2-AZABICYCLO[3.2.0]HEPTANE-3,4-DIONE (8): A NOVEL ACID CATALYZED SKELETAL REARRANGEMENT OF 7-OXY-7-VINYL DERIVATIVES TO 2-AZATRICYCLO[4.3.0.0.^{4,9}]NONANE-3,7-DIONES[1]

Takehiro Sano* and Jun Toda
Showa College of Pharmaceutical Sciences, Setagaya-ku, Tokyo 154, Japan
Yoshisuke Tsuda
Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa 920, Japan

Abstract— Treatment of 7-trimethylsilyloxy-7-vinyl-2-azabicyclo-[3.2.0]heptane-3,4-diones with various acids yielded novel caged compounds, 2-azabicyclo[4.3.0.0^{4,9}]nonane-3,7-diones, whose formation is explained in terms of intramolecular Prins type cyclization with concomitant 1,2-shift.

7-Vinyl-2-azabicyclo[3.2.0]heptane-3,4-diones are vulnerable to thermolysis or base treatment and are known to give at least four types of reaction products depending on reaction conditions and the nature of the substituent X.[2-5]

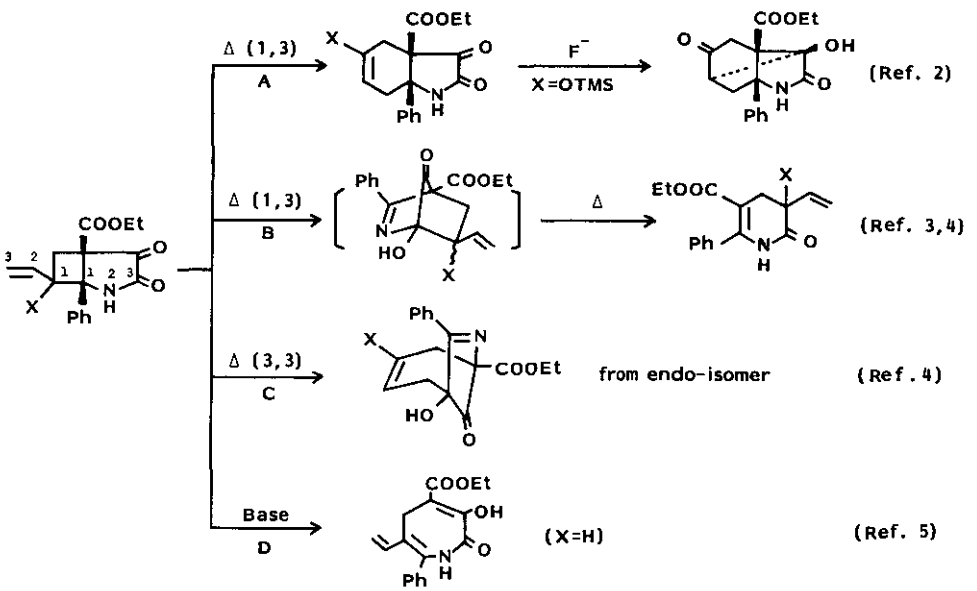


Chart 1

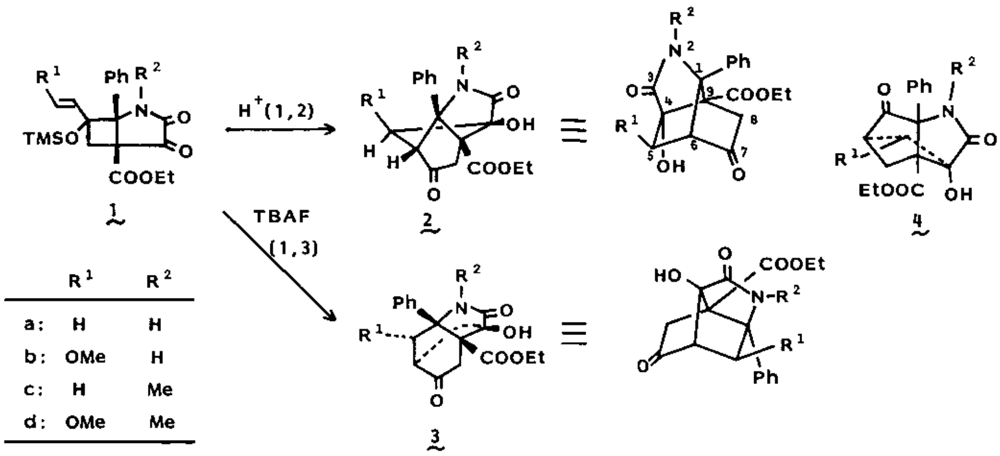
The path A, B, and C are the thermal reactions and the path D is the ionic reaction. Among those, the path B and C are essentially the reactions through lactim intermediates and accelerated by transforming the compound to the imidate.[3-4] The path A is facilitated when X is oxygenated substituent such as OTMS, for those compounds this pathway exceeds to the others yielding hydroindoles as major products.[2] The similar 1,3-shift occurs, probably in an ionic fashion, at a low temperature when the compound was treated with tetrabutylammonium fluoride.[6]

In this communication we wish to demonstrate that 7-oxy-7-vinyl derivatives 1 under acidic conditions undergo completely different skeletal rearrangement to afford novel caged compounds having a norbornane skeleton.

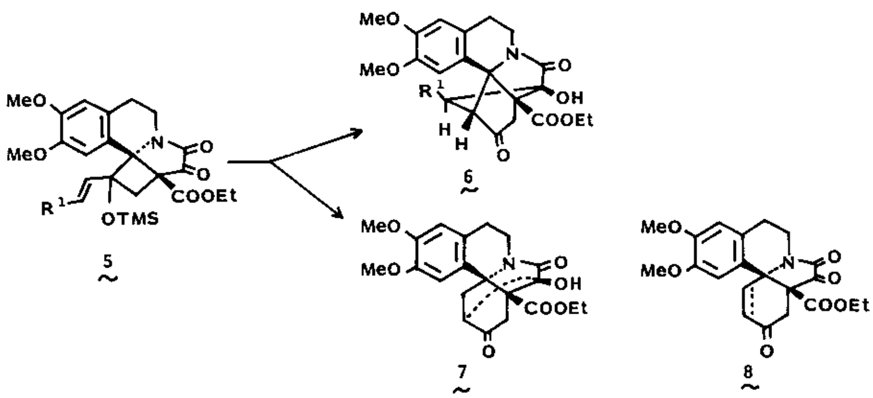
Treatment of 1a with BF_3.etherate in CH_2Cl_2 or 5% HCl in THF(1:1) at room temperature afforded a ketol 2a[7] in good yield. The methoxyvinyl derivative 1b on a similar acidic treatment readily rearranged to yield the similar product 2b. The N-methyl derivatives 1c and 1d on BF_3 treatment also gave the similar rearrangement products 2c and 2d, respectively. In the tetracyclic congeners 5a and 5b, hydrochloric acid caused the same rearrangement to yield the ketols 6a and 6b, respectively. However, BF_3.etherate produced complex mixtures from which the isomeric ketol 7 and the enone 8b (both of which are 1,3-shift products)[8] were isolated in low yields, respectively. The results are summarized in Table 1.

The products 2a-d and 6a showed very close spectroscopic properties with the ketols 3a-d and 7 (1,3-shift products of the same substrates) ; that is, the presence of a tertiary OH, a five membered-ring ketone, $-\overset{|}{\underset{|}{C}}-CH_2CO-$, and $-\overset{|}{\underset{|}{C}}-\underset{R}{\overset{|}{C}}H-\overset{|}{\underset{|}{C}}H-CO-$ together with the other expected functional groups, but they were isomeric each other. These spectral evidences coupled with the mechanistic consideration (intramolecular Prins reaction accompanied by 1,2-shift of C_1-C_7 bond) lead to the structures as depicted in Chart 2. The alternative structure 4 resulting from C_6-C_7 bond migration was eliminated from the ^1H- and ^{13}C-NMR spectral data.

The configuration of the methoxy group (R^1) in 2b, 2d, and 6b was assigned as exo in norbornane system since $J_{H^5-H^6}$ in those compounds are zero, while in 2a and 2c, $J(H^5_{endo}-H^6)$ and $J(H^5_{exo}-H^6)$ are shown to be 0 and 6 Hz, respectively.



	R^1	R^2
a:	H	H
b:	OMe	H
c:	H	Me
d:	OMe	Me



a: 3,4-dihydro
b: $\Delta^{3,4}$

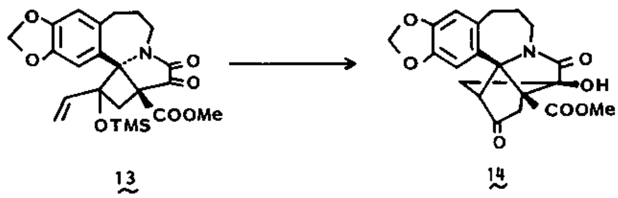


Chart 2

Table 1. Reactions of Trimethylsilyloxy-vinyl(or methoxyvinyl)-cyclobutanes 1 and 5 with Various Cationic Reagents

	Conditions			Product(Yield %)		
	Reagents	Temp.(°C)	Time	[1,2]shift	[1,3]shift	others
1a	A	20	18h	2a(75)	----	----
	B	20	4h	2a(57)	----	----
	C	20	18h	10a(47)	11a(39)	----
	D[a)]	-30	10min	2a(28)	3a(57)	----
1b	A	0	5min	2b(46)	----	----
	B	20	4h	2b(86)	----	----
	C	20	18h	10b(12)	11b(69)	----
	D[a)]	-30	3min	----	3b(88)	----
1c	A	40	4h	2c(98)	----	----
	B	20	4h	----	----	9c(60)
	D[a)]	-30	2min	2c(32)	3c(63)	----
1d	A	20	30min	2d(55)	----	----
	B	20	4h	2d(85)	----	----
	D[a)]	-30	2min	----	3d(83)	----
5a	A	20	1h	---- [c)]	7 (8)	(11)[d)]
	B	20	3h	6a(97)	----	----
	D[b)]	-30	5min	6a(11)	8a(51)	----
5b	A	20	1h	6b(18)	8b(10)	(25)[d)]
	B	20	1h	6b(85)	----	----
	D[b)]	-30	10min	----	8b(82)	----

A: BF_3·etherate(5-10 equiv.) in CH_2Cl_2 B: 5% HCl-THF(1:1)
C: Et_3OBF_4 in CH_2Cl_2 D: n-Bu_4NF in THF
a) T. Sano, J. Toda, and Y. Tsuda, Chem. Pharm. Bull., submitted (ref.6)
b) T. Sano, J, Toda, and Y. Tsuda, and T. Ohshima, Heterocycles, accompanying paper (ref.8). c) not detected on TLC. d) The structures were not clarified.

Table 2. Chemical Shifts of Ring Protons and Carbons of 2

^{1}H-NMR(δ, J, Hz in $CDCl_3$)

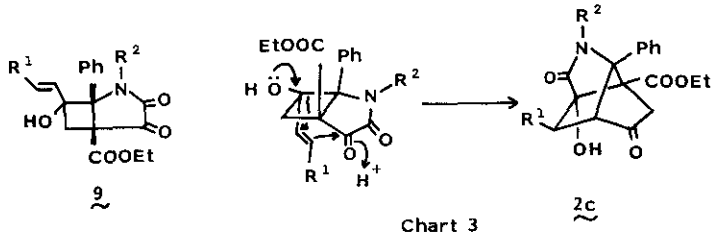
	C_5-H (exo)	C_5-H (endo)	C_6-H	C_8-H[a)] (ΔAB, J)
2a	2.44 (dd,6,14)	1.94 (d,14)	3.26 (d,6)	2.74 (0.26,20)
2b	----	3.77 (s)	3.27 (s)	2.64 (0.21,20)
2c	2.26 (dd,6,14)	1.92 (d,14)	3.33 (d,6)	2.71 (0.21,20)
2d	----	3.76 (s)	3.29 (bs)	2.62 (0.25,20)

a) The signal appeared as ABq of 2H.

^{13}C-NMR(δ, $CDCl_3$)

	1	3	4	5	6	7	8	9
2a	71.0(s)	168.0(s)	83.7(s)	35.8(t)	53.5(d)	208.6(s)	35.1(t)	67.3(s)
2b	70.5(s)	167.5(s)	89.4(s)	84.2(d)	64.5(d)	206.7(s)	36.7(t)	69.8(s)

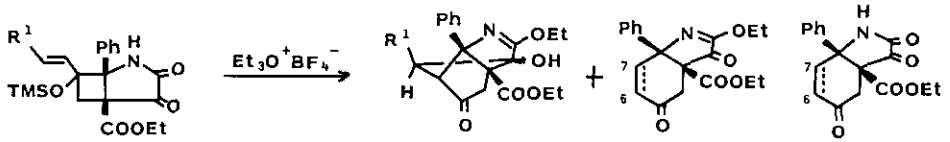
The following evidence shows that this rearrangement reaction proceeds via a 7-hydroxy-7-vinyl derivative 9.[9] On treatment of 1c with 5% HCl-THF at room temperature, it gave a hydroxy compound 9c which on further treatment with BF_3.etherate in CH_2Cl_2 under reflux yielded the rearranged ketol 2c in 90% yield.



9 2c

Chart 3

Triethyloxonium fluoroborate was the reagent to effect two reactions, 1,2- and 1,3-shifts, competitively. Thus, treatment of 1a and 1b with this reagent in CH_2Cl_2 produced two imidates 10a,b and 11a,b, which were proved by conversion of 2a,b and 12a,b to 10a,b and 11a,b, respectively.



1a,b

10 11 12

a: R^1=H
b: R^1=OMe

a: 6,7-dihydro
b: $\Delta^{6,7}$

Chart 4

As shown previously,[6] tetra-n-butylammonium fluoride (TBAF) induces oxy-vinyl 1,3-shift, but the above 1,2-shift was observed as a side reaction in some instances, in which ammonium cation may promote the Prins reaction. In a particular case, the substrate 13 gave the 1,2-shift product 14 as a major product on treatment with TBAF.[10]

The facts reported in this and preceding papers[6] clearly demonstrated that which type of shifts predominantly occur is dependent not only on the reagents, acidity or basicity of the reaction media, but also on the structures of the substrates.

REFERENCES AND NOTES

1. Dioxopyrrolines XXXI: Part XXVIII and 2-azabicyclo[3.2.0]Heptane-3,4-dione (7): see Ref.6
2. T. Sano, J. Toda, Y. Horiguchi, K. Imafuku, and Y. Tsuda, Heterocycles, 1981, 16, 1463.
3. T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, 1981, 16, 889.
4. T. Sano, Y. Horiguchi, S. Kambe, J. Toda, J. Taga, and Y. Tsuda, Heterocycles, 1981, 16, 893.
5. T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, 1981, 12, 1427.
6. T. Sano, J. Toda, and Y. Tsuda, Chem. Pharm. Bull., 1983, 31, 2960.
7. All new compounds gave correct molecular formula. Mp's and IR(Nujol, cm^{-1}) are as follows.

   2a: mp 226°C. IR: 3470, 3175, 3090, 1760, 1725.

   2b: mp 235-237°C. IR: 3270, 3200, 3100, 1760, 1720, 1690.

   2c: mp 163.5-165°C. IR: 3400, 1760, 1725, 1700.

   2d: mp 178-180°C. IR: 3390, 1755, 1720.

   6a: mp 212-215°C. IR: 3340, 1750, 1730, 1705.

   6b: mp 212-213°C. IR: 3350, 1745, 1725, 1705.

   9c: mp 144-146°C. IR: 3370, 1780, 1720, 1705. ^{1}H-NMR δ: 1.01(3H, t, J=7 Hz) 2.66 and 3.26(each 1H, d, J=13 Hz), 5.35(1H, dd, J=2 and 11 Hz), 5.64 (1H, dd, J=2 and 17 Hz), 6.37(1H, dd, J=11 and 17 Hz), 7.35(5H, bs).

   10a: mp 165-168°C. IR: 3400, 1740, 1705, 1615.

   10b: mp 124-125°C. IR: 3475, 1750, 1715, 1630.

   11a: mp 111-113°C. IR: 1760, 1735, 1720, 1640.

   11b: mp 70-72°C. IR: 1760, 1730, 1675, 1630.
8. T. Sano, J. Toda, T. Ohshima, and Y. Tsuda, Heterocycles, accompanying paper.
9. Occurrence of this rearrangement suggests that the vinyl group in 1 is of endo configuration since otherwise the intramolecular Prins reaction could be difficult to occur. However, this is not rigid proof of the configuration of the vinyl group in 1, since if rapid epimerization at C_7 prior to cyclization took place, the exo-isomer would give the same product. In fact, very recent X-ray analysis of 1c revealed that the compound has exo-vinyl, endo-OTMS configuration (unpublished results).
10. Y. Tsuda and T. Ohshima, unpublished result.

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