

REGIO- AND STEREO-CONTROLLED DIELS-ALDER REACTION OF DIOXOPYRROLINES
 WITH ACTIVATED BUTADIENES: FACILE SYNTHESSES OF RING D
 FUNCTIONALIZED ERYTHRINANS¹⁾

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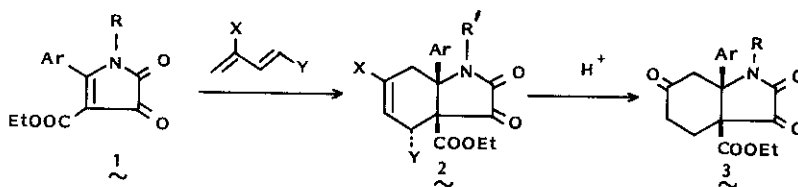
Diels-Alder reaction of Δ^2 -pyrrolidine-4,5-diones with activated butadienes proceeds in regio- and stereo-selective manner. Thus, isoquinolinopyrrolinediones (prepared in 3 steps from β -arylethylamines) gave single erythrinan derivatives which are functionalized at ring D in acceptable yields. The structure and stereochemistry of the adducts were established by chemical and spectroscopic means and finally by X-ray analysis of the derived diacetate (19).

Hydroindole synthesis by Diels-Alder reaction of Δ^2 -pyrrolidine-4,5-diones with butadiene exploited by Tsuda et al,²⁾ prompted us to use of activated butadienes such as 1-methoxy-3-trimethylsilyloxybutadiene³⁾ instead of butadiene, since it seems to promise yielding variously functionalized hydroindoles directly. In that case the regio- and stereo-chemistry of the product must be clarified. This communication treats this subject mainly.

Table 1 summarizes the present result on Diels-Alder reaction of 2-aryl- Δ^2 -pyrrolinediones (1) with some previous results^{2c)} for comparison. It indicates that 2-phenyl- Δ^2 -pyrrolinedione is poorly reactive to butadiene unless the nitrogen is negatively substituted and 2-(3',4'-methylenedioxyphenyl) derivative is less reactive. However, with activated butadienes they are moderately reactive to yield single adduct suggesting that the reaction proceeds in regio- and stereo-selective manner (structures of the products are given on analogy with the results described below).

We therefore examined Diels-Alder reaction of isoquinolinopyrrolinediones (7), in which free rotation of an aromatic ring is prohibited by formation of a new

Table 1. Diels-Alder Reaction of 2-Aryl- Δ^2 -pyrroline-4,5-diones (1) with Butadienes.



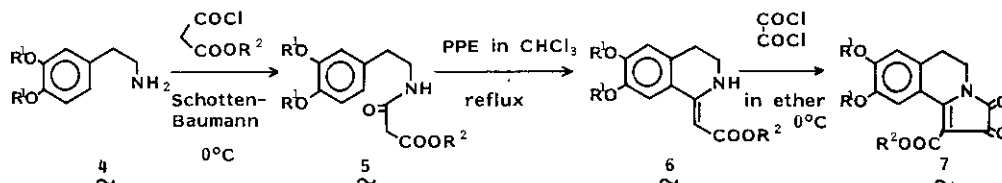
dienophiles (<u>1</u>)		diene	reaction condition			products (<u>2</u>)				
Ar	R		solvent	temp.	time	X	Y	R'	yield	mp
Ph	H	A	CH ₂ Cl ₂	180°	28hr	H	H	H	10% ^{a)}	228-230° ^{a)}
Ph	H	A	Ac ₂ O	160°	8hr	H	H	Ac	60% ^{a)}	164-166° ^{a)}
Ph	H	C	toluene	150°	8hr	H	OTMS	H	11% ^{b)}	(212-214°) ^{b)}
Ph	H	D	toluene	160°	10min	OTMS	OMe	H	35%	146-150°
Ph	Me	A	CH ₂ Cl ₂	160°	8hr	H	H	Me	10% ^{a)}	158-160° ^{a)}
Ph	Me	A	Ac ₂ O	160°	8hr	H	H	Me	10%	158-160°
Ph	Me	C	toluene	150°	7hr	H	OTMS	Me	15% ^{b)}	(154-156°) ^{b)}
3,4-(OCH ₂ O)C ₆ H ₃	H	A	CH ₂ Cl ₂	180°	28hr	H	H	H	c)	c)
3,4-(OCH ₂ O)C ₆ H ₃	H	A	Ac ₂ O	160°	8hr	H	H	Ac	10%	gum

A: butadiene, C: 2-trimethylsilyloxybutadiene, D: 1-methoxy-3-trimethylsilyloxybutadiene.

a) see ref. 2c.

b) Isolated as the ketone 3 after acid hydrolysis.

c) Not isolable.



a: R¹=Me, R²=Et; b: R¹=Me, R²=Me; c: R¹-R¹=-CH₂-, R²=Et; d: R¹-R¹=-CH₂-, R²=Me

Chart 1

Table 2. Syntheses of Isoquinolinopyrrolinediones (7) (mp and yield %)

	<u>5</u>	<u>6</u>	<u>7</u>
a	57-58°, 98%	82-85°, 90%	209-212°, 89%
b	75-76°, 99%	gum, 90%	244-246°, 60%
c	98-100°, 86%	148-150°, 80%	219-223°, 94%
d	98-99°, 95%	138-141°, 80%	221-224°, 89%

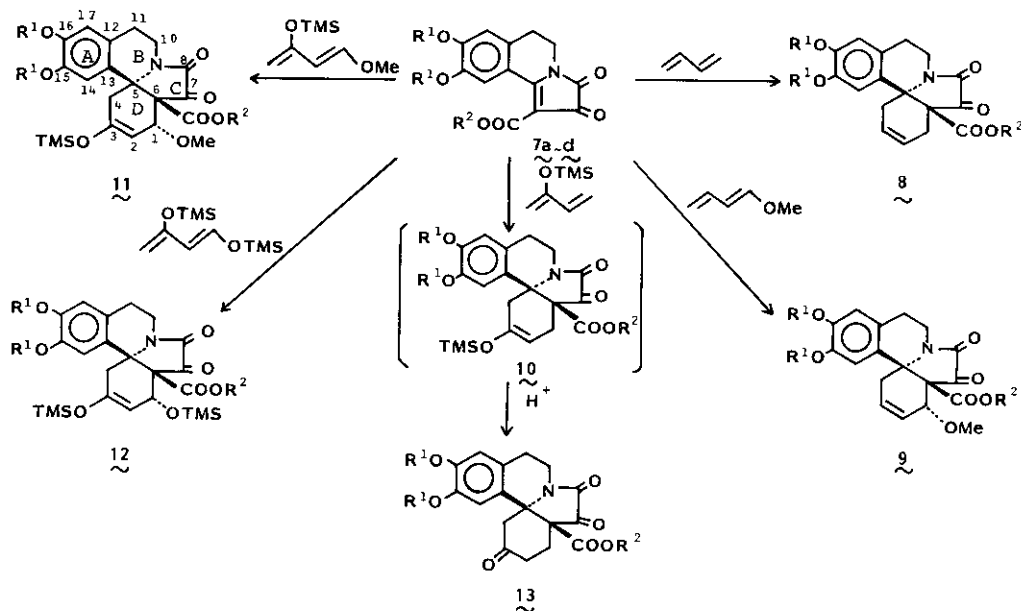


Chart 2

 Table 3. Diels-Alder Reaction of **7** with Butadienes.

dienophile	diene	solvent	temp.	time (hr)	1,4-adduct (mp)	yield (%)
7a	A	toluene	170°	30	8a 175-176°	6
	B	toluene	140°	9	9a gum	80 ^{b)}
	C	toluene	160°	17	10a a)	33
	D	neat	130°	3	11a 124-126°	58
	E	neat	140°	0.5	12a 142-145°	58
7b	D	dioxane	130°	1	11b 142-144°	82
	E	dioxane	130°	0.5	12b 141-143°	65
7c	A	toluene	170°	20	8c c)	c)
	B	toluene	140°	5	9c 191-192°	36
	C	toluene	170°	13	10c a)	23
	D	neat	130°	3	11c 176-179°	49
	E	neat	130°	2	12c 202-205°	76
7d	D	dioxane	120°	1	11d 174-177°	51
	E	neat	130°	2	12d 173-176°	64

A: butadiene. B: 1-methoxybutadiene. C: 2-trimethylsilyloxybutadiene.

D: 1-methoxy-3-trimethylsilyloxybutadiene. E: 1,3-bis(trimethylsilyloxy)butadiene.

a) Isolated as a keto compound (**13**) after acid hydrolysis.

b) Yield given as a crude gum.

c) Not isolable.

Table 4. IR and NMR Spectra of the Cycloadducts.

cycloadducts	IR (cm ⁻¹)		NMR (CDCl ₃ , δ) olefinic protons
	ν C=O	absorptions	
<u>8a</u>	1770, 1730, 1715		5.57-6.27 (2H, m.)
<u>9a</u>	1770, 1740, 1710		5.68-6.48 (2H, m.)
<u>9c</u>	1775, 1740, 1715		5.91, 6.27 (each 1H, m.)
<u>11a</u>	1770, 1725, 1710		5.34 (1H, d., J=5 Hz)
<u>11b</u>	1780, 1745, 1720		5.38 (1H, d., J=5 Hz)
<u>11c</u>	1770, 1745, 1720		5.33 (1H, d., J=5 Hz)
<u>11d</u>	1766, 1720, 1710		5.31 (1H, d., J=5 Hz)
<u>12a</u>	1760, 1740, 1715		5.35 (1H, d., J=6 Hz)
<u>12b</u>	1760, 1740, 1715		5.38 (1H, d., J=6 Hz)
<u>12c</u>	1760, 1730, 1710		5.33 (1H, d., J=6 Hz)
<u>12d</u>	1765, 1740, 1720		5.31 (1H, d., J=5 Hz)

ring. The desired dienophiles, 7a-d were prepared as shown in Chart 1, which were obtained as red-reddish yellow crystals in yield of 60-80% starting from the β-arylethylamines (4) (Table 2).

Table 3 summarizes the result of Diels-Alder reaction of 7 with various butadienes: reaction conditions, products, and yields. 7a-d were more reactive to butadienes than 1 apparently due to gaining planarity in a dienophile. The reaction was again highly regio- and stereo-selective to give single 1,4-cycloadducts in acceptable yields (IR and NMR listed in Table 4). The adducts 10a and 10c were characterized as the corresponding ketones (13a), mp 223-225°, and (13c), mp 272-275°, after acid hydrolysis (2.5% HCl-THF).

The regiochemistry of the adducts was elucidated as shown in Chart 3 as follows. Treatment of 11c and 12c with acid (2.5% HCl-THF) caused not only cleavage of the O-Si bond but also opening of the ring D to give the same keto-aldehyde (16), mp 243-246°, δ 8.07 (1H, br s, CHO). Trituration of 11c with methanol again gave the ring D cleaved product, the enol-ether (17), mp 182-186°, δ 3.67 (3H, s, OCH₃), 5.45 and 7.47 (each 1H, d, J=12 Hz, olefinic protons). While on treatment with KF in THF, 11c and 12c gave the ketone (14) (52%), mp 210-213°, and (15) (54%), mp 208-211°, respectively, which changed into 16 and 17, respectively, on treatment with base (DBU at r.t.). Those ring opening reactions were rationalized in term of the reverse Michael reaction of a 1,5-diketo derivative. The above results indicate that the 1,4-cycloaddition of Δ²-pyrrolinediones proceeds in a fashion acceptable from the ground state electron interaction of the diene and the dienophile.

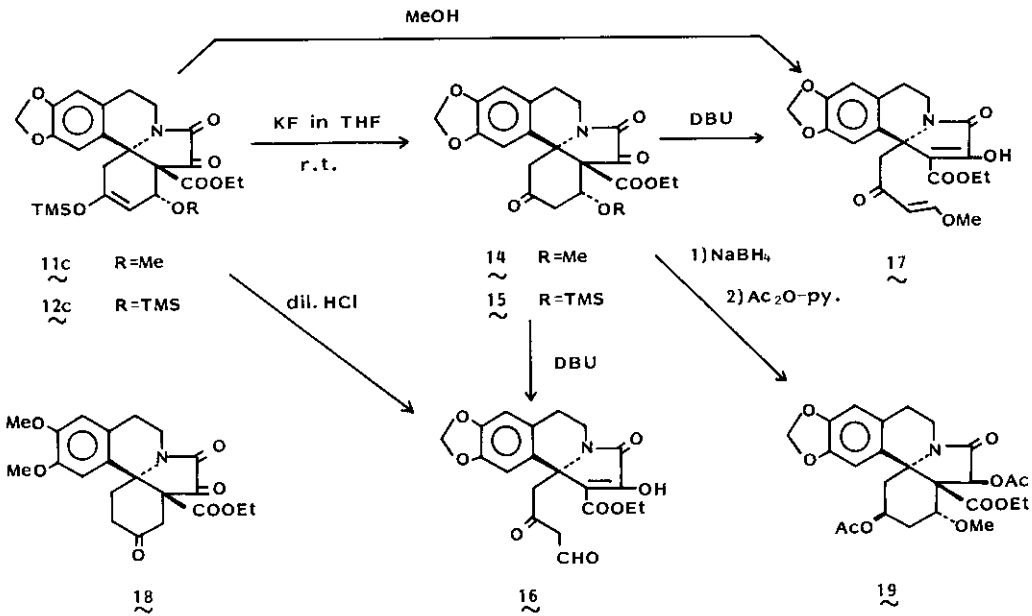
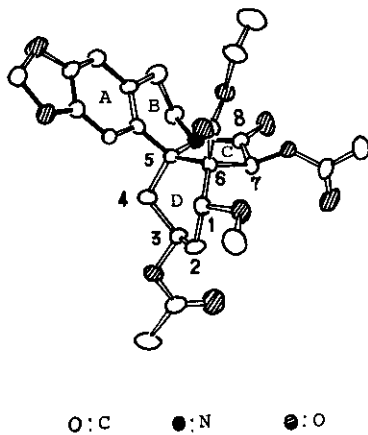


Chart 3



crystal data

monoclinic crystals
 space group, $P2_1/a$
 $a=15.660$, $b=12.142$, $c=13.682\text{\AA}$
 $\beta=109.09^\circ$
 $Z=4$

Fig. 1 The computer-plotted structure of the diacetate (19)

The structure of the adduct(10) was elucidated as shown in Chart 2 based on the above consideration. In fact, the derived ketone (13a) was isomeric with 2-keto derivative (18) reported previously.⁵⁾

The structure of 11c including the stereochemistry of C₁-substituent was finally established by X-ray crystallographic analysis. The X-ray analysis was carried out for the diacetate (19), mp 242-244°, which was prepared by NaBH₄ reduction of the methoxy-ketone (14c) followed by acetylation. The intensity data were collected on a Philips PW-1100 diffractometer using graphite-monochromated Cu-Kα radiation. The structure was solved by direct methods with the MULTAN program.⁶⁾ Block-diagonal least-squares refinements of positional and thermal parameters based on 1483 observed reflections reduced R value to 0.04. The resulting structure is shown in Fig. 1, which rigidly established not only the α-configuration of C₁-OMe but also the β-configurations of the C₃ and C₇-OAc. The latter asymmetric centers are newly produced by hydride reduction. Furthermore, it is worthwhile to note that both the ring B and D have boat conformation in the crystalline state.

The stereochemistry of 9 was assumed as shown in Chart 2 based on the above results, though rigid proof was not available.

The present method may provide a simple route to erythrina alkaloids, since 6-alkoxycarbonyl group is easily removable from the above prepared 6-alkoxycarbonyl-7,8-dioxoerythrinans.⁷⁾

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