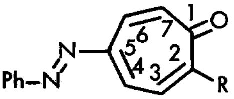
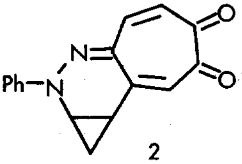
In the previous papers (1), we have reported the cycloaddition reaction of 2-hydroxy- and 2-methoxy-5-arylazotropones with cyclopentadiene, in which these tropones reacted exclusively utilizing their N=N-C=C heterodiene system. Although the nature of the reactions was largely clarified, their stereochemical requirement was not elucidated because of the complexity of PMR spectra of the products. In this paper, we describe the reactions of 2-chloro-, 2-hydroxy-, and 2-methoxy-5-phenylazotropones with cyclopropene, which were designed to determine the stereoselectivity and to test the generality of this rather unusual reaction.

Excess cyclopropene was bubbled at 0° through a CH_2Cl_2 solution of 5-phenylazotropolone **1**. After 6 hrs, the reaction mixture was oxidized with O_2 in the presence of a base (K_2CO_3 or organic base) and chromatographed through basic SiO_2, to give the quinone **2**, red prisms, m.p. 55°, and αβ-unsaturated ketone **3**, yellowish orange needles, m.p. 83°, in 28% and 21% yields, respectively (2). Although the structures of these products were secured spectroscopically, **2** was further characterized as its quinoxaline derivative **4**, red prisms, m.p. 230° (dec.). In order to determine the product ratio more quantitatively, the reaction mixture was devided in two portions, and one was acetylated while the other was heated with o-phenylenediamine. Thus, acetate **5**, yellowish orange granules, m.p. 134°, (20% yield) and a quinoxaline **6**, orange prisms, m.p. 238° (dec.) (54% yield) were obtained, respectively. **6** can be oxidized to **4** with DDQ. Therefore, the primary products of the cycloaddition reaction must be **3** and **7**.

2-Methoxy-5-phenylazotropone **8** (3) reacted with cyclopropene under the same conditions (3 hrs). After chromatography through acidic SiO_2, the reaction mixture yielded similar products **9**, reddish orange prisms, m.p. 75° (dec.) (47% yield) and **10**, yellowish orange needles, m.p. 95° (28% yield), while chromatography through neutral SiO_2 yielded the known pyridotropone **11** (4) in 3% yield besides the



1 R=OH
8 R=OMe
12 R=Cl



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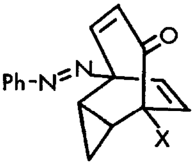
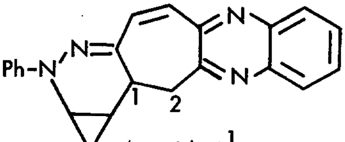
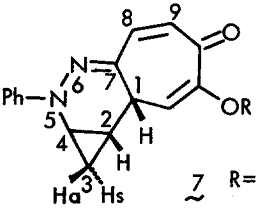


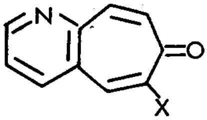
3 X=OH
5 X=OAc
10 X=OMe
13 X=Cl



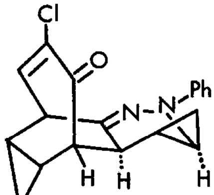
4 with Δ^1
6 without Δ^1



7 R=H
9 R=Me



11 X=OMe
15 X=Cl



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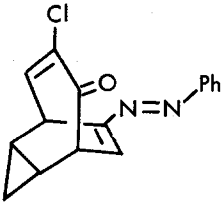

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complex green product. 9 showed its H_1 and H_2 well separated in PMR spectra, allowing the assignment of the endo configuration ($J_{1,2}=7$, $J_{1,3a}=1.5$, $J_{2,3a}=9$). The same stereochemistry should apply to the reactions described in the previous paper (1) as well as those in the present paper. 9 afforded 2 upon treatment with mild base (K_2CO_3 or NH_3, etc.) in dil. methanol (5), while acidic treatment (conc. HCl, r.t. 2 hrs) afforded 11 in 30% yield (6).

Likewise, 2-chloro-5-phenylazotropone 12 (7) underwent reaction with cyclopropene under the same conditions. The reaction completed within 45 min. By SiO_2 shromatography, the 1 : 1 adduct 13, yellowish orange prisms, m.p. 75° (8%), the 1 : 2 adduct 14, yellow prisms, m.p. 166° (11%) and the pyridotropone 15, colorless needles, m.p. 180°, (13%) were isolated. Although the structures of 13, and 15 followed the spectral comparison, that of 14 was based on the detailed PMR analysis (Table II). 14 should be, derived from the 1 : 1 adduct 16 by the attack of the 2nd molecule of cyclopropene from the sterically less hindered side.

Thus, these three reactions with cyclopropene revealed a considerable decrease in regioselectivity; three modes of the [4+2] cycloadditions, involving $N=N-C_5=C_4$ (Type A), $C_2=C_3-C_4=C_5$ (Type B) and $C_4=C_5-C_6=C_7$ (Type C), were observed as shown in the Table I.

The stabilization energy for these cycloadditions was calculated using Fukui's equation (8). The experimental results are in good accord with the magnitude of stabilization energy (SE) which are also listed in the Table I.

Table I. Yield of Primary Products and Stabilization Energy in Cycloaddition of 5-Phenylazotropones with Cyclopropene

group at C_2		addition at $N{=}N{-}C_5{=}C_4$ (A)	addition at $C_2{=}C_3{-}C_4{=}C_5$ (B)	addition at $C_4{=}C_5{-}C_6{=}C_7$ (C)
OH	yield (%)	54	21	—
	SE (γ^2/β)	0.52	0.29	0.12
OMe	yield (%)	47	28	—
	SE (γ^2/β)	0.52	0.27	0.16
Cl	yield (%)	13	8	11
	SE (γ^2/β)	0.77	0.48	0.34

The calculation further suggested that the Type A addition is largely stabilized by the interaction of LUMO of the tropones and HOMO of cyclopropene ("inverse electron demand"), whereas the Types B and C additions are stabilized nearly equally from both LUMO-HOMO interactions. Similar situation was revealed for the reaction of methoxyphenylazotropone and cyclopentadiene but in this case only Type A mode receives enough stabilization energy.

Table II. Spectral Data of the Pertinent Compounds

2: λ_{max}^{MeOH} 225 (ϵ 11900), 238 (11400), 265 (3220 sh), 299 (2150), 340 (3380), 500 nm (20500), ν^{CHCl_3} 1612, 1572 cm^{-1}, δ^{CDCl_3+Py} 0.86 (1H, td, J=5.8, 4.3), 2.06 (1H, ddd, J=10.0, 7.0, 5.8), 2.60 (1H, br.ddd, J=10.0, 8.0, 5.8), 3.96 (1H, ddd, J=8.0, 7.0, 4.3), 6.63(1H, d, J=13.5), 6.78 (1H, s), 7.37 (1H, d, J=13.5), 7.2-7.8 (5H, Arom.).

3: m/e 266 (M^+), 161 (M^+-PhN_2), 77 (base peak), λ_{max}^{MeOH} 215.5 (ϵ 15900), 270 (14200), 406 nm (244), ν^{KBr} 3460, 1665 cm^{-1}, δ^{CDCl_3} 0.89 (1H, td, J=7.5, 5.5), 1.31 (1H, dddd, J=8.5, 7.5, 4.3, 1.8), 1.50 (1H, dt, J=5.5, 4.3), 1.95 (1H, dddd, J=8.5, 7.5, 4.3, 1.8), 4.30 (1H, br.s), 5.71 (1H, dd, J=9.5, 1.8), 5.89 (1H, d, J=11.5), 6.40 (1H, dd, J=9.5, 1.8), 7.64 (1H, d, J=11.5), 7.4-7.85 (5H, Arom.).

5: m/e 308 (M^+), 203 (M^+-PhN_2), 161 (base peak), ν^{KBr} 1745, 1683, 1620 cm^{-1}.

9: m/e 187, 93 (base peak), λ_{max}^{MeOH} 239 (ϵ 9520), 285 (11000), 447 nm (16300), ν^{CHCl_3} 1616, 1596, 1520, 1493 cm^{-1}, δ^{CDCl_3} 0.97 (1H, ddd, J=6, 6, 4), 1.28 (1H, dddd, J=9, 6.5, 6, 1.5), 1.93 (1H, dddd, J=9, 8.5, 7, 6), 3.23 (1H, ddd, J=8.5, 6.5, 4), 3.59 (3H, s), 3.95 (1H, ddd, J=7, 3.5, 1.5), 5.14 (1H, br.d, J=3.5), 6.02 (1H, d, J=12.5), 6.81 (1H, dt, J=12.5, 0.5), 6.8-7.5 (5H, Arom.).

10: m/e 280 (M^+), 175 (base peak, M^+-PhN_2), 77, λ_{max}^{MeOH} 215 (ϵ 14800), 270.5 (11800), 408 nm (213),

ν^{KBr} 1677, 1635 (sh) cm^{-1}, δ^{CCl_4} 0.93 (1H, td, J=7.5, 5.5), 1.43 (1H, dt, J=5.5, 4.5), 1.59 (1H, dddd, J=9, 7.5, 4.5, 1.8), 2.06 (1H, dddd, J=9, 7.5, 4.5, 1.8), 3.98 (3H, s), 5.71 (1H, d, J=11.5), 5.78 (1H, dd, J=9.5, 1.8), 6.46 (1H, dd, J=9.5, 1.8), 7.45 (1H, d, J=11.5), 7.38-7.82 (5H, Arom.).

13: m/e 286, 284 (1:3, M$^+$), 77 (base peak), λ_{max}^{MeOH} 215.5 (ϵ 15200), 271.5 (14000), 408 nm (187), ν^{CHCl_3} 1687, 1640 cm^{-1}, δ^{CCl_4} 1.05 (1H, td, J=7.5, 6.0), 1.54 (1H, dt, 6.0, 4.5), 1.77 (1H, dddd, J=8.5, 7.5, 4.5, 1.8), 2.19 (1H, dddd, J=8.5, 7.5, 4.5, 1.8), 5.83 (1H, dd, J=9.5, 1.8), 5.86 (1H, d, J=11.3), 6.54 (1H, dd, J=9.5, 1.8), 7.52 (1H, d, J=11.3), 7.4-7.85 (5H, Arom.).

14: m/e 326, 324 (1:3, M$^+$), 289 (M$^+$-Cl), 77 (base peak), λ_{max}^{MeOH} 247.5 (ϵ 12200), 282 (11700), 352 nm (2540), ν^{CCl_4} 1687 cm^{-1}, δ^{CDCl_3} 0.66 (1H, td, J=6.5, 4.5), 0.71 (1H, dtd, J=8.5, 6.0, 1.5), 0.99 (1H, td, J=8.0, 6.0), 1.16 (1H, dt, J=6.0, 4.0), 1.32 (1H, m, J=8.0, 4.0, 3.3, etc.), 1.69 (1H, m, J=8.0, 4.0, 3.6, etc.), 1.76 (1H, m, J=9.3, 8.5, 6.0, 4.0), 2.77 (1H, br.td, J=4.0, 1.5), 3.27 (1H, dddd, J=9.3, 6.0, 4.0, 0.7), 3.57 (1H, ddd, J=4.4, 3.3, 1.0), 3.72 (1H, dd, J=9.3, 3.6), 6.9-7.3 (5H, Arom.), 7.42 (1H, d, J=9.3).

15: m/e 193, 191 (1:3, M$^+$), 165, 163 (1:3, base peak), λ_{max}^{MeOH} 241.5 (ϵ 31900), 261 (14300, sh), 290 (4670 sh), 305 (5590), 319 (6140), 334.7 (6230), 350.3 nm (3950), ν^{KBr} 1633, 1610, 1601 cm^{-1}, δ^{CDCl_3} 7.22 (1H, d, J=13.3), 7.57 (1H, dd, J=8.2, 5.0), 7.92 (1H, d, J=13.3), 8.02 (1H, dd, J=8.2, 1.8), 8.10 (1H, s), 8.93 (1H, dd, J=5.0, 1.8).

References and Notes

1) S. Itô and I. Saito, Tetrahedron Letters, 1203 (1977).

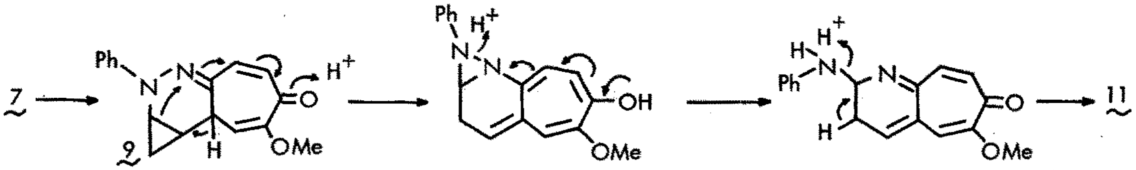
2) Structures of new products were assigned on the basis of spectral data together with the detailed NMDR analysis. The data of the pertinent compounds are listed in Table II at the end of text.

3) J. Griffiths, J. Chem. Soc. (B), 801 (1971).

4) G. Queguiner, C. Fugier and P. Pastour, Bull. Soc. Chim. Fr., 3636 (1970).

5) Extreme ease of the oxidative hydrolysis may reflect the nonbonded π-π interaction between N=C and C=C-OMe. Similar interaction was observed by J. Streith, et al. (G. Kiehl, J. Streith and G. Taurand, Tetrahedron, 30, 2851 (1974)).

6) Although experimental support is lacking, the reaction is considered proceeding as follows.



The formation of **15** should also involve this type of addition at the initial step.

7) Prepared by the action of $SOCl_2$ on **1** in benzene (80°, 3 hrs). Orange needles, m.p. 131-132°.

8) K. Fukui, in "Molecular Orbitals in Chemistry, Physics and Biology", P.O. Lowdin and B. Pullman, ed., Academic Press, N.Y. (1964).