Beckmann Rearrangements of 1-Indanone Oxime Derivatives Using Aluminum Chloride and Mechanistic Considerations

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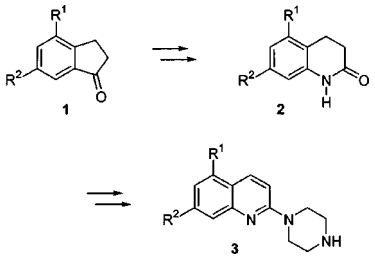
Hydrocarbostyril, which is a key intermediate in our new synthetic route to 6-nitroquipazine, can be prepared from 1-indanone oxime by Beckmann rearrangement. We have optimized the reaction by using a Lewis acid, aluminum chloride, in the yield of 91% instead of common acids such as polyphosphoric acid, and sulfuric acid used in conventional Beckmann rearrangement (20% in the literature, 10% in our experiment). The optimized condition is established by using three equivalents of aluminum chloride in CH_2Cl_2 at -40 °C - room temperature for 40 min. We have applied this condition to other 1-indanone derivatives, such as 4-methyl-, 4-methoxy-, 4-nitro and 6-nitro-1-indanones. The mechanism of this BR has been proposed on the basis of the effect of temperature and substituent on product ratio, with the aid of PM3 calculation for a model system.

Introduction

Since the first discovery of Beckmann rearrangement (BR) by Beckmann in 1886,[1] successive investigations have largely carried out and applied in many ways.[2] The BR of ketoximes or aldoximes in the presence of certain acid, including Lewis acids, give amides or lactams. The BR is a skeletal rearrangement, which have become a useful way for not only the incorporation of nitrogen atom efficiently in both cyclic and acyclic system, but also the synthesis of various alkaloids. The basic mechanism of BR was suggested as shown in Figure 1.[2a] Concerted [1,2]-sigmatropic rearrangement occurs in transition state, and then primary product is tautomerized to give target compound immediately.

Recently, we have reported BR of 1-indanone oxime (**1**) providing hydrocarbostyril (**2**) as a major product in 91% yield *via* tosylate at from -40 °C to room temperature using a Lewis acid, aluminum chloride (Scheme 1).[3] This method is very efficient as well as mild because the reaction undergoes at room temperature and even at lower temperatures like -40 °C. Thus, this method will be useful for the synthesis of other hydrocarbostyril derivatives from corresponding 1-indanone derivatives. There has been reported only one example of BR using aluminum chloride in literature,[4] however the role of aluminum chloride has not been studied.



Scheme 1

Our continuing interest in developing new neurotransmitters, which have good binding affinity to serotonin reuptake site *in vivo*, has led us to synthesize 6-nitroquipazine (**3**, $R^1 = NO_2$, $R^2 = H$). Recently we have reported a new efficient synthesis of 6-nitroquipazine from hydrocarbostyril.[5] Key intermediate, 2-chloro-6-nitroquinoline, was synthesized successfully from hydrocarbostyril, which was a major product of BR of 1-indanone oxime. We have applied to other 1-indanone derivatives in order to synthesize multi-substituted quinoline derivatives. Consequently, our method was found to be excellent for the synthesis of substituted hydrocarbostyril. Labeling of these compounds with radioactive isotope, such as F-18, make it possible to image its binding site in our bodies by means of positron emission tomography (PET).[6] In order to prepare labeled 6-nitroquipazine derivatives, it is required to synthesize highly substituted hydrocarbostyrils.

We have designed a new synthetic route involving BR as core step. Consequently, this process was applied to other 1-indanone derivatives such as 4-methyl, 4-methoxy, 4-nitro and 6-nitro-1-indanone. In this paper, we now report the BRs of other 1-indanone oxime derivatives using this method, considering the mechanism of this rearrangement and the role of aluminum chloride.

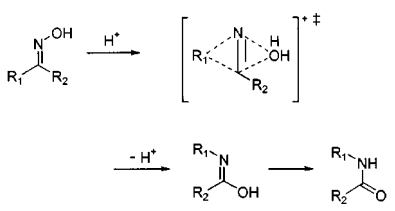


Figure 1. Suggested mechanism for conventional BR of ketoxime.

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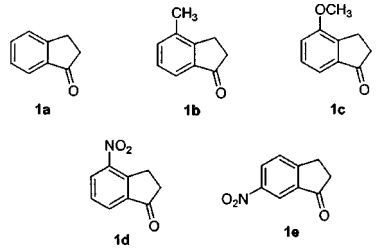


Figure 2. 1-1ndanone derivatives studied in this work.

Results and Discussion

The Preparation of 1-Indanone Derivatives. The 1-indanone derivatives chosen as starting molecules (Figure 2) were prepared by the following procedure except for commercially available 1-indanone (**1a**).

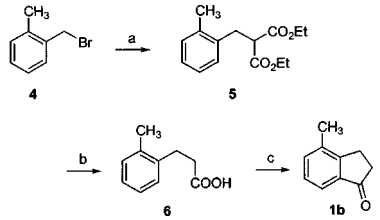
As shown in Scheme 2, 2-methylbenzylbromide (**4**) was reacted with diethylmalonate in alcoholic sodium ethoxide to give diethyl (2-methylbenzyl)malonate (**5**) in 75% yield. 3-(2-Methylphenyl)propionic acid (**6**) was prepared by saponification of **5** in ethanolic NaOH followed by decarboxylation in dimethylformamide at 120 °C in overall yield of 90%. The intramolecular ring formation of **6** in polyphosporic acid (PPA) at 110 °C provided 4-methyl-1-indanone (**1b**) in 90% yield.

4-Methoxy-1-indanone (**1c**) was synthesized by Fries rearrangement of dihydrocoumarin (**7**) with three equivalents of aluminum chloride followed by *O*-methylation of 4-hydroxy-1-indanone (**8**) with 0.6 equivalents of dimethylsulfate (Scheme 3).

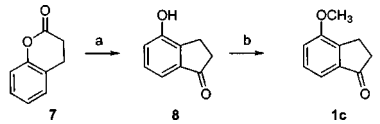
The nitration of 1-indanone (Scheme 4) gave 6-nitro-1-indanone (**1e**) as a major product and 4-nitro-1-indanone (**1d**) as a minor product in 9 : 1 ratio.

Synthesis of 1-Indanone Oxime Tosylates and Their Beckmann Rearrangements. The BRs of these 1-indanone derivatives were carried out by the process illustrated in Scheme 5.

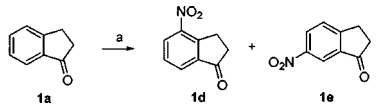
As shown in Scheme 5, various 1-indanone derivatives



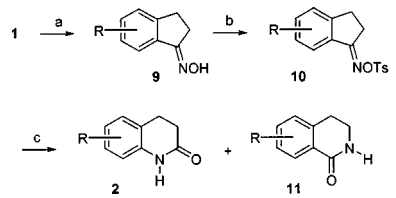
Scheme 2. Reaction conditions: (a) $CH_2(CO_2Et)_2$, EtONa/EtOH, -40 °C - rt; (b) (i) aq. NaOH, EtOH, 90 °C, 3 h; (ii) DMF, 120 °C, 2 h. c) PPA, 110 °C, 20 min.



Scheme 3. Reaction conditions: (a) $AlCl_3$, 190 °C, 6 h; (b) $(Me)_2SO_4$, dioxane, NaOH, 50 °C, 2 h.



Scheme 4. Reaction conditions: (a) HNO_3, H_2SO_4, -10 °C - rt.

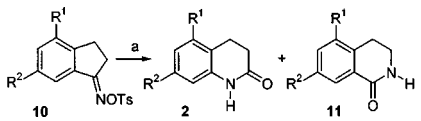


Scheme 5. Reaction conditions: (a) NH_2OHHCl, 4 N NaOH, MeOH, -10 °C - rt; (b) TsCl, 4 N NaOH, acetone, -10 °C - rt; (c) $AlCl_3$, CH_2Cl_2, -40 °C - rt.

were treated under similar condition. After 1-indanones, **1a-e**, and hydroxylamine hydrochloride were dissolved in methanol, 4 N NaOH was added to the solution at -10 °C. After 5 min, the reaction was continued for additional 40-150 min at room temperature. All of the 1-indanones provided the corresponding oximes as a mixture of isomers (*trans* and *cis*) in 95% yield. To a solution of 1-indanone oximes and *p*-toluenesulfonyl chloride in acetone was added 4 N NaOH at -10 °C. The reaction was completed within 40 min to provide corresponding 1-indanone oxime tosylates as a mixture of isomers in 95% yield as well.

The BRs of these tosylates were carried out both with a mixture and with pure *trans* isomer. The results using aluminum chloride catalyst were described in Table 1. The *trans*/*cis* ratio of tosylates was calculated on the basis of NMR integration, and the ratio of 3,4-dihydro-2(1*H*)-quinolinones (**2**) to 3,4-dihydro-1(2*H*)-quinolinones (**11**) was obtained by isolation with flash column chromatography. The final products, 3,4-dihydro-2(1*H*)-quinolinone and 3,4-dihydro-1(2*H*)-quinolinone derivatives synthesized from 1-indanone derivatives were characterized by clear assignment of the ^1H and ^{13}C NMR spectra.

Table 1. The Beckmann Rearrangement of 1-Indanone Oxime Tosylates

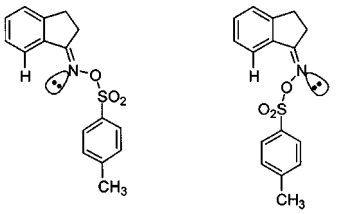


Compd	Tosylateratio		Reaction temp. (°C)	Total yield (%)	Product ratio	
	trans	*cis*			**2**	**11**
10a	97	3	-40 °C - rt	99	92	8
	21	79[a]	-40 °C - rt	98	13	87
10b	100	0	-40 °C - rt	88	85	15
10c	100	0	-40 °C - rt	80	74	26
10d	80	20	-40 °C - rt	84	27	73
10e	84	16	-40 °C - rt	40	96	4

[a]Since *cis* tosylate is formed in a small ratio and has very similar R_f to *trans* isomer, this was the best ratio we got.

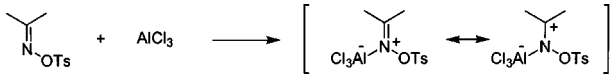
Mechanistic Consideration. The fact that both pure *trans* and *cis* oxime were isomerized on TLC covered with silica gel is one of strong evidence of isomerization even under mild acidic condition such as on silica gel. Although *cis* tosylate could not purely be obtained like *trans* tosylate, it was collected as a mixture containing a little amount of *trans*.

One can imagine that the relative stability of *trans*-oxime tosylate (*trans*-**10**) is greater than that of *cis* isomer (*cis*-**10**) due to the steric repulsion between the tosyl group and C_{Ar}-H as shown below.

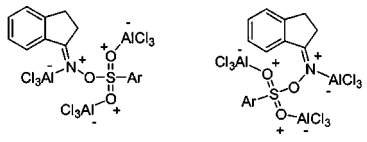


trans-**10** *cis*-**10**

Table 1 shows that the relative amount of 3,4-dihydro-1(2*H*)-quinolinone produced was slightly increased more than the amount of *cis* tosylate used. It indicates that rotational barrier of C=N double bond would be fairly high. But in the presence of Brønsted or Lewis acids such as silica gel or $AlCl_3$, rotational barrier would be lowered. The complex formation of tosylate and $AlCl_3$ makes the double bond rotation possible.



There are three equivalents of $AlCl_3$ needed at optimized condition for the BR reaction. At least one equivalent of $AlCl_3$ coordinates to nitrogen lone pair and the other two equivalents coordinate to oxygen lone pair of tosylate.



Considering the mechanism of conventional BR (Figure 1), *trans*-tosylate would give 3,4-dihydro-2(1*H*)-quinolinone and *cis*-tosylate gives 3,4-dihydro-1(2*H*)-quinolinone. We have proposed the plausible mechanism of BR of 1-indanone oxime tosylate based on the experimental results with substituted 1-indanone oxime tosylate (Figure 3).

One can easily guess that the reactant complex formation step with $AlCl_3$, enol product formation step from product complex, and enol-keto tautomerization step would be very faster than the other steps. So the product distribution would be determined by the relative reactivities of the *cis*-*trans* isomerization between reactant complexes (k_r and k_{-r}) and of the product complex formation steps (k_t and k_c).

In order to clarify the above mentioned point, temperature-dependence of product distribution for the BR reaction of *trans*-1-indanone oxime tosylate was carried out and the result is summarized in Table 2. Logarithm of the ratio of product **2** to **11** is plotted against 1/T in Figure 4. The reaction was carried out using more than 99% pure *trans* isomer of **1** with excess $AlCl_3$ for 30 min.

Arrhenius type plot of log([**2**]/[**11**]) *vs* 1/T in Figure 4, shows non-linear characteristics, and the downward curvature of this plot suggests that the relative magnitude of k_r and k_t, and that of k_{-r} and k_c, is comparable and varied due to the change of reaction temperature. In other words, the rate-determining step for the product formation is dependent on the temperature.

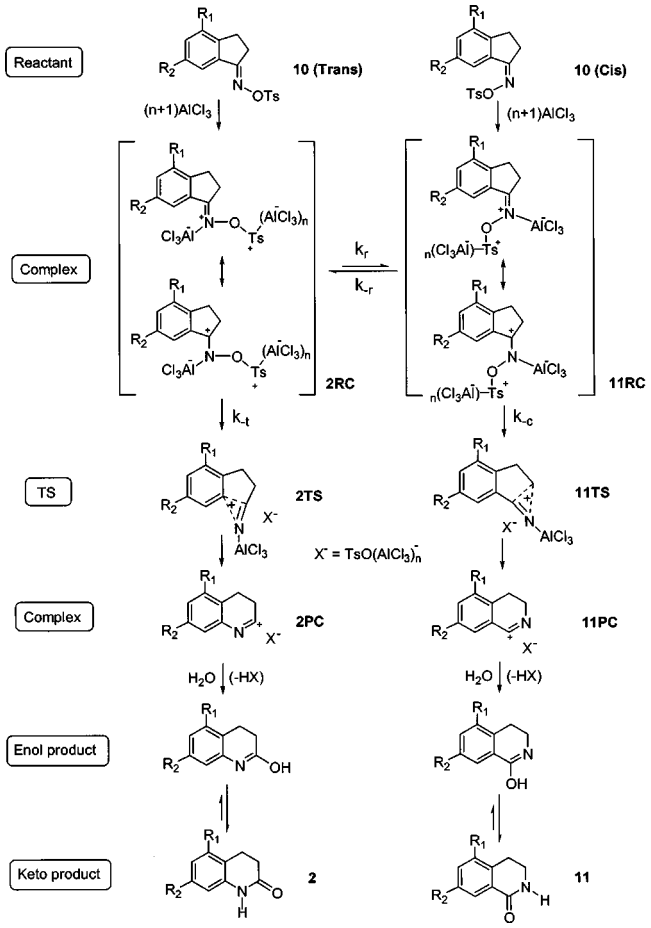


Figure 3. Proposed mechanism of BR of 1-indanone oxime tosylate.

Table 2. Product Ratio of 3,4-Dihydro-2(1*H*)-quinolinone (2) and 3,4-Dihydro-1(2*H*)-quinolinone (11) in BR of 1-Indanone Oxime Tosylate in CH_2Cl_2, with Excess $AlCl_3$ for 30 min at Four Temperatures

Temp. (°C)	Product ratio (%)	
	2	**11**
-40	95.6	4.4
-7	94.5	5.5
4	92.1	7.9
23	75.9	24.1

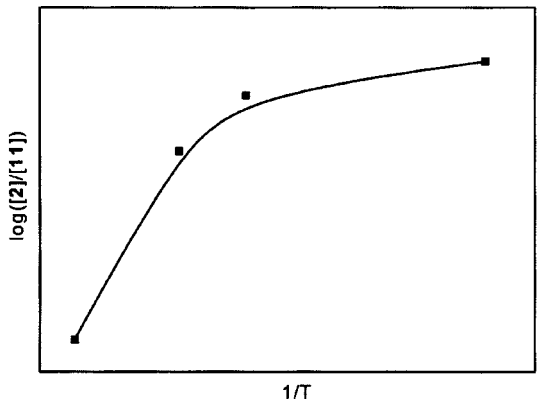


Figure 4. Plot of log ([**2**]/[**11**] *vs*. 1/T for BR reaction of 1-indanone oxime tosylate (cf. Table 2).

At low temperature region around -40 ~ -7 °C, the selectivity of **2** over **11** is very high. These results indicate that the isomerization via the rotation around C-N bond (k_r) would be the rate determining step for the formation of **11**. On the other hand, the relatively increased selectivity of **11** at higher temperature region above -7 °C indicates that the rate determining step for the formation of **11** is changed to the *cis*-product formation step (k_c) from the *cis*-reactant complex.

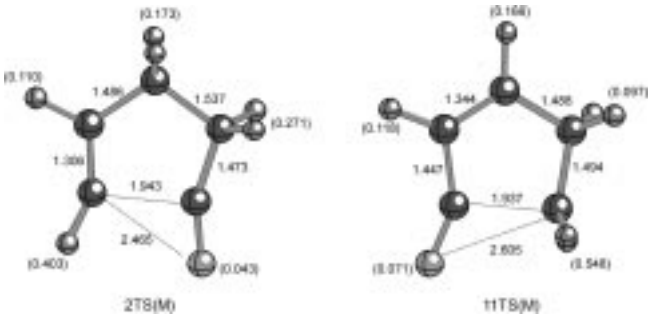


Figure 5. Structures of two TS model, 2TS(M) and 11TS(M) by PM3 calculation. Values in the parenthesis are group charges.

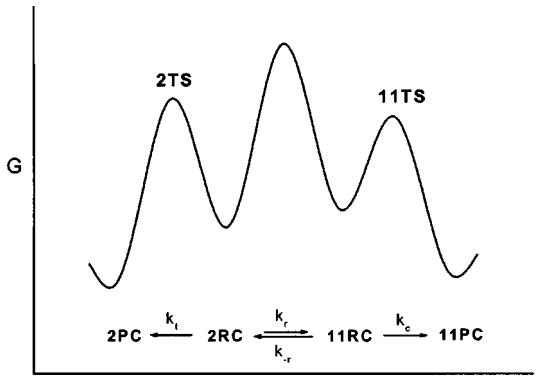


Figure 6. Schematic reaction profile for the product determining step for BR of **10a**.

We have calculated the structures and energies of the model system for **2TS** (**2TS**(**M**)) and **11TS** (**11TS**(**M**)) to understand the electronic nature of both TSs by PM3, one of the semi-empirical quantum mechanical calculation methods. The dehydroxylated cation of 2-cyclopentenone oxime is used as a model system for the complex between $AlCl_3$ and 1-indanone oxime tosylate, and the results of calculation are summarized in Figure 5.

According to the result of PM3 calculation for the model of both TSs, **2TS**(**M**) could be considered as a structure that vinyl cation part attacks alkyl cyanide part, while **11TS**(**M**) could be considered as a structure that alkyl cation part attacks vinyl cyanide part. Because vinyl cyanide is a little bit stabler than alkyl cyanide due to π - conjugation between C=N and C=C π orbitals, and alkyl cation is also more stable than σ - type vinyl cation, **11TS**(**M**) is expected to be more stable than **2TS**(**M**). On the basis of these interpretation, the experimental results that *cis*-**10a** goes completely to **11** but *trans*-**10a** goes partially to **2** at the reaction conditions in Table 1 is easily understandable. These characteristics could be summarized with a schematic reaction profile which is shown in Figure 6.

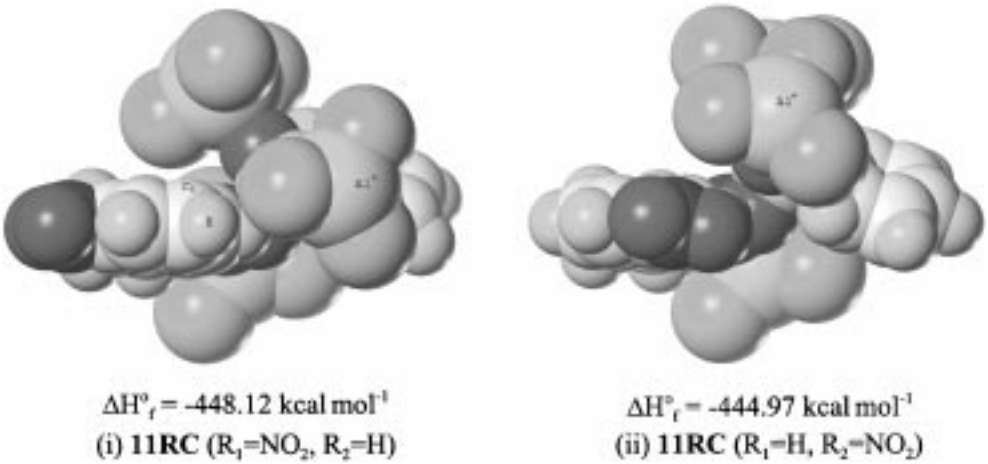


Figure 7. Space filling models whose optimized structures were calculated by AM1 QM method. In (i), stabilization by electrostatic attraction of C_6-$H^{\delta+}$ and $^{\delta-}$Cl-Al^* is shown. In (ii), one can see that Al^*Cl_3 group move away from aromatic ring plane, and NO_2 group rotates slightly from the molecular plane in order to decrease Van der Waals and electrostatic repulsion between and (Cl_2-Al^*)-$Cl^{\delta-}$ and $^{\delta-}$O-(NO), leading to net destabilization of 3.15 kcal mol^{-1}.

Considering the electronic nature of **2TS(M)** and **11TS(M)**, one can easily understand the results of substituent effects on the product distribution in Table 1. If the substituent is changed from H to more electron withdrawing Me, MeO and NO_2 at R_1, which is meta to phenyl cationic reaction center, in **2TS**, it will be destabilized. However, since the same variation of substituent at R_1, which is far from phenethyl cation center due to the intervening methylene group in **11TS**, it destabilizes **11TS** less than **2TS**. Therefore, the product ratio of **2** to **11** decreases along with the electron withdrawing power of the substituents, H > Me > MeO > NO_2.

Nitro substituent on C_6 (R_2=NO_2) is expected to decrease reactivity due to the strong electron withdrawing effect, but the most important effect is the drastic reversal of product ratio. This effect could be interpreted by the destabilization of **11TS**, due to the Van der Waals and electrostatic repulsion between $AlCl_3$ of [tosylate $(AlCl_3)_n$]$^-$ leaving group and adjacent NO_2 group in **11TS** as shown in space filling model which were calculated by AM1 QM method.

Experimental Section

Materials and Methods. Column chromatography was done by Flash chromatography with silica gel (EM Science, 230-400 mesh ASTM). Solvents and reagents were purchased from the following commercial sources: Aldrich, Kanto, Acros. Analytical thin layer chromatography (TLC) was performed with Merck silica gel F-254 glass-backed plates. Visualization was achieved by phosphomolybdic acid (PMA), $KMnO_4$, or anisaldehyde spray reagents, iodine, or UV illumination. ^{1}H and ^{13}C NMR spectra were obtained on Varian Gemini-2000 spectrometers and are reported in parts per million downfield from internal tetramethylsilane. Mass spectra were obtained on HP590 GC/MS 5972 MSD spectrometer.

General Procedure of 1-Indanone Oxime Derivatives 9a-e. Hydroxylamine hydrochloride (0.68 g, 9.84 mmol) in 2 mL of water was added to a solution of 1-indanone (1.00 g, 7.57 mmol) in 20 mL of methanol. To the stirred mixture was added 4 N NaOH (3.78 mL, 15.13 mmol) at -10 °C dropwise. After 5 min, the cooling bath was removed. The reaction was maintained for 1 h at rt, and then quenched by adding 50 mL of water. The resulting mixture was extracted with ethylacetate (20 mL × 4). The combined extracts were dried over sodium sulfate, and evaporated under reduced pressure. The 1.05 g (94%) of 1-indanone oxime was obtained by flash chromatography (20% EtOAc/Hx) as a white crystal: **Indan-1-one Oxime (9a)**: commercially available.: ***trans*-4-Methylindan-1-one Oxime (9b)**: 99% yield as a white crystal; IR (KBr) 3170, 3160, 2930, 1660, 1470, 1380 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.92-7.60 (br s, 1H), 7.58-7.53 (m, 1H), 7.23-7.16 (m, 2H), 3.03-2.92 (m, 4H), 2.28 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 162.8, 145.9, 133.9, 133.3, 129.4, 125.7, 117.4, 25.7, 247.1, 16.7; MS (EI) m/z (relative intensity) 161 (M^+, 100), 146 (17), 128 (28), 115 (37), 91 (14), 77 (11); Anal. Calcd for $C_{10}H_{11}NO$: C, 74.50; H, 6.88; N, 8.69. Found: C, 74.52; H, 7.01; N, 8.61.: ***trans*-4-Methoxyindan-1-one Oxime (9c)**: 94% yield as a white crystal; IR (KBr) 3260, 3180, 2940, 1590, 1455, 1265 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.78 (br s, 1H), 7.26-7.24 (m, 2H), 6.82 (dd, *J* = 5.6, 3.2 Hz, 1H), 3.86 (s, 3H), 2.97 (s, 4H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 160.3, 155.3, 137.2, 134.4, 127.7, 111.7, 109.9, 54.1, 24.5, 23.9; MS (EI) m/z (relative intensity) 177 (M^+, 100), 162 (7) 146 (7), 133 (11), 116 (18), 103 (20), 91 (11), 77 (15).: ***trans*-4-Nitroindan-1-one Oxime (9d)**: 94% yield as a brown crystal; ^{1}H NMR (200 MHz, acetone-d_6) δ 10.37 (s, 1H), 8.17 (d, *J* = 8 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 3.53-3.46 (m, 2H), 3.00-2.92 (m, 2H); ^{13}C NMR (50 MHz, acetone-d_6) δ 159.2, 142.5, 139.8, 127.5, 125.5, 123.94, 28.43, 24.23; MS (EI) m/z (relative intensity) 192 (M^+, 100), 175 (33), 144 (51), 127 (38), 114 (41), 103 (44), 77 (26).: ***trans*-6-Nitroindan-1-one Oxime (9e)**: 94% yield as a brown crystal; ^{1}H NMR (200 MHz, acetone-d_6) δ 10.46 (s, 1H), 8.28 (d, *J* = 2.0 Hz, 1H), 8.17 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 3.21-3.14 (m, 2H), 3.02-2.95 (m, 2H); ^{13}C NMR (50 MHz, acetone-d_6) δ 159.1, 154.1, 146.7, 137.6, 125.7, 123.3, 114.5, 27.3, 24.8; MS (EI) m/z (relative intensity) 192 (M^+, 100), 175 (4), 145 (11), 128 (36), 115 (21), 101 (31), 89 (15), 77 (22).

General Procedure of 1-Indanone Oxime Tosylate Derivatives 10a-e. To a stirred solution of 1-indanone oxime (0.90 g, 6.12 mmol) and *p*-toluenesulfonyl chloride (1.28 g, 6.73 mmol) in 30 mL of acetone was added 4 N NaOH at -10 °C dropwise. After 5 min, the cooling bath was removed. The reaction was continued for 1h at rt, and then quenched by being poured into 200 mL of ice-crashed water. The resulting mixture was extracted with ethylacetate (20 mL × 4). The combined extracts were dried over sodium sulfate, and evaporated under reduced pressure. The 1.76 g (96%) of 1-indanone oxime was obtained by flash chromatography (20% EtOAc/Hx) as a white crystal.: ***trans*-*O*-(*p*-Toluenesulfonyl)indan-1-one Oxime (10a)**: IR (KBr) 3440, 3070, 2930, 1600, 1450, 1380 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.46-7.22 (m, 5H), 3.03 (br s, 4H), 2.44 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.7, 148.4, 143.3, 131.9, 131.5, 130.8, 127.9, 127.3, 125.6, 124.1, 121.3, 26.7, 26.0, 19.9; MS (EI) m/z (relative intensity) 301 (M^+, 2), 260 (6), 209 (11), 155 (22), 139 (28), 130 (100), 116 (45), 106 (44), 91 (43), 77 (33).: ***trans*-4-Methyl-*O*-(*p*-toluenesulfonyl)indan-1-one Oxime (10b)**: 95% as a white crystal; IR (KBr) 3055, 2920, 1635, 1340 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 6.6 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.17 (dd, *J* = 13.6, 6.6 Hz, 1H), 7.15 (d, *J* = 13.6 Hz, 1H), 3.02-2.96 (m, 2H), 2.92-2.86 (m, 2H), 2.41 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.2, 147.5, 143.3, 133.5, 131.6, 131.2, 127.9, 127.3, 125.9, 118.7, 25.9, 25.6, 19.9, 16.7; MS (EI) m/z (relative intensity) 315 (M^+, 0.3), 225 (3), 160 (4), 155 (5), 144 (100), 130 (35), 118 (22), 105 (16), 91 (31), 77 (15); Anal. Calcd for $C_{17}H_{17}NO_3S$: C, 64.74; H, 5.43; N, 4.44; S, 10.17. Found: C, 64.46; H, 5.48; N, 4.39; S, 9.81.: ***trans*-4-Methoxy-*O*-(*p*-toluenesulfonyl)-indan-1-one Oxime (9c)**: 96% yield as a white crystal; IR (KBr) 3435, 3010, 2970, 1640, 1440, 1360, 1315 cm^{-1}; ^{1}H

NMR (200 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2, 2H), 7.26-7.12 (m, 2H), 6.84 (dd, J = 5.8, 3.0 Hz, 1H), 3.81 (s, 3H), 2.99-2.87 (m, 4H), 2.41 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.1, 154.8, 143.3, 137.0, 133.4, 131.2, 127.9, 127.3, 127.2, 113.1, 111.0, 53.6, 26.1, 23.7, 19.9; MS (EI) m/z (relative intensity) 331 (M^+, 8), 267 (3), 239 (5), 177 (9), 162 (17), 155 (33), 146 (20), 139 (33), 105 (25), 91 (100), 77 (34).: ***trans*-4-Nitro-*O*-(*p*-toluenesulfonyl)indan-1-one Oxime (10d)**: 95% yield as a brown crystal; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.30 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 7.8 Hz, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.50 (t, J = 7.8 Hz, 1H), 7.36 (d, J = 8.6 Hz, 2H), 3.57-3.52 (m, 2H), 3.13-3.06 (m, 2H); MS (EI) m/z (relative intensity) 346 (M^+, 0.3), 262 (4), 175 (15), 155 (36), 139 (8), 128 (15), 114 (7), 105 (22), 91 (100), 77 (7).: ***trans*-6-Nitro-*O*-(*p*-toluenesulfonyl)indan-1-one Oxime (10e)**: 96% yield as a brown crystal; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.44 (d, J = 2.0 Hz, 1H), 8.25 (dd, J = 8.6, 2.0 Hz, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.6 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 3.13 (m, 4H), 2.44 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.6, 154.5, 142.1, 143.8, 133.7, 130.7, 128.2, 127.3, 125.3, 125.0, 116.7, 27.0, 26.4, 20.0; MS (EI) m/z (relative intensity) 346(M^+, 0.2), 282 (8), 176 (100), 129 (46), 106 (81), 91 (61).

General Procedure of 3,4-Dihydro-2(1*H*)-quinolinone Derivatives 2a-e. Aluminum chloride (0.66 g, 4.98 mmol) was added to a solution of *O*-(*p*-toluenesulfonyl)indan-1-one oxime (0.50 g, 1.66 mmol) in 15 mL of CH_2Cl_2 at -40 ºC portionwise. After 10 min, The cooling bath was removed. The mixture was stirred for additional 1h at rt, and then quenched by adding 50 mL of water carefully. The mixture was extracted from aqueous phase with CH_2Cl_2 (20 mL × 4). The extract was dried over sodium sulfate, and evaporated under reduced pressure. The 222 mg (91%) of 3,4-dihydro-2(1*H*)-quinolinone (**2a**) and 20 mg (7%) of 3,4-dihydro-1(2*H*)-quinolinone (**11a**) was obtained by flash chromatography (40% EtOAc/Hx) as a white crystal. The 174 mg (55%) of *p*-toluensulfonyl chloride was also recovered.: **3,4-Dihydro-2(1*H*)-quinolinone (2a)**: IR (KBr) 3470, 3140, 2985, 1685, 1590, 1440, 1340, 1280 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.78 (br s, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 6.99 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 7.8 Hz, 1H), 2.96 (t, J = 7.5 Hz, 2H), 2.64 (t, J = 7.5 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.1, 135.8, 126.2, 125.9, 121.9, 121.4, 114.1, 29.0, 23.6; MS (EI) m/z (relative intensity) 147 (M^+, 87), 128 (8), 118 (100), 104 (20), 91 (22), 77 (12); Anal. Calcd for C_9H_9NO: C, 73.44; H, 6.16; N, 9.52. Found: C, 73.84; H, 6.44; N, 9.50.: **3,4-Dihydro-1(2*H*)-quinolinone (11a)**: IR (Kr) 3450, 3085, 2965, 1670, 1600, 1485 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.04 (dd, J = 7.6, 1.4 Hz, 1H), 7.46-7.28 (m, 3H), 7.19 (d, J = 7.2 Hz, 1H), 3.55 (td, J = 6.7, 3.0 Hz, 2H), 2.96 (t, J = 6.7 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.2, 137.3, 130.5, 127.4, 126.2, 125.3, 125.4, 38.4, 26.5; MS (EI) m/z (relative intensity) 147 (M^+, 61), 128 (10), 118 (100), 90 (56), 77 (4).: **5-Methyl-3,4-dihydro-2(1*H*)-quinolinone (2b)**: 75% yield as a white crystal; IR (KBr) 3460, 3150, 2930, 1680, 1480 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.48 (br s, 1H), 7.06 (t, J = 7.8 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.72 (d, J = 7.8 Hz, 1H), 2.91 (t, J = 7.8 Hz, 2H), 2.63 (t, J = 7.8 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.6, 135.7, 134.3, 125.5, 123.3, 120.3, 112.1, 28.6, 20.2, 17.6; MS (EI) m/z (relative intensity) 161 (M^+, 100), 146 (11), 132 (78), 128 (5), 115 (16), 91 (27), 77 (14); Anal. Calcd for $C_{10}H_{11}NO$: C, 74.50; H, 6.88; N, 8.69. Found: C, 74.64; H, 6.52; N, 8.65.: **5-Methyl-3,4-dihydro-1(2*H*)-quinolinone (11b)**: 13% yield as a white crystal; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.94 (dd, J = 7.4, 1.4 Hz, 1H), 7.34 (br s, 1H), 7.31 (dd, J = 7.4, 1.4 Hz, 1H), 7.24 (t, J = 7.4 Hz, 1H), 3.55 (td, J = 6.8, 1.0 Hz, 2H), 2.90 (t, J = 6.8 Hz, 2H), 2.30 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.5, 135.9, 133.2, 132.0, 127.4, 124.8, 124.2, 37.9, 23.2, 17.5; MS (EI) m/z (relative intensity) 161 (M^+, 68), 149 (11), 133 (10), 117 (3), 104 (36), 91 (4), 77 (20).: **5-Methoxy-3,4-dihydro-2(1*H*)-quinolinone (2c)**: 59% yield as a white crystal; IR (KBr) 3455, 3065, 2960, 1690, 1510, 1430 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.44 (br s, 1H), 7.11 (t, J = 8.0 Hz, 1H), 6.55 (d, J = 8.6 Hz, 1H), 6.50 (d, J = 8.0 Hz, 1H), 3.82 (s, 3H), 2.93 (t, J = 7.7 Hz, 2H), 2.59 (t, J = 7.7 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.8, 155.2, 136.8, 126.3, 109.9, 106.9, 103.7, 53.8, 28.4, 16.7; MS (EI) m/z (relative intensity) 177 (M^+, 100), 162 (7), 148 (34), 134 (19), 118 (30), 106 (24), 91 (8), 76 (9).: **5-Methoxy-3,4-dihydro-1(2*H*)-quinonlinone (11c)**: 21% yield as a white crystal; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.65 (d, J = 7.8 Hz, 1H), 7.46 (br s, 1H), 7.27 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.82 (s, 3H), 3.50 (td, J = 6.7, 2.4 Hz, 2H), 2.92 (t, J = 6.7 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.2, 154.0, 128.4, 126.1, 125.6, 118.1, 111.9, 53.9, 38.1, 19.6; MS (EI) m/z (relative intensity) 177 (M^+, 100), 160 (19), 147 (49), 133 (4), 120 (21), 105 (18), 90 (50), 77 (22).: **5-Nitro-3,4-dihydro-2(1*H*)-quinolinone (2d)**: 23% yield as a brown crystal; IR (KBr) 3460, 3090, 2940, 1700, 1520, 1455 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.15 (br s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 8.1 Hz, 1H), 7.09 (d, J = 7.8 Hz, 1H), 3.30 (t, J = 7.6 Hz, 2H), 2.66 (t, J = 7.6 Hz, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 168.8, 147.8, 139.5, 127.0, 118.7, 117.6, 116.5, 28.1, 20.5; MS (EI) m/z (relative intensity) 177 (M^+, 100), 160 (19), 147 (49), 133 (4), 120 (21), 105 (18), 90 (50), 77 (22).: **5-Nitro-3,4-dihydro-1(2*H*)-quinolinone (11d)**: 61% yield as a pale brown crystal; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.40 (dd, J = 7.8, 1.2 Hz, 1H), 8.13 (dd, J = 8.2, 1.2 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 6.70 (br s, 1H), 3.59 (td, J = 6.6, 3.0 Hz, 2H), 3.33 (t, J = 6.6 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 161.7, 146.8, 133.1, 131.2, 130.7, 126.5, 126.4, 37.1, 23.7; MS (EI) m/z (relative intensity) 192 (M^+, 7), 175 (100), 163 (5), 146 (13), 117 (53), 103 (46), 91 (7), 77 (10), 63 (19).: **7-Nitro-3,4-dihydro-2(1*H*)-quinolinone (2e)**: 38% yield as a brown crystal; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.87 (dd, J = 8.2, 2.2 Hz, 1H), 7.61 (d, J = 2.2 Hz, 1H), 7.33 (d, J = 8.2 Hz, 1H), 3.80 (t, J = 7.6 Hz, 2H), 2.69 (d, J = 7.6 Hz, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 169.1, 145.6, 138.5, 130.7, 127.9, 115.6, 108.1, 28.3, 23.7.: MS (EI) m/z (relative intensity) 192 (M^+, 100), 164 (86), 146 (13), 137 (15), 117 (45), 91 (4), 77 (39).: **7-Nitro-3,4-dihydro-1(2*H*)-quinolinone (11e)**: 2% yield as a brown crystal;

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.91 (d, J = 2.4 Hz, 1H), 8.30 (dd, J = 8.4, 2.4 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 6.43 (br s, 1H), 3.64 (t, J = 6.5 Hz, 2H), 3.13 (t, J = 6.5 Hz, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 161.6, 145.9, 145.6, 129.6, 128.4, 125.0, 120.6, 37.5, 26.5; MS (EI) m/z (relative intensity) 192 (M^+, 78), 164 (100), 135 (17), 89 (34), 77 (14).

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