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Table I. Modifications of the 10-Hydroxyl Substituent of Ryanodine and the Cyclohexane Ring of Dehydroryanodine in Relation to Action at Calcium Release Channels

no.	10-substituent or modification of cyclohexane ring	activity relative to ryanodine[a]			
		ryanodine receptor			rat ventricular strip assay
		rabbit muscle	mouse brain	canine ventricle	
1	ryanodine	100	100	100	100
Modifications of the 10-Hydroxyl Substituent of **1**					
3	oxo	30			
4	10-epi-hydroxy	97	69	78	34
5	oxime	26			
6	methoxime	13	13	17	34
7	benzyloxime	13			
8	hydrazone	18			
9	epi-hydroxyamine	32			
10	epi-benzoyloxyamine	8.5	11		
11	epi-methoxyamine	68		36	31
12	epi-benzyloxyamine	14	6.3		
13	epi-amine	68	65		
14	epi-benzamide	9.5			
15	epi-4-azidobenzoylhydrazide	67			
16	lactam	42		7.4	11
Modifications of the Cyclohexane Ring of **2**					
17	10-benzoyloxy	3.9	17		
18	Δ^8 (10-hydroxy)	26		27	11
19	Δ^8-10-oxo	12			
20	10-oxo-2	4.2	1.3		

[a] Values for **1** are: IC_{50}s of 3.5 and 3.3 nM for rabbit muscle and mouse brain; K_i of 1.8 nM for cardiac ventricle preparation; and IC_{50} of 34 nM for rat ventricular muscle strip assay.

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Table II. Defunctionalization of the Cyclohexane Ring of Dehydroryanodine in Relation to Action at Calcium Release Channels

		activity relative to ryanodine[a] = 100			
		ryanodine receptor			rat
no.	modifications of cyclohexane ring	rabbit muscle	mouse brain	canine ventricle	ventricular strip assay
21	21-*nor*-9-oxo(EtB)	13	8.3		
22	21-*nor*-9_{ax}-hydroxy(EtB)	0.82	2.1		
23	21-*nor*-9-oxo	10	7.1	6.5	5.9
24	21-*nor*-9_{ax}-hydroxy	0.62	0.50	2.7	26
25	21-*nor*-9_{eq}-hydroxy	1.2	0.90	0.66	<3.5
26	21-*nor*-9-oxo-10-acetoxy	8.3	8.3		
27	21-*nor*-10-deoxy-9-oxo	1.0	0.20	0.79	4.7
28	21-*nor*-10-deoxy-9_{ax}-hydroxy	0.20	0.40	0.42	28
29	21-*nor*-10-deoxy-9_{eq}-hydroxy	2.4	4.3	1.6	<3.5
30	10-deoxydehydro	37	77	45	121
31	21-*nor*-10-deoxy	6.5	78		
32	21-*nor*-10-deoxy-6,9-oxido	0.16	<0.10	0.13	<3.5
33	21-*nor*-10-deoxy-Δ^8/Δ^9	0.57[b]	1.3[b]		

[a] Values for **1** are: IC_{50}s of 3.5 and 3.3 nM for rabbit muscle and mouse brain preparations; K_i of 1.8 nM for cardiac ventricle preparation; and IC_{50} of 34 nM for rat ventricular muscle strip assay.

[b] Single assay of Δ^8/Δ^9 mixture.