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NOVEL SYNTHESIS OF OXADIAZINONE AND OXADIAZEPINONE DERIVATIVES BY RING EXPANSION OF DIAZIRIDINONE#

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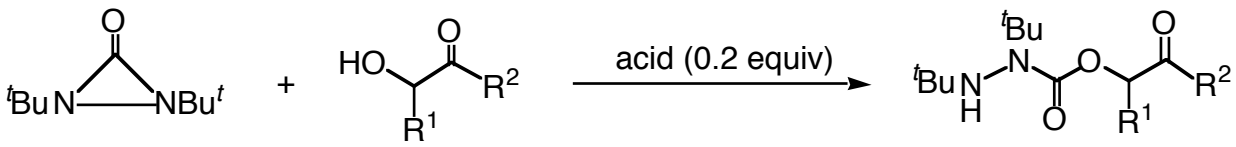
Abstract-Treatment of *N, N'*-di-*tert*-butyldiaziridinone with α-hydroxy ketones in the presence of a catalytic amount of BF_3•OEt_2 gave carbazate derivatives in excellent yields. Acid-catalyzed recyclization of these compounds easily proceeded to give oxadiazinone derivatives. The reaction was applicable to the synthesis of oxadiazepinone derivatives and also to one-pot process.

Three-membered heterocycles have served as potential building blocks for the synthesis of numerous types of heterocycles.[1] Among these small rings, diaziridinones[2] show unique ring opening reactivity because of their highly strained three-membered structures which consist of a carbonyl carbon and two nitrogen atoms.[1-3] Previously, we reported the ring enlargement reactions of *N, N'*-di-*tert*-butyldiaziridinone (**1**) with anionic species, which are metalated isocyanides,[4a] α-metalated nitriles,[4b] metalated active methylene compounds,[4c] and 1-sodio-2-formylpyrrole,[4d] *via* ring opening and recyclization. Although diaziridinone (**1**) bears two *tert*-butyl groups on nitrogen atoms to stabilize the three-membered ring, the substituents on products can be readily removed under acidic conditions, and hence diaziridinone (**1**) can be regarded as the non-substituted diaziridinone. On the other hand, we have already showed the ring expansion of **1** with benzonitrile in the presence of Lewis acid.[5] Thus, this property forced us to investigate the reaction of diaziridinone with other neutral neucleophiles. Here we report the acid-catalyzed ring opening and subsequent recyclization reactions of diaziridinone (**1**) with several alcohols having a carbonyl group.



1 (1 equiv) **2a-c** (1 equiv) **3a-c**

Acid-catalyzed ring opening reactions of *N, N'*-di-*tert*-butyldiaziridinone (**1**) with α-hydroxy ketones (**2a-c**) are summarized in Table 1. Treatment of **1** with hydroxyacetone (**2a**) in the presence of a catalytic amount

#Dedicated to Professor Teruaki Mukaiyama on the occasion of his 73rd birthday.

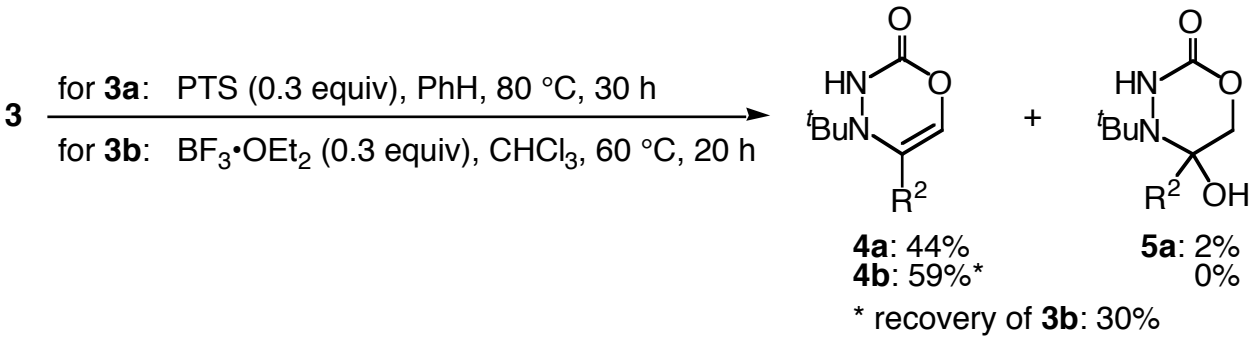
of BF_3•OEt_2 in $CHCl_3$ at 0 ℃ for 0.5 h gave acetylmethyl carbazate (**3a**) in 92% yield. The reaction proceeded with high yields in any of the other solvents, such as THF, Et_2O or PhMe. Although *p*-toluenesulfonic acid (PTS) did not catalyze the reaction at 0 ℃, the desired product was obtained in 81% yield by raising the reaction temperature to 60 ℃. 2-Hydroxyacetophenone (**2b**) also reacted with **1** in good yield to give a benzoyl derivative (**3b**). The reaction was applicable to a hydroxy ester having a secondary hydroxy group. The substituents on the carbonyl group of **2** did not prevent the formation of **3**.

Table 1. Acid-Catalyzed Ring Opening Reactions of **1** with **2a**-**c**

R^1	R^2		acid	solv.	temp. (°C)	time (h)	yield (%)
H	Me	(**2a**)	$BF_3 \cdot OEt_2$	$CHCl_3$	0	0.5	92 (**3a**)
H	Me	(**2a**)	$BF_3 \cdot OEt_2$	THF	0	0.5	89 (**3a**)
H	Me	(**2a**)	$BF_3 \cdot OEt_2$	Et_2O	0	0.5	88 (**3a**)
H	Me	(**2a**)	$BF_3 \cdot OEt_2$	PhMe	0	0.5	90 (**3a**)
H	Me	(**2a**)	PTS[a)]	PhMe	0	0.5	0 (**3a**)
H	Me	(**2a**)	PTS	$CHCl_3$	60	1	81 (**3a**)
H	Ph	(**2b**)	$BF_3 \cdot OEt_2$	$CHCl_3$	0	0.5	90 (**3b**)
Me	OEt	(**2c**)	$BF_3 \cdot OEt_2$	$CHCl_3$	0	0.5	90 (**3c**)

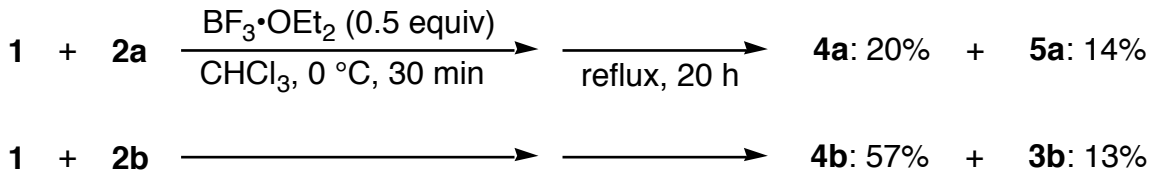
a) *p*-toluenesulfonic acid.

Since no cyclic product was formed under the above mentioned conditions, recyclizations of isolated **3** were examined under heating in the presence of acid catalysts. When **3a** was treated with a catalytic amount of PTS in benzene at 80 ℃, oxadiazinone derivatives (**4a** and **5a**) were obtained. The position of *tert*-butyl group on **4a** was confirmed by existence of nOe between methyl and *tert*-butyl groups. While BF_3•OEt_2 was found to be a good catalyst for the recyclization of **3b** to **4b**, the recyclization of **3c** did not proceed under these conditions.

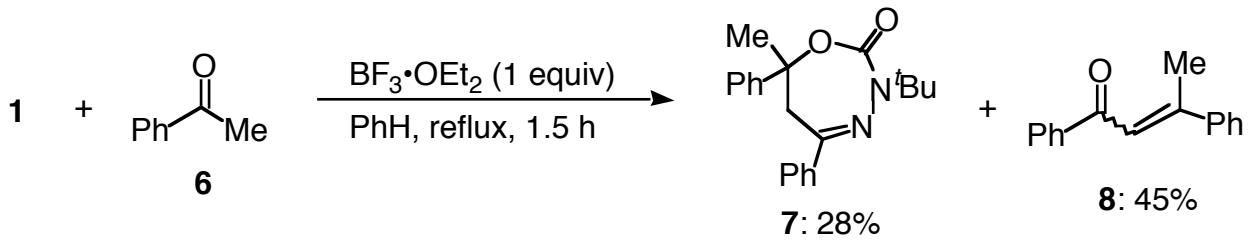


One-pot ring expansion reactions were studied because both the ring opening and recyclization reactions proceeded under the same conditions using acid catalysts except for the factor of the temperature. When the reaction of **1** with **2a** was carried out under the following conditions, the cyclic products (**4a** and **5a**) were

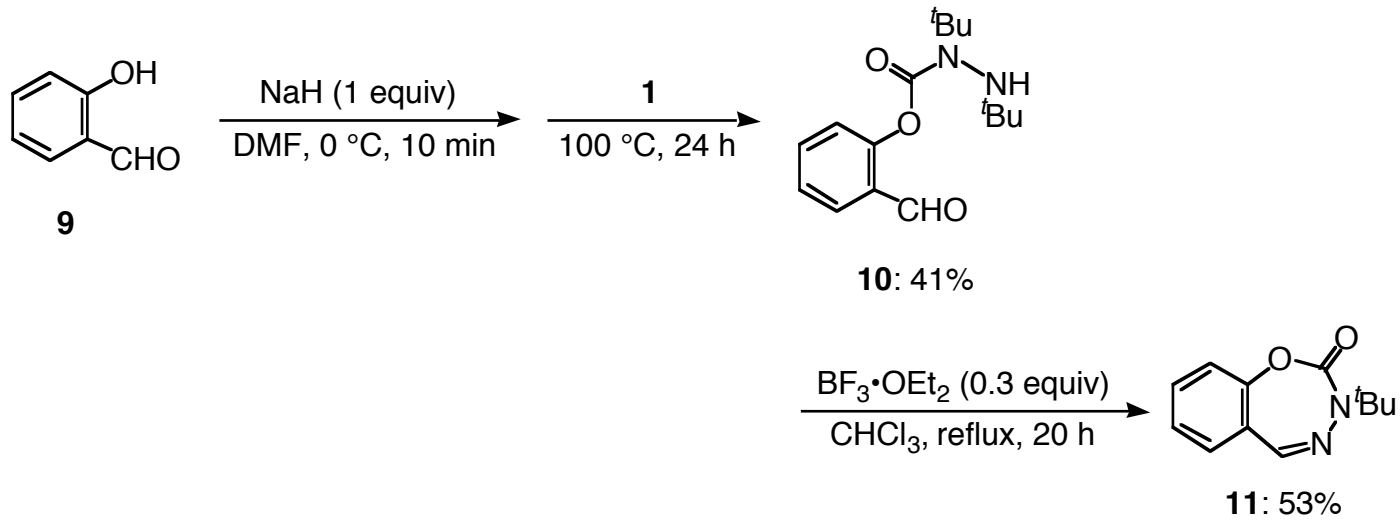
obtained. The hydroxy ketone (**2b**) also reacted with **1** to give the corresponding oxadiazinone (**4b**) in good yield, as well as the non-cyclized product (**3b**).



Then, β-hydroxy ketones were employed in the present reaction with the intention of obtaining seven-membered heterocycles. Since acetophenone is readily converted into β-hydroxy ketone by aldol condensation under acidic conditions, the reaction of **1** with acetophenone (**6**) in the presence of BF_3•OEt_2 gave an expected oxadiazepinone derivative (**7**) in one-pot process.



Furthermore, salicylaldehyde was used as a substrate to synthesize a bicyclic seven-membered heterocycle. Although the reaction of salicylaldehyde (**9**) with **1** gave a complicated mixture under the acidic conditions, treatment of **9** with an equimolar amount of NaH followed by addition of **1** afforded the ring opening product (**10**) in 41% yield. Subsequently, isolated **10** was heated in the presence of BF_3•OEt_2 (0.3 equiv) to give benzoxadiazepinone (**11**) in 53% yield.



In summary, we have demonstrated here a novel synthesis of oxadiazinones *via* carbazate derivatives prepared effectively by the reaction of *N*, *N*'-di-*tert*-butyldiaziridinone with α-hydroxy ketones. The present reactions are applicable to one-pot process and also to the synthesis of oxadiazepinone derivatives by employing acetophenone and salicylaldehyde as a β-hydroxy carbonyl compound or its precursor. The reactions of **1** with various types of hydroxy and mercapto ketones are under investigation.

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6. Selected spectroscopic data for **4a**: IR (neat) 3300, 1762, 1670, 1132 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 1.17 (s, 9H), 1.99 (d, *J* = 1.7 Hz, 3H), 4.08 (br s, 1H), 6.48 (q, *J* = 1.7 Hz, 1H); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 8.4, 27.9, 56.3, 121.2, 126.9, 156.5; EI-MS *m/z* 170 (M^+, 28), 114 M^+-^{t}Bu, 100). **4b**: IR (neat) 3308, 3020, 2980, 1758, 1666 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 1.00 (s, 9H), 4.40 (br s, 1H), 6.85 (s, 1H), 7.33-7.73 (m, 5H); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 27.9, 57.2, 122.0, 127.2, 127.9, 128.2, 128.8, 130.5, 156.2; EI-MS *m/z* 232 (M+, 24), 176 (M^+-^{t}Bu, 100). **7**: IR (nujol) 1750, 1570 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.30 (s, 3H), 5.32 (d, J = 1.0 Hz, 1H), 5.37 (d, *J* = 1.0 Hz, 1H), 7.22-7.80 (m, 10H); EI-MS *m/z* 336 (M^+). **11**: IR (neat) 2980, 1732, 1658 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 1.43 (s, 9H), 7.09-7.68 (m, 4H), 8.25 (s, 1H); EI-MS *m/z* 218 (M^+, 29), 162 (M^+-^{t}Bu, 100).