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HETERO DIELS–ALDER TYPE REACTIONS BETWEEN DANISHEFSKY'S DIENES IN THE PRESENCE OF LEWIS BASE CATALYSTS.
AN EFFICIENT METHOD FOR THE SYNTHESIS OF SUBSTITUTED 2,3-DIHYDROPYRAN-4-ONES

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Dedicated to Professor Satoshi Omura on the occasion of his 70th birthday

Abstract – Alkoxy anion such as methoxide anion works effectively as Lewis base catalyst to activate silicon–carbon bond of 1-methoxy-3-trimethylsilyl-oxy-1,3-butadiens (Danishefsky's dienes) in the reaction between aldehydes and ketones. By using Lewis base as catalyst, acid sensitive substrates and Lewis basic moiety containing substrates can be used in this reaction. The hetero Diels–Alder type reaction proceeds through stepwise mechanism between silyl enolates and carbonyl compounds.

INTRODUCTION

2,3-Dihydropyran-4-ones are often found in number of biologically active compounds such as pharmaceuticals, agrochemicals and natural products. One of the most efficient methods for the synthesis of these heterocyclic compounds is a reaction of Danishefsky's dienes (1-methoxy- 3-trimethyl-silyoxy-1,3-butadienes) with carbonyl compounds which is well known as hetero Diels–Alder reactions[1]. These hetero Diels–Alder reactions are generally considered to proceed via either stepwise pathways or

concerted pathways by the promotion of Lewis acids. Although a number of effective Lewis acid catalysts are reported, there was no example of using Lewis base as a catalyst in this hetero Diels–Alder reaction. Since substrates having Lewis basic moieties such as an amino group are not generally employed in Lewis acid catalyzed reactions, Lewis base catalyzed hetero Diels–Alder reactions were desired. Recent reports show that the activation of silyl enolates by Lewis base catalysts is an efficient alternative to perform the reactions between electrophiles having Lewis basic functionalities. Recently, several Lewis base catalyzed reactions such as aldol reactions[2], Michael reactions[3], Mannich–type reactions[4], Strecker–type reactions[5], trifluoromethylation[6], cyanomethylation[7] and alkynylation[8] reactions were studied intensively in our laboratory and it was shown that most of the substrates having Lewis basic moieties are successively employed since these reactions proceed under Lewis basic conditions. In these reactions, it was assumed that silicon–oxygen bonds or silicon–carbon bonds were effectively activated with various oxygen or nitrogen Lewis bases, and then these considerations led us to examine that heterocyclic compounds would be formed via the activation of other silyl enolates. In this paper, we would like to report the effective activations of silyl enolates such as Danishefsky's dienes with Lewis base catalysts.

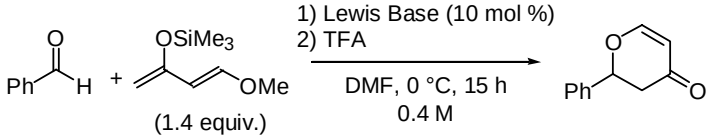
RESULTS AND DISCUSSION

In the first place, the suitable conditions for the activation of Danishefsky's diene were examined by screening the reaction between benzaldehyde using 10 mol% of various Lewis base catalysts, followed by treatment with trifluoroacetic acid (Table 1). Lewis base catalysts generated from carboxylic acids such as acetate anions or benzoate anions were not effective for this reaction, and the yield of the desired cycloadducts were very low. Phenoxide anions, stronger Lewis basic catalysts gave better results than the above mentioned acetate anion. When pyridine or THF was used as a solvent instead of DMF, the yields decreased except when ammonium phenoxide was used in rather lower concentration to give the desired product up to 77 % yield. The yield was dramatically improved when the alkoxide anion was used as a Lewis base catalyst and the best result was obtained when lithium methoxide was used. When the equivalent of lithium methoxide was reduced to 5 mol%, the yield lowered slightly. Thus, use of 10 mol % of lithium methoxide in DMF at 0 ˚C was determined as the optimized conditions.

Based on this promising result, hetero Diels–Alder type reactions of Danishefsky's diene between various aldehydes were examined (Table 2). Aromatic aldehydes with electron withdrawing– or donating–group reacted smoothly under the optimized conditions and the desired cycloadducts were obtained in

excellent yields. Other aryl aldehydes and hetero aryl aldehydes also reacted smoothly under the conditions and the desired cycloadducts were obtained in good to excellent yields. In addition to aromatic aldehydes, aliphatic aldehydes including tertiary aldehydes also reacted smoothly to afford the corresponding cycloadducts in high yields and α,β–unsaturated ketones also gave the desired cycloadducts in good yield.

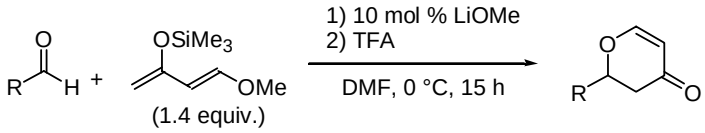
Table 1. Screening of catalyst and reaction conditions in the hetero Diels–Alder type reaction



Entry	Lewis Base	Yield (%)	Entry	Lewis Base	Yield (%)	Entry	Lewis Base	Yield (%)
1	AcOLi	9	7	PhONa	5	13	MeOLi[5]	50
2	$AcONBu_4$	36	8	PhOK	20	14	MeONa	28
3	$PhCOONBu_4$	32	9	$PhONBu_4$	77[1,3]	15	BnOLi	43
4	PhOLi	57	10	$PhONBu_4$	64	16	^{i}PrOLi	40
5	PhOLi	N.R.[1]	11	MeOLi	96	17	^{t}BuOLi	59
6	PhOLi	18[2]	12	MeOLi	79[4]	18	^{t}BuOK	25

[1] The reaction was carried out in THF.
[2] The reaction was carried out in pyridine.
[3] 0.1 M.
[4] 5 mol % catalyst was used.
[5] Prepared from MeOH and MeLi.

Table 2. LiOMe catalyzed hetero Diels–Alder type reactions with various aldehydes

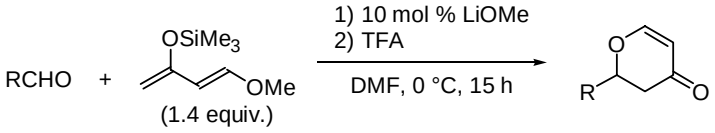


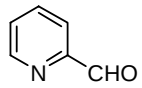
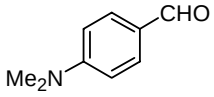
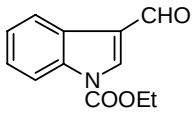
Entry	R	Yield (%)	Entry	R	Yield (%)	Entry	R	Yield (%)
1	Ph	96	7	4-$MeOC_6H_4$	79	12	$Ph(CH_2)_2$	81
2	2-ClC_6H_4	88	8	4-MeC_6H_4	76	13	c-Hex	78
3	4-ClC_6H_4	94	9	1-Naphthyl	93	14	*t*Bu	54
4	4-NCC_6H_4	93	10	2-Naphthyl	88	15	$BnOCH_2$	75
5	4-$MeOOCC_6H_4$	91	11	2-Furyl	75	16	(*E*)-PhCH=CH	80
6	2-$MeOC_6H_4$	80						

[1] 2.0 eq of Danishefsky's Diene was used.
[2] Determined by 1H-NMR analysis (270 Hz) using 1,1,2,2,-tetrachloroethane as an internal standard.

To demonstate the advantage of using Lewis base as a catalyst, the substrates having Lewis basic moieties were tried (Table 3). As expected, the reaction also proceeded smoothly with pyridine-carboxaldehyde, N-ethoxycarbonylindole-3-carboxyaldehyde, and 4-dimethylaminobenzaldehyde. These substrates generally interact with the Lewis acid catalyst, therefore, it is difficult to employ this substrate under commonly known Lewis acidic conditions.

Table 3. LiOMe catalyzed hetero Diels–Alder type reactions with aldehydes containing Lewis basic moiety

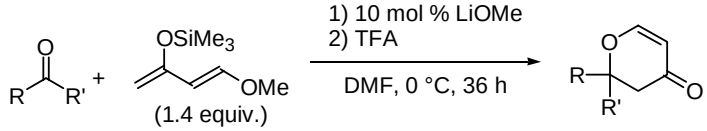


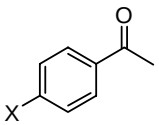
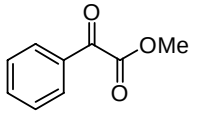
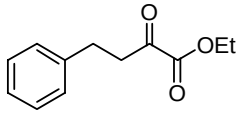
Entry	RCHO	Yield (%)
1		60[1]
2		50[1,2]
3		82

[1] Determined by 1H-NMR analysis (270 Hz) using 1,1,2,2,-tetrachloroethane as an internal standard.
[2] 2.0 eq of Danishefsky's Diene was used.

Next, various ketones were used in this hetero Diels–Alder type reactions (Table 4). When simple acetophenone was used, the reaction did not proceed smoothly as in the case with aldehydes. By using

Table 4. LiOMe catalyzed hetero Diels–Alder type reactions with various ketones

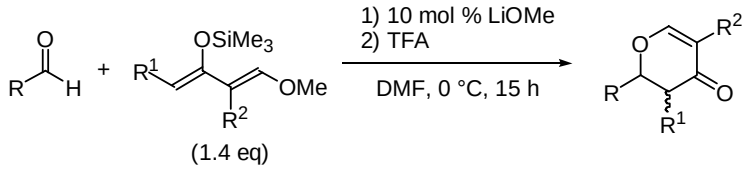


Entry	Ketone		Yield (%)	Entry	Ketone	Yield (%)
1		X = H	19	4		83
2		X = Br	26			
3		X = NO_2	66	5		82

more reactive ketones such as electron withdrawing group substituted acetophenones and α–ketoesters, the reactions were also successful to afford the desired tertiary carbon containing cycloadducts in high yields.

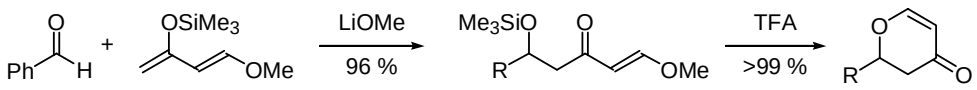
Then, other Danishefsky's dienes were tried under the same conditions (Table 5). It was found that various Danishefsky's dienes were successfully employed in the present hetero Diels–Alder type reaction. Danishefsky's dienes with methyl group at 2-position reacted smoothly and the desired cycloadducts were obtained in high yields. In the case when the substituent at 4-position was methyl group, the diastereoselectivities were rather small, but the reaction proceeded smoothly to afford the corresponding cycloadducts in excellent yields.

Table 5. LiOMe catalyzed hetero Diels–Alder type reactions with substituted Danishefsky's Dienes



Entry	R	R^1	R^2	Yield (%)	d.r.
1	Ph	H	Me	96	-
2		Me	Me	quant.	65 / 35
3	$Ph(CH_2)_2$	H	Me	68	-
4		Me	Me	80	59 / 41

Under the reaction conditions, the cycloadducts were not directly formed, and the corresponding aldol adducts were first obtained in 96 % yield. These aldol adducts were converted into the desired 2,3-dihydropyan-4-ones in almost quantative yields on treatment with trifluoroacetic acid. Thus, these hetero Diels–Alder reactions proceeded via stepwise aldol pathway, that is, first an aldol reaction and the following acid mediated annulation (Scheme 1).



Scheme 1. A stepwise mechanism of the hetero Diels-Alder type reaction promoted by Lewis Base catalysts

In conclusion, the first Lewis base promoted hetero Diels–Alder type reaction, an alternative synthetic method to Lewis acid mediated cyclization was established. Because Lewis base catalyst such as lithium methoxide is used, the substrates having Lewis basic moiety, which generally deactivate Lewis

acid catalysts, can be used. This method would provide a variety of 2,3-dihydropyran-4-ones in excellent yield under mild conditions.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a JEOL JNM-EX270L (270 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on a JEOL JNM-EX270L (68 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$; δ = 77.0 ppm). HRMS spectra were recorded on a JEOL JMS-700 mass spectrometer. Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF254, 0.25 mm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Kokusan Chemical, Wako Pure Chemical Industries, or Aldrich Chemical.

Typical experimental procedure for the hetero Diels-Alder raction. (Table 1, entry 10).

To a stirred solution of LiOMe (1.6 mg, 0.0421 mmol) in dry DMF (0.1 mL) was added a solution of 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (104.4 mg, 0.603 mmol) in DMF (0.3 mL) and a solution of benzaldehyde (44.0 mg, 0.415 mmol) in DMF (0.6 mL) at 0 °C under argon atmosphere. The mixture was stirred for 15 h at the same temperature and 5 ml saturated aqueous NH_4Cl solution was added to quench the reaction. The mixture was extracted with EtOAc and the combined organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated. The residue was dissolved in Et_2O (5 mL) and TFA (0.3 mL) was added at 0 °C. The mixture was stirred for 30 min at the same temperature and saturated aqueous $NaHCO_3$ solution was added carefully. After usual workup, the crude product was purified by preparative TLC (hexane / EtOAc / benzene = 10 / 2 / 1) to give the corresponding 2,3-di-hydro-pyran-4-one (70.6 mg, 96 %) as a colorless oil.

2-Phenyl-2,3-dihydropyran-4-one.[9]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.47 (1H, d, J = 6.2 Hz), 7.42-7.40 (5H, m), 5.52 (1H, d, J = 6.2 Hz), 5.43 (1H, dd, J = 14.4, 3.0 Hz), 2.97-2.62 (2H, m), ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.8, 162.9, 137.7, 128.8, 128.7, 126.0, 107.3, 81.0, 43.4.

2-(2-Chloro-phenyl)-2,3-dihydropyran-4-one.[10]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.59 (1H, dd, J = 7.4, 2.2 Hz), 7.51 (1H, d, J = 5.9 Hz), 7.42-7.26 (3H, m) 5.82 (1H, dd, J = 13.0, 4.6 Hz), 5.55 (1H, d, J = 6.2 Hz), 2.85-2.72 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.4, 162.9, 135.7, 131.6, 129.7, 127.3, 107.5, 78.1, 42.2.

2-(4-Chloro-phenyl)-2,3-dihydropyran-4-one. [10]

Colorless crystals. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.48-7.32 (5H, m), 5.53 (1H, d, J = 5.9 Hz), 5.40 (1H, dd, J = 14.2, 3.5 Hz), 2.91-2.61 (m, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.5, 162.8, 136.2, 128.9, 128.7, 127.3, 107.4, 80.2, 43.2.

4-(4-Oxo-3,4-dihydro-2H-pyran-2-yl)benzonitrile. [11]

Colorless crystals. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.73 (2H, d, J = 8.8 Hz), 7.55-7.49, (3H, m), 5.57-5.48 (2H, m), 2.89-2.66 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 190.5, 162.4, 142.8, 132.5, 126.4, 118.1, 112.6, 107.7, 79.8, 43.3.

4-(4-Oxo-3,4-dihydro-2H-pyran-2-yl)benzoic acid methyl ester.

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.09 (2H, d, J = 8.4 Hz), 7.51-7.46 (3H, m), 5.56-5.46 (2H, m), 3.93 (3H, s), 2.87 (1H, dd, J = 16.7, 14.0 Hz), 2.69 (1H, dd, J = 16.8, 3.9 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.1, 166.3, 162.6, 142.6, 130.5, 125.7, 80.4, 52.2, 43.4. HRMS (EI^+) cacld for $C_{13}H_{12}O_4$ $[M]^+$ 232.0736, found *m/z* 232.0732.

2-(2-Methoxy-phenyl)-2,3-dihydropyran-4-one. [10]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.52-7.46 (2H, m), 7.34 (1H, t, J = 7.8 Hz), 7.03 (1h ,t J = 8.1 Hz), 5.62 (1H, dd, J = 11.2, 6.5 Hz), 5.51 (1H, d, J = 5.9 Hz), 3. 84 (3H, s), 2.83-2.69 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.6, 163.3, 155.7, 129.5, 126.4, 126.2, 120.7, 110.5, 107.1, 77.5, 55.3, 42.3.

2-(4-Methoxy-phenyl)-2,3-dihydropyran-4-one. [12]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.45 (1H, d, J = 5.9 Hz), 7.32 (2H, d, J = 8.9 Hz), 6.93 (2H, d, J = 8.8 Hz), 5.50 (1H, d, J = 7.0 Hz), 5.36 (1H, dd, J = 14.2, 2.7 Hz), 3.82 (3H, s), 2.98-2.59 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.1, 163.1, 159.9, 129.7, 127.6, 114.1, 107.2, 80.9, 55.3, 43.2.

2-p-Tolyl-2,3-dihydropyran-4-one. [13]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.43 (1H, d, J = 5.9 Hz), 7.28- 7.19 (4H, m), 5.49 (1H, d, J = 6.2 Hz), 5.36 (1H, dd, J = 14.3, 3.5 Hz), 2.88 (1H, dd, J = 16.7, 14.3 Hz), 2.61 (1H, dd, J = 16.5, 2.4 Hz), 2.36 (3H, s). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.0, 163.0, 138.6, 134.6, 129.1, 125.9, 107.0, 80.9, 43.2, 21.1.

2-Naphthalen-1-yl-2,3-dihydropyran-4-one. [14]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.96-7.83 (3H, m), 7.61 (1H, d, J = 7.0 Hz), 7.57-7.45 (4H, m), 6.14 (1H, dd, J = 14.0, 2.7 Hz), 5.58 (1H, d, J = 5.9 Hz), 3.11-2.79 (2H, m)7.30–7.14 (m, 5H), 5.82 (br s, 1H), 3.30–3.22 (m, 2H), 2.62 (t, J = 7.6 Hz, 2H), 2.08–1.98 (m, 1H), 1.88–1.63 (m, 7H), 1.46–1.15 (m, 5H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.0, 163.1, 133.6, 133.1, 129.9, 129.4, 128.9, 126.6, 125.9, 125.1, 123.7, 122.4, 107.4, 78.3, 42.7.

2-Naphthalen-2-yl-2,3-dihydropyran-4-one. [15]

Colorless crystals. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.89-7.82 (4H, m), 7.53-7.45 (4H, m) 5.59-5.53 (2H, m), 2.98 (1H, dd, J = 16.7, 14.3 Hz), 2.72 (1H, ddd, J = 16.9, 3.6, 1.1 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.7, 162.9, 135.0, 133.2, 132.9, 128.6, 128.0, 127.6, 126.5, 126.5, 125.3, 123.4, 107.3, 81.1, 43.4.

2-Furan-2-yl-2,3-dihydropyran-4-one. [14]

Light yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.48 (1H, d, J = 6.2 Hz), 7.36 (1H, d, J = 5.9 Hz), 6.46-6.40 (2H, m), 5.51-5.44 (2H, m), 3.14-2.69 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.1, 162.2, 144.9, 143.5, 110.5, 109.6, 107.4, 73.6, 45.1.

2-Phenethyl-2,3-dihydropyran-4-one. [14]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.37 (1H, d, J = 5.9 Hz), 7.32-7.17 (5H, m), 5.40 (1H, d, J = 5.9 Hz), 4.44-4.33 (1H, m), 2.89-1.87 (6H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.1, 162.9, 140.5, 128.4, 128.2, 126.1, 106.9, 78.4, 41.8, 36.0, 30.9.

2-Cyclohexyl-2,3-dihydropyran-4-one. [14]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.39 (1H, d, J = 5.9 Hz), 5.41 (1H, d, J = 5.9 Hz), 4.22-4.13 (1H, m), 2.62-2.36 (2H, m), 1.91-1.62 (6H, m), 1.34-1.00 (5H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.3, 163.7, 106.6, 83.5, 41.4, 39.0, 28.0, 26.2, 25.8.

2-tert-Butyl-2,3-dihydropyran-4-one. [16]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.41 (1H, d, J = 5.7 Hz), 5.40 (1H, d, J = 5.9 Hz), 4.03 (1H, dd, J = 14.7, 3.5 Hz), 2.59-2.35 (2H, m), 1.00 (9H, s). ^{13}C NMR (68 MHz, $CDCl_3$) δ 193.3, 163.6, 106.5, 86.8, 37.2, 33.8, 25.4.

2-Benzyloxymethyl-2,3-dihydropyran-4-one. [9]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.39-7.30 (6H, m), 5.42 (1H, dd, J = 7.3, 3.8 Hz), 4.68-4.54 (3H, m), 3.73-3.68 (2H, m), 2.79-2.38 (2h, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.7, 162.6, 137.3, 128.4, 127.6, 107.0, 78.3, 73.5, 70.6, 28.4.

2-Styryl-2,3-dihydropyran-4-one. [15]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.44-7.25 (5H, m), 6.70 (1H, d, J = 16.0 Hz), 6.28 (1H, dd, J = 16.5, 6.8 Hz), 5.46 (1H, d, J = 5.9 Hz), 5.09-5.01 (1H, m), 2.78-2.48 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.2, 162.9, 135.4, 133.6, 128.6, 126.6, 124.8, 107.1, 79.6, 41.9.

2-Pyridin-2-yl-2,3-dihydropyran-4-one.[13]

^{1}H NMR (270 MHz, $CDCl_3$) δ 8.62 (1H, d, J = 4.6 Hz), 7.80-7.22 (4H, m), 5.54-5.29 (2H, m), 3.02-2.56 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.4, 162.3, 156.4, 148.7, 138.1, 123.9, 121.1, 107.8, 80.3, 41.6.

2-(4-Dimethylaminophenyl)-2,3-dihydropyran-4-one.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.45–7.43 (2H, m), 7.28-7.26 (1H, m), 5.49 (1H, d, J = 5.4 Hz), 5.33 (1H, dd, J = 14.9, 3.5 Hz), 3.09-2.92 (8H, m). HRMS (EI^+) cacld for $C_{13}H_{15}NO_2$ $[M]^+$ 217.1103, found *m/z* 217.1104.

3-(4-Oxo-3,4-dihydro-2H-pyran-2-yl)indole-1-carboxylic acid ethyl ester.

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.21 (1H, d, J = 8.1 Hz), 7.66-7.63 (2H, m), 7.47-7.27 (3H, m), 5.76 (1H, dd, J = 12.6, 4.1 Hz), 5.54 (1H, d, J = 6.2 Hz), 4.74 (2H, q, J = 7.3 Hz), 3.10 (1H, dd, J – 23.4, 12.7 Hz), 2.86 (1H, dd, J = 16.7, 4.1 Hz), 1.48 (3H, t, J = 7.3 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.5, 162.7, 146.9, 132.2, 128.0, 125.2, 123.5, 123.2, 119.5, 118.3, 115.5, 107.5, 107.5, 74.8, 41.5, 14.5. HRMS (EI^+) cacld for $C_{13}H_{12}O_4$ $[M+H]^+$ 286.1079, found *m/z* 286.1094.

2-Methyl-2-phenyl-2,3-dihydropyran-4-one.

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.41-7.30 (6H, m), 5.38 (1H, d, J = 5.9 Hz), 3.10-2.83 (2H, m), 1.71 (3H, s). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.1, 161.1, 128.5, 127.9, 124.6, 106.9, 84.3, 77.5, 47.5, 28.4. HRMS (EI^+) cacld for $C_{13}H_{12}O_4$ $[M]^+$ 188.0837, found *m/z* 188.0852.

2-(4-Bromophenyl)-2-methyl-2,3-dihydropyran-4-one.

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.49 (2H, d, J = 8.6 Hz), 7.30-7.23 (3H, m), 5.38 (1H, d, J = 6.2 Hz), 3.04-2.82 (2H, m), 1.69 (3H, s). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.2, 160.8, 131,7, 126.5, 121.9, 107.0, 84.0, 77.5, 47.3, 28.3. HRMS (EI^+) cacld for $C_{13}H_{12}O_4$ $[M]^+$ 267.1185, found *m/z* 267.0030.

2-Methyl-2-(4-nitrophenyl)-2,3-dihydropyran-4-one.

Yellow crystal. ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.23 (2H, d, J = 8.6 Hz), 7.58 (2H, d, J = 8.6 Hz), 7.35 (1H, d, J = 6.2 Hz), 5.43 (1H, d, J = 6.2 Hz), 3.08-2.89 (2H, m), 1.75 (3H, s). ^{13}C NMR (68 MHz, $CDCl_3$) δ 190.1, 160.6, 149.7, 125.7, 123.8, 107.3, 83.8, 47.2, 28.0. HRMS (EI^+) cacld for $C_{13}H_{12}O_4$ $[M]^+$ 233.0688, found *m/z* 233.0681.

4-Oxo-2-phenyl-3,4-dihydro-2H-pyran-2-carboxylic acid methyl ester.[15]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.54-7.36 (6H, m), 5.51 (1H, d, J = 5.9 Hz), 3.73 (3H, s), 3.51-3.03 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ 189.3, 169.8, 161.2, 136.5, 129.0, 128.7, 124.8, 108.2, 85.7, 53.5, 44.3.

4-Oxo-2-phenethyl-3,4-dihydro-2H-pyran-2-carboxylic acid ethyl ester.

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.42 (1H, d, J = 6.2 Hz), 7.32-7.15 (5H, m), 5.45 (1H, d, J = 6.2 Hz), 4.25-4.17 (2H, m), 3.02-2.96 (1H, m), 2.89-2.74 (3H, m), 2.32-2.22(2H, m), 1.27 (3H, t, J = 7.0 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.4, 169.5, 161.8, 128.5, 128.2, 126.3, 107.5, 85.4, 77.5, 62.4, 43.5, 39.3, 29.6, 14.2. HRMS (EI^+) cacld for $C_{13}H_{12}O_4$ $[M]^+$ 274.1205, found *m/z* 274.1207.

5-Methyl-2-phenyl-2,3-dihydropyran-4-one.[17]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.44-7.33 (6H, m), 5.37 (1H, dd, J = 14.4, 3.8 Hz), 2.94-2.64 (2H, m), 1.73 (3H, s). ^{13}C NMR (68 MHz, $CDCl_3$) δ 190.9, 169.3, 139.0, 128.7, 125.9, 125.6, 109.9, 80.9, 43.3, 14.4.

3,5-Dimethyl-2-phenyl-2,3-dihydropyran-4-one (less polar isomer).[18]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.41-7.31 (6H, m), 4.91 (1H, d, J = 13.2 Hz), 2.86-2.73 (1H, m), 1.73 (3H, s), 0.93 (3H, d, J = 7.0 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 194.9, 158.7, 137.5, 129.0, 128.7, 127.3, 113.1, 86.9, 44.7, 10.7, 10.3.

3,5-Dimethyl-2-phenyl-2,3-dihydropyran-4-one (more polar isomer). [18]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.39-7.32 (6H, m), 5.47 (1H, d, J = 3.2 Hz), 2.65-2.55 (1H, m), 1.74 (3H, s), 0.90 (3H, d, J = 7.3 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 197.7, 158.8, 136.8, 128.5, 127.9, 125.4, 112.5, 82.9, 45.7, 10.7, 9.9.

5-Methyl-2-phenethyl-2,3-dihydropyran-4-one. [19]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.32-7.17 (6H, m), 4.38-4.27 (1H, m), 2.82-2.67 (2H, m), 2.58-2.41 (2H, m), 1.99-1.86 (2H, m), 1.66 (3H, d, J = 1.1 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.5, 159.4, 140.7, 128.4, 128.3, 126.1, 118.1, 78.3, 41.7, 36.2, 31.0, 10.6.

3,5-Dimethyl-2-phenethyl-2,3-dihydropyran-4-one (less polar isomer). [20]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.32-7.17 (6H, m), 4.04-3.95 (1H, m), 2.93-2.67 (3H, m), 2.49-2.39 (1H, m), 2.08-1.98 (1H, m), 1.66 (3H, d, J = 11.1 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ 195.3, 158.4, 141.2, 128.5, 128.4, 126.0, 112.7, 82.8, 43.5, 34.3, 30.8, 10.7.

3,5-Dimethyl-2-phenethyl-2,3-dihydropyran-4-one (more polar isomer). [20]

Colorless oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.32-7.17 (6H, m), 4.31-4.27 (1H, m), 2.87-2.62 (1H, m), 2.40-2.31 (1H, m), 2.22-2.08 (1H, m), 1.86-1.66 (5H, m), 1.07 (3H, d, J = 7.6 Hz). ^{13}C NMR (68 MHz, $CDCl_3$) δ196.6, 158.5, 141.6, 128.3, 128.0, 125.7, 112.2, 82.8, 43.5, 35.0, 30.9, 10.7.

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