通过氰基亚胺与香豆灵酸甲酯的 1,3-偶极环加成反应 合成二氢吡喃并吡唑酮

王 博 王奇君 刘洪蕾 廖健宁 黄家兴* 郭红超*

(中国农业大学应用化学系 北京 100193)

摘要 室温条件下, 氰基亚胺与香豆灵酸甲酯或吡喃酮的[3+2]环加成反应可高效地进行, 以较高至优秀的产率和优秀的非对映选择性生成二氢吡喃并吡唑酮衍生物。

关键词 环加成; 氰基亚胺; 香豆灵酸酯; 吡喃酮; 吡唑酮

Synthesis of Dihydropyrano[3,2-c]pyrazolone through 1,3-Dipolar Cycloaddition of Nitrilimines with Methyl Coumalate

Wang, Bo Wang, Qijun Liu, Honglei Liao, Jianning
Huang, Jiaxing* Guo, Hongchao*

(Department of Applied Chemistry, China Agricultural University, Beijing 100193)

Abstract The 1,3-dipolar cycloaddition of nitrilimines with methyl coumalate or pyranone worked efficiently in the presence of $^i\text{Pr}_2\text{NEt}$ under room temperature to give functionalized dihydropyrano[3,2-c]pyrazol-5(1H)-one derivatives in high to excellent yields with excellent diastereoselectivities.

Keywords cycloaddition; nitrilimine; coumalate; pyranone; pyrazoline

1 Introduction

Pyrazolines is an important type of structure skeleton, widely existing in drug, agrochemicals, fluorescent probe, material, whitening agent.^[1] Pyrazoline derivatives displayed various biological activities such as local anaesthetic, anticonvulsant, anti-inflammatory, anthelmintic, antipyretic, antidepressant, analgesic, antitubercular, antimicrobial, anti-HIV, antiamebic, antidiabetic, antitumor, antihypertensive, insecticidal, and tranquilizing anti-oxidant activity.^[2]

Nitrilimines that are generated *in situ* from the corresponding hydrazone halides in the presence of a base are important 1,3-dipolar species,^[3] which can react with a variety of dipolarophiles such as nitrile, olefin, thiophene, enamine, alkyne and allene.^[4] Since Et_3N -catalyzed formal [3+2] cycloaddition of nitrilimines and nitriles was reported to form triazoles in 1962,^[5] nitrilimines has been exploited as a highly reactive dipole in cycloaddition reactions for synthesis of heterocyclic compounds.^[3,4] The cy-

cloaddition of nitrilimines with carbon-carbon unsaturated bond is one of the most concise approaches to access functionalized pyrazole derivatives.

Coumalates have been recognized as a very useful synthon for various transformations in organic synthesis.^[6] A large number of reactions involving coumalates have been reported.^[6] Among these reactions, cycloaddition and formal cycloaddition reactions of coumalates have extensively been used for synthesis of carbo- and hetero-cyclic compounds. Generally, alkyl coumalates may function as dienes, dienophiles, or dipolarophiles in cycloaddition reactions depending on their reaction partners. They have often been used as dienophiles with substituted dienes or dienes with different dienophiles for the Diels-Alder reaction.^[7,8] These coumalates may also perform inter- or intra-molecular [2+2] cycloaddition reactions.^[9] In addition, a few examples with coumalates as dipolarophiles for 1,3-dipolar cycloaddition reactions have been reported.^[10-13] Coumalates reacted as 4π electron partners or 2π electron partners towards 1,3-dipoles for [4+3] or [2+3] cycloadd-

* Corresponding authors. E-mail: hchgao@cau.edu.cn; 05084@cau.edu.cn

Received October 14, 2018; revised December 27, 2018; published online February 19, 2019.

Project supported by the National Natural Science Foundation of China (No. 21572264).

国家自然科学基金(No. 21572264)资助项目.

dition. For examples, Pd-catalyzed cycloaddition of trimethylenemethane with methyl coumalate led to a mixture of [2+3] and [4+3] cycloadducts.^[10] Phosphine-catalyzed annulation of Morita-Baylis-Hillman carbonates with methyl coumalate only gave [4+3] cycloadduct.^[11] Et₃N-catalyzed formal [4+3] cycloaddition of methyl coumalate with azomethine ylides provided an access to functionalized azepine derivatives.^[12] [3+2] cycloaddition of 4-aryl-6-(trifluoromethyl)-2-pyrones with the nonstabilized azomethine ylide obtained from sarcosine and formaldehyde afforded pyrrolopyrones.^[13] As shown above, although these successfully examples have been achieved, the study on 1,3-dipolar cycloaddition reactions of coumalates is still very limited. New discovery on the reactivity of coumalates is highly desirable. Due to excellent biological activity of both pyrazole and pyran derivatives, combining pyrazole and pyran moieties into one structure is very interesting. As our continuous efforts on cycloaddition reactions,^[14] the synthesis of dihydropyrano[3,2-*c*]-pyrazol-5(1*H*)-one derivatives was reported through 1,3-dipolar cycloaddition of nitrilimines with methyl coumalate (Scheme 1).

Scheme 1 [3+2] cycloaddition of nitrilimines with methyl coumalate

2 Results and discussion

Initially, the [3+2] cycloaddition was investigated with nitrilimine precursor (**1a**) and methyl coumalate (**2**) as model substrates (Table 1). With the use of Et₃N as the base, the reaction was performed in dichloromethane at room temperature for 48 h to give the cycloadduct **3a** in 60% yield (Entry 1). Solvent screening was next performed (Entries 2, 3). The medium polar THF resulted in decreasing of the yield to 29% (Entry 2). Using CHCl₃ as the solvent, the yield was increased to 76% yield (Entry 3). Then different bases were screened to improve the yield (Entries 4~8). To our delight, with the use of *i*-Pr₂NEt, the yield was increased to 82% yield (Entry 4). The bases such as *t*-BuOK and Cs₂CO₃ led to proximate yields to that through *i*-Pr₂NEt (Entries 5, 6). Only a trace of product was observed with the use of Na₂CO₃ as the base (Entry 7). There was no reaction when NaOH was used (Entry 8). When the reaction temperature was increased to 40 °C, the yield had not been improved (Entry 9). In the presence of *i*-Pr₂NEt,

further solvent screening revealed that the polar solvents such as DMSO, DMF, and MeCN were unfavorable to the reaction (Entries 10~12). On the basis of the above screening results, the optimized reaction conditions were determined as: with *i*-Pr₂NEt as the base in CHCl₃ at room temperature.

Table 1 Screening of the reaction conditions^a

Entry	Base	Solvent	Yield ^b /%
1	Et ₃ N	CH ₂ Cl ₂	60
2	Et ₃ N	THF	29
3	Et ₃ N	CHCl ₃	76
4	<i>i</i> -Pr ₂ NEt	CHCl ₃	82
5	<i>t</i> -BuOK	CHCl ₃	79
6	Cs ₂ CO ₃	CHCl ₃	77
7	Na ₂ CO ₃	CHCl ₃	Trace
8	NaOH	CHCl ₃	NR ^d
9 ^c	<i>i</i> -Pr ₂ NEt	CHCl ₃	81
10	<i>i</i> -Pr ₂ NEt	DMSO	16
11	<i>i</i> -Pr ₂ NEt	DMF	24
12	<i>i</i> -Pr ₂ NEt	MeCN	38

^a Unless indicated otherwise, the reaction was carried out with 0.15 mmol of **1a**, 0.1 mmol of **2** and 0.15 mmol of base in 1 mL of solvent at room temperature for 48 h. ^b Isolated yield; >20 : 1 *dr*, determined by ¹H NMR data. ^c The reaction was carried out at 40 °C. ^d No reaction.

With the optimal reaction conditions in hand, we explored the scope of the nitrilimine precursors. As shown in Table 2, the reaction could tolerate a wide scope of nitrilimines bearing different R¹ groups, giving the products **3** in high yields (Entries 1~16). Regardless of the electronic nature (electron-donating or electron-withdrawing) of the substituents on the benzene ring, the corresponding products **3a**~**3m** were obtained in good yields (72%~84%) (Entries 1~13). However, substrates bearing substituents at the 3-position of the aryl showed relative weak reactivities, leading to the corresponding products in lower yields (Entries 3, 5 and 8). In comparison, the electron-donating groups such as 3-methyl, 4-methyl, 3-methoxy and 4-methoxy nitrilimine precursors gave the product in relatively lower yields (Entries 10~13) than electron-withdrawing group (Entries 2~9). The fused aromatic and hetero-aromatic group-substituted substrates performed the reaction well, providing the corresponding products in 69%~84% yields (Entries 14~16). In addition, different R²-substituted nitrilimines also displayed good reactivity, producing the cycloadducts in good to excellent yields (Entries 17~26). The electron-donating groups such as 2-methyl, 3-methyl and 4-methyl led to the products in relatively higher yields (Entries 24~26) than electron-withdrawing groups (Entries 17~23). Alkyl substituted nitrilimines did not perform the reaction at room

temperature, and even at 80 °C (Entries 27, 28). Delightedly, 2*H*-pyran-2-one (**2b**) underwent the reaction at 40 °C to give the corresponding cycloadduct **3zc** in 68% yield (Entry 29). The relative configuration of the cycloaddition product was determined through X-ray crystallographic data of the product **3w** (Figure 1).^[15] To further demonstrate the practical utility of the synthetic method, the reaction of **1a** was performed on the gram scale, producing the desired product **3a** in 80% yield (Scheme 2).

Table 2 Substrate scope of nitrilimines **1**^a

Entry	R ¹ , R ²	1	R ³	2	3	Time/h	Yield ^b /%
1	Ph, Ph	1a	CO ₂ Me	2a	3a	48	81
2	2-FC ₆ H ₄ , Ph	1b	CO ₂ Me	2a	3b	48	80
3	3-FC ₆ H ₄ , Ph	1c	CO ₂ Me	2a	3c	48	76
4	4-FC ₆ H ₄ , Ph	1d	CO ₂ Me	2a	3d	48	83
5	3-ClC ₆ H ₄ , Ph	1e	CO ₂ Me	2a	3e	48	79
6	4-ClC ₆ H ₄ , Ph	1f	CO ₂ Me	2a	3f	48	84
7	2-BrC ₆ H ₄ , Ph	1g	CO ₂ Me	2a	3g	48	83
8	3-BrC ₆ H ₄ , Ph	1h	CO ₂ Me	2a	3h	48	79
9	4-BrC ₆ H ₄ , Ph	1i	CO ₂ Me	2a	3i	48	83
10	3-MeC ₆ H ₄ , Ph	1j	CO ₂ Me	2a	3j	48	75
11	4-MeC ₆ H ₄ , Ph	1k	CO ₂ Me	2a	3k	24	77
12	3-OMeC ₆ H ₄ , Ph	1l	CO ₂ Me	2a	3l	48	72
13	4-OMeC ₆ H ₄ , Ph	1m	CO ₂ Me	2a	3m	48	76
14	1-Naphthyl, Ph	1n	CO ₂ Me	2a	3n	48	84
15	2-Naphthyl, Ph	1o	CO ₂ Me	2a	3o	48	80
16	2-Furanyl, Ph	1p	CO ₂ Me	2a	3p	48	69
17	Ph, 2-FC ₆ H ₄	1q	CO ₂ Me	2a	3q	48	75
18	Ph, 3-FC ₆ H ₄	1r	CO ₂ Me	2a	3r	48	81
19	Ph, 2-ClC ₆ H ₄	1s	CO ₂ Me	2a	3s	48	75
20	Ph, 3-ClC ₆ H ₄	1t	CO ₂ Me	2a	3t	48	76
21	Ph, 4-ClC ₆ H ₄	1u	CO ₂ Me	2a	3u	48	79
22	Ph, 3-BrC ₆ H ₄	1v	CO ₂ Me	2a	3v	48	80
23	Ph, 4-BrC ₆ H ₄	1w	CO ₂ Me	2a	3w	48	81
24	Ph, 2-MeC ₆ H ₄	1x	CO ₂ Me	2a	3x	24	95
25	Ph, 3-MeC ₆ H ₄	1y	CO ₂ Me	2a	3y	24	96
26	Ph, 4-MeC ₆ H ₄	1z	CO ₂ Me	2a	3z	24	93
27	Ph, Me	1za	CO ₂ Me	2a	3za	48	NR ^d
28	Ph, <i>n</i> -C ₅ H ₁₁	1zb	CO ₂ Me	2a	3zb	48	NR
29 ^c	Ph, Ph	1a	Bz	2b	3zc	36	68

^a The reaction was carried out with 0.45 mmol of **1a**, 0.3 mmol of **2** and 0.45 mmol of *i*Pr₂NEt in 3 mL of CHCl₃ at room temperature for 48 h. ^b Isolated yield; >20 : 1 *dr*, determined by ¹H NMR data. ^c The reaction of 5-benzoyl-2*H*-pyran-2-one (**2b**, 0.1 mmol) was performed at 40 °C. ^d No reaction.

Figure 1 X-ray structure of the product **3w**

Scheme 2 Reaction on the gram scale

3 Conclusions

In summary, we have developed *i*Pr₂NEt-promoted [3+2] cycloaddition reaction of nitrilimine with methyl coumalate or pyranone. The reaction is operationally simple and works efficiently under mild reaction conditions to furnish a broad range of biologically important functionalized dihydropyrano[3,2-*c*]pyrazol-5(1*H*)-one derivatives in good to excellent yields with excellent diastereoselectivities.

4 Experimental

4.1 General

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Organic solutions were concentrated under reduced pressure using a rotary evaporator or oil pump. Reactions were monitored through thin-layer chromatography (TLC) on silica gel-precoated glass plates. Chromatograms were visualized by fluorescence quenching under UV light at 254 nm. Flash column chromatography was performed using a Qingdao Haiyang flash silica gel (200~300 mesh). ¹H NMR and ¹³C NMR spectra were recorded using a Bruker-300 spectrometer. Accurate mass measurements were performed using an Agilent instrument with the EI-MS technique. X-ray crystallographic data were collected using a Bruker SMART CCD-based diffractometer equipped with a low-temperature apparatus operated at 100 K.

4.2 General procedure for [3+2] cycloaddition of hydrazone chlorides **1** and methyl coumalate **2**

Hydrazone chlorides **1** (1.5 equiv., 0.45 mmol), methyl coumalate **2** (0.3 mmol) and *i*Pr₂NEt (1.5 equiv., 0.45

mmol) were dissolved in 3 mL of chloroform, and the resulting mixture was stirred at room temperature. Once starting material was consumed (monitored by TLC), the mixture was concentrated to dryness. The residue was purified through flash column chromatography [$V(\text{ethyl acetate})/V(\text{petroleum ether})=1/12$] to afford the corresponding cycloaddition product. When 2*H*-pyran-2-one (**2b**) was used, the reaction was performed with hydrazonyl chlorides **1** (1.5 equiv., 0.15 mmol), pyranone **2b** (0.1 mmol) and $^i\text{Pr}_2\text{NEt}$ (1.5 equiv., 0.15 mmol) in 3 mL of chloroform.

Methyl 5-oxo-1,3-diphenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3a**): Yellow solid (85 mg, 81% yield). m.p. 134~136 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.98~7.95 (s, 2H), 7.51~7.35 (m, 5H), 7.24~7.21 (m, 2H), 7.13 (t, $J=7.3$ Hz, 1H), 6.96~6.92 (m, 1H), 6.45 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.2, 158.0, 145.3, 141.9, 136.1, 129.4, 129.1, 128.5, 126.3, 123.1, 121.6, 117.2, 86.1, 66.8, 53.7; IR (film) ν_{max} : 2956, 1743, 1596, 1495, 1448, 1385, 1240, 1120, 1067, 1017, 874, 822, 750, 691, 660, 483 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{17}\text{N}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 349.1183, found 349.1185.

Methyl 3-(2-fluorophenyl)-5-oxo-1-phenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3b**): Yellow solid (88 mg, 80% yield). m.p. 118~212 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.94 (td, $J=1.6, 7.6$ Hz, 1H), 7.42~7.35 (m, 2H), 7.30~7.08 (m, 6H), 7.03 (d, $J=10.3$ Hz, 1H), 6.52 (d, $J=1.6$ Hz, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.8, 160.0 (d, $J=252.9$ Hz), 158.1, 142.4 (d, $J=2.9$ Hz), 141.7, 135.8, 131.0 (d, $J=8.5$ Hz), 129.1, 129.0 (d, $J=3.1$ Hz), 124.2 (d, $J=3.3$ Hz), 123.2, 121.7, 117.1, 116.2 (d, $J=21.9$ Hz), 113.5, 86.5, 86.4, 66.8, 53.6; IR (film) ν_{max} : 3068, 2957, 1740, 1598, 1496, 1456, 1385, 1242, 1108, 1071, 1006, 947, 891, 824, 756, 693, 656, 508 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{FN}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 367.1089, found 367.1085.

Methyl 3-(3-fluorophenyl)-5-oxo-1-phenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3c**): creamy white solid (84 mg, 76% yield). m.p. 140~144 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.74~7.65 (m, 1H), 7.48~7.35 (m, 2H), 7.23~7.20 (m, 1H), 7.17~7.09 (m, 1H), 6.95 (d, $J=10.3$ Hz, 1H), 6.42 (s, 1H), 6.26 (d, $J=10.3$ Hz, 1H), 3.93 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.9, 162.6 (d, $J=246.3$ Hz), 157.8, 144.1 (d, $J=3.1$ Hz), 141.6, 135.8, 131.3 (d, $J=8.3$ Hz), 130.1 (d, $J=8.3$ Hz), 129.2, 123.4, 122.0 (d, $J=2.9$ Hz), 121.6, 117.3, 116.3 (d, $J=21.5$ Hz), 112.9 (d, $J=23.5$ Hz), 85.8, 67.0, 53.7; IR (film) ν_{max} : 3073, 2958, 1746, 1595, 1567, 1495, 1455, 1434, 1385, 1244, 1189, 1119, 1071, 878, 822, 787, 750, 688, 522 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{FN}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 367.1089, found 367.1093.

Methyl 3-(4-fluorophenyl)-5-oxo-1-phenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3d**): White solid (91 mg, 83% yield). m.p. 114~116 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.99~7.91 (m, 1H), 7.41~7.36 (m,

1H), 7.23~7.10 (m, 2H), 6.92 (d, $J=10.3$ Hz, 1H), 6.42 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.93 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.1, 163.3 (d, $J=250.9$ Hz), 157.9, 144.5, 141.9, 136.1, 129.2, 128.3 (d, $J=8.4$ Hz), 125.4 (d, $J=3.2$ Hz), 123.2, 121.6, 117.3, 115.7 (d, $J=22.0$ Hz), 86.0, 66.9, 53.7; IR (film) ν_{max} : 3069, 2957, 1745, 1599, 1513, 1496, 1435, 1384, 1236, 1159, 1120, 1069, 889, 840, 823, 750, 693, 625, 544 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{FN}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 367.1089, found 367.1087.

Methyl 3-(3-chlorophenyl)-5-oxo-1-phenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3e**): Yellow solid (91 mg, 79% yield). m.p. 172~175 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.95~7.97 (m, 1H), 7.83~7.76 (m, 1H), 7.46~7.36 (m, 1H), 7.23~7.20 (m, 1H), 7.13 (t, $J=7.3$ Hz, 1H), 6.96 (d, $J=10.3$ Hz, 1H), 6.41 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.92 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.8, 157.8, 143.9, 141.6, 135.8, 134.6, 131.0, 129.8, 129.3, 129.2, 126.1, 124.3, 123.4, 121.6, 117.3, 85.7, 66.9, 53.8; IR (film) ν_{max} : 3069, 2957, 2923, 2851, 1747, 1595, 1557, 1497, 1435, 1372, 1240, 1072, 888, 824, 787, 750, 687 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{15}\text{ClN}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 405.0613, found 405.0618.

Methyl 3-(4-chlorophenyl)-5-oxo-1-phenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3f**): Yellow solid (96 mg, 84% yield). m.p. 59~62 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.94~7.85 (m, 1H), 7.45~7.35 (m, 1H), 7.24~7.17 (m, 1H), 7.13 (t, $J=7.3$ Hz, 1H), 6.92 (d, $J=10.3$ Hz, 1H), 6.42 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.93 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.0, 157.9, 144.3, 141.7, 136.0, 135.3, 129.2, 128.8, 127.7, 127.5, 123.3, 121.6, 117.3, 85.9, 67.0, 53.8; IR (film) ν_{max} : 3065, 2956, 1746, 1597, 1557, 1494, 1435, 1408, 1384, 1241, 1091, 1070, 1012, 889, 822, 749, 694, 541, 498 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{ClN}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 383.0790, found 383.0793.

Methyl 3-(2-bromophenyl)-5-oxo-1-phenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3g**): Yellow solid (106 mg, 83% yield). m.p. 150~153 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.70 (d, $J=8.0$ Hz, 1H), 7.64~7.61 (m, 1H), 7.46~7.35 (m, 1H), 7.34~7.27 (m, 1H), 7.23 (d, $J=8.0$ Hz, 1H), 7.13 (t, $J=7.3$ Hz, 1H), 6.94 (d, $J=10.3$ Hz, 1H), 6.72 (s, 1H), 6.27 (d, $J=10.3$ Hz, 1H), 3.93 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.0, 158.2, 146.0, 141.9, 136.0, 133.7, 131.2, 130.6, 129.8, 129.2, 127.3, 123.4, 121.9, 121.8, 117.4, 86.4, 67.4, 53.7; IR (film) ν_{max} : 3065, 2956, 2925, 1746, 1598, 1496, 1434, 1371, 1239, 1117, 1090, 927, 889, 823, 752, 693, 644 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{BrN}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 427.0288, found 427.0292.

Methyl 3-(3-bromophenyl)-5-oxo-1-phenyl-1,3*a*-dihydropyrano[3,2-*c*]pyrazole-7*a*(5*H*)-carboxylate (**3h**): Yellow solid (101 mg, 79% yield). m.p. 164~166 °C; ^1H NMR (300 MHz, CDCl_3) δ : 8.12~8.11 (m, 1H), 7.91~7.79 (m, 1H), 7.57~7.54 (m, 1H), 7.44~7.29 (m, 1H), 7.24~7.19 (m, 1H), 7.14 (t, $J=7.3$ Hz, 1H), 6.95 (d, $J=10.3$ Hz, 1H), 6.40 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.92 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.8, 157.8, 143.8,

141.6, 135.9, 132.2, 131.3, 130.0, 129.2, 128.9, 124.8, 123.4, 122.7, 121.6, 117.3, 85.7, 66.9, 53.8; IR (film) $\nu_{\max}$: 3067, 2956, 2924, 1745, 1595, 1553, 1497, 1434, 1372, 1239, 1119, 1071, 888, 823, 786, 749, 686, 514 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{BrN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 427.0288, found 427.0290.

Methyl 3-(4-bromophenyl)-5-oxo-1-phenyl-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3i**): Yellow solid (106 mg, 83% yield). m.p. 64~67 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.86~7.79 (m, 1H), 7.62~7.56 (m, 1H), 7.41~7.35 (m, 1H), 7.21~7.19 (m, 1H), 7.13 (t, $J=7.3$ Hz, 1H), 6.92 (d, $J=10.3$ Hz, 1H), 6.42 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.93 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.9, 157.8, 144.3, 141.7, 135.9, 131.7, 129.2, 128.1, 127.7, 123.7, 123.4, 121.6, 117.3, 85.8, 67.0, 53.8; IR (film) $\nu_{\max}$: 3065, 2956, 1746, 1597, 1493, 1435, 1382, 1241, 1119, 1070, 1008, 888, 822, 749, 694, 539, 496 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{BrN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 427.0288, found 427.0292.

Methyl 5-oxo-1-phenyl-3-(*m*-tolyl)-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3j**): Pale yellow solid (82 mg, 75% yield). m.p. 115~119 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.84~7.70 (m, 1H), 7.45~7.33 (m, 2H), 7.33~7.19 (m, 2H), 7.13 (t, $J=7.3$ Hz, 1H), 6.95 (d, $J=10.3$ Hz, 1H), 6.44 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.92 (s, 1H), 2.45 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.1, 158.1, 145.6, 142.0, 138.2, 136.1, 130.3, 129.1, 129.0, 128.4, 126.8, 123.6, 123.1, 121.6, 117.2, 86.0, 66.8, 53.7, 21.1; IR (film) $\nu_{\max}$: 3063, 2956, 2924, 1747, 1599, 1496, 1435, 1385, 1244, 1118, 1072, 925, 884, 825, 787, 750, 693, 513 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 363.1339, found 363.1344.

Methyl 5-oxo-1-phenyl-3-(*p*-tolyl)-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3k**): Yellow solid (84 mg, 77% yield). m.p. 140~144 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.86 (d, $J=8.2$ Hz, 1H), 7.43~7.34 (m, 1H), 7.28 (d, $J=8.1$ Hz, 1H), 7.23~7.20 (m, 1H), 7.11 (t, $J=7.3$ Hz, 1H), 6.92 (d, $J=10.3$ Hz, 1H), 6.43 (s, 1H), 6.24 (d, $J=10.3$ Hz, 1H), 3.92 (s, 1H), 2.43 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.3, 158.1, 145.6, 142.1, 139.7, 136.2, 129.2, 129.1, 126.3, 122.9, 121.6, 117.1, 86.2, 66.8, 53.6, 21.1; IR (film) $\nu_{\max}$: 2956, 1740, 1597, 1496, 1435, 1385, 1317, 1241, 1187, 1119, 1068, 1016, 927, 888, 823, 750, 694, 544, 499 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 363.1339, found 363.1343.

Methyl 3-(3-methoxyphenyl)-5-oxo-1-phenyl-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3l**): Yellow solid (82 mg, 72% yield). m.p. 64~67 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.57~7.48 (m, 1H), 7.42~7.34 (m, 1H), 7.25~7.19 (m, 1H), 7.13 (t, $J=7.3$ Hz, 1H), 7.03~6.97 (m, 1H), 6.94 (d, $J=10.3$ Hz, 1H), 6.42 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.92 (s, 1H), 3.90 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.1, 159.5, 158.0, 145.2, 141.9, 136.0, 130.4, 129.5, 129.1, 123.1, 121.6, 119.0, 117.2, 115.7, 111.1, 86.0, 66.9, 55.1, 53.7; IR (film) $\nu_{\max}$: 2957, 1746, 1598, 1568, 1495, 1456, 1434, 1384, 1246, 1178, 1119, 1045, 874, 825, 786, 750, 690, 664 cm^{-1} ; HRMS (ESI)

calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_5$ $[\text{M} + \text{H}]^+$ 379.1288, found 379.1291.

Methyl 3-(4-methoxyphenyl)-5-oxo-1-phenyl-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3m**): Pale Yellow solid (86 mg, 76% yield). m.p. 132~134 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.92~7.89 (m, 1H), 7.40~7.35 (m, 1H), 7.21~7.19 (m, 1H), 7.10 (t, $J=7.3$ Hz, 1H), 7.01~6.97 (m, 1H), 6.90 (d, $J=10.3$ Hz, 1H), 6.41 (s, 1H), 6.23 (d, $J=10.3$ Hz, 1H), 3.92 (s, 1H), 3.88 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.3, 160.6, 158.2, 145.4, 142.2, 136.3, 129.1, 127.9, 122.8, 121.7, 121.5, 117.1, 114.0, 86.3, 66.8, 55.0, 53.6; IR (film) $\nu_{\max}$: 3064, 2958, 2840, 1744, 1597, 1516, 1496, 1425, 1384, 1256, 1179, 1120, 1067, 888, 823, 750, 694, 614, 547 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_5$ $[\text{M} + \text{H}]^+$ 379.1288, found 379.1288.

Methyl 3-(naphthalen-1-yl)-5-oxo-1-phenyl-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3n**): Orange solid (100 mg, 84% yield). m.p. 60~63 °C; ^1H NMR (300 MHz, CDCl_3) δ : 8.32 (s, 1H), 8.17 (dd, $J=1.7$, 8.7 Hz, 1H), 8.00~7.83 (m, 1H), 7.61~7.52 (m, 1H), 7.47~7.37 (m, 1H), 7.32~7.24 (m, 1H), 7.15 (t, $J=7.3$ Hz, 1H), 6.99 (d, $J=10.3$ Hz, 1H), 6.57 (s, 1H), 6.28 (d, $J=10.3$ Hz, 1H), 3.93 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.1, 158.1, 145.4, 141.9, 136.1, 133.5, 132.9, 129.2, 128.4, 128.3, 127.4, 126.74, 126.68, 126.3, 126.3, 123.3, 123.1, 121.7, 117.2, 86.1, 66.9, 53.7; IR (film) $\nu_{\max}$: 3061, 2956, 1740, 1598, 1496, 1435, 1384, 1248, 1118, 1069, 1018, 952, 861, 822, 749, 694, 639, 475 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 399.1339, found 399.1342.

Methyl 3-(naphthalen-2-yl)-5-oxo-1-phenyl-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3o**): Orange solid (96 mg, 80% yield). m.p. 99~102 °C; ^1H NMR (300 MHz, CDCl_3) δ : 8.32 (s, 1H), 8.16 (dd, $J=1.7$, 8.7 Hz, 1H), 8.01~7.81 (m, 1H), 7.60~7.52 (m, 1H), 7.46~7.37 (m, 1H), 7.30~7.26 (m, 1H), 7.15 (t, $J=7.3$ Hz, 1H), 6.99 (d, $J=10.3$ Hz, 1H), 6.57 (s, 1H), 6.28 (d, $J=10.3$ Hz, 1H), 3.94 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.1, 158.1, 145.4, 141.9, 136.1, 133.5, 132.9, 129.2, 128.4, 128.3, 127.4, 126.74, 126.67, 126.3, 126.3, 123.3, 123.1, 121.7, 117.2, 86.1, 66.9, 53.7; IR (film) $\nu_{\max}$: 3061, 2956, 1740, 1598, 1496, 1435, 1384, 1248, 1118, 1069, 1018, 952, 861, 822, 749, 694, 639, 476 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 399.1339, found 399.1344.

Methyl 3-(furan-2-yl)-5-oxo-1-phenyl-1,3a-dihydropyrano[3,2-c]pyrazole-7a(5H)-carboxylate (**3p**): Black solid (70 mg, 69% yield). m.p. 56~60 °C; ^1H NMR (300 MHz, CDCl_3) δ : 7.61~7.60 (m, 1H), 7.39~7.33 (m, 1H), 7.22~7.16 (m, 1H), 7.15~7.08 (m, 1H), 7.00~6.97 (m, 1H), 6.82 (dd, $J=0.7$, 10.3 Hz, 1H), 6.56 (dd, $J=1.8$, 3.5 Hz, 1H), 6.33 (d, $J=0.7$ Hz, 1H), 6.24 (d, $J=10.3$ Hz, 1H), 3.94 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.0, 156.0, 144.3, 141.8, 138.2, 135.9, 129.1, 123.4, 121.7, 117.6, 112.5, 111.7, 85.8, 66.8, 53.7; IR (film) $\nu_{\max}$: 2958, 1747, 1597, 1496, 1435, 1385, 1360, 1257, 1124, 1091,

1070, 1012, 926, 885, 816, 750, 694, 592 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_5$ $[\text{M} + \text{H}]^+$ 339.0975, found 339.0979.

Methyl 1-(2-fluorophenyl)-5-oxo-3-phenyl-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3q**): White solid (82 mg, 75% yield). m.p. 115~118 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 8.04~7.85 (m, 2H), 7.57~7.33 (m, 4H), 7.25~7.08 (m, 3H), 6.72 (dd, $J=1.6, 10.3$ Hz, 1H), 6.47 (s, 1H), 6.19 (d, $J=10.3$ Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.5, 158.1, 154.0 (d, $J=245.5$ Hz), 147.1, 136.6 (d, $J=4.6$ Hz), 129.8, 129.6, 129.0, 128.5, 126.5, 126.3 (d, $J=7.9$ Hz), 124.8, 124.7 (d, $J=3.4$ Hz), 121.5, 116.0 (d, $J=20.5$ Hz), 86.0, 67.6, 53.4; IR (film) ν_{max} : 3067, 2957, 1747, 1614, 1595, 1496, 1448, 1385, 1262, 1120, 1064, 929, 890, 820, 759, 692, 591, 556 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{FN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 367.1088, found 367.1087.

Methyl 1-(3-fluorophenyl)-5-oxo-3-phenyl-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3r**): White solid (89 mg, 81% yield). m.p. 123~127 $^{\circ}\text{C}$; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ : 7.96~7.92 (m, 2H), 7.52~7.38 (m, 3H), 7.38~7.24 (m, 1H), 7.04 (dt, $J=2.3, 11.0$ Hz, 1H), 6.98 (d, $J=10.4$ Hz, 1H), 6.87 (dd, $J=8.2, 1.7$ Hz, 1H), 6.77 (td, $J=8.2, 2.3$ Hz, 1H), 6.42 (s, 1H), 6.27 (d, $J=10.3$ Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.9, 163.3 (d, $J=245.7$ Hz), 157.7, 145.8, 143.5 (d, $J=10.3$ Hz), 135.6, 130.4 (d, $J=9.7$ Hz), 129.7, 128.8, 128.6, 126.4, 121.9, 111.2, 111.2, 109.3 (d, $J=21.5$ Hz), 104.1 (d, $J=26.4$ Hz), 86.1, 66.4, 53.9; IR (film) ν_{max} : 3068, 2957, 1745, 1613, 1586, 1492, 1448, 1386, 1243, 1187, 1156, 1126, 1064, 1017, 856, 818, 764, 691, 551 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{FN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 367.1088, found 367.1086.

Methyl 1-(2-chlorophenyl)-5-oxo-3-phenyl-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3s**): Yellow solid (86 mg, 75% yield). m.p. 147~149 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 8.04~7.87 (m, 2H), 7.51~7.38 (m, 4H), 7.34~7.22 (m, 2H), 7.21~7.16 (m, 1H), 6.66 (d, $J=10.3$ Hz, 1H), 6.52 (s, 1H), 6.14 (d, $J=10.3$ Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.0, 158.1, 148.7, 139.5, 136.7, 130.5, 130.2, 129.7, 129.1, 128.7, 128.5, 128.3, 127.3, 126.6, 121.4, 85.6, 68.0, 53.4; IR (film) ν_{max} : 3070, 2957, 1747, 1593, 1481, 1434, 1385, 1243, 1083, 1017, 872, 824, 764, 737, 691, 550 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{ClN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 383.0794, found 383.0793.

Methyl 1-(3-chlorophenyl)-5-oxo-3-phenyl-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3t**): Yellow solid (87 mg, 76% yield). m.p. 128~131 $^{\circ}\text{C}$; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ : 8.04~7.85 (m, 2H), 7.57~7.38 (m, 3H), 7.31~7.27 (m, 2H), 7.14~6.91 (m, 3H), 6.41 (s, 1H), 6.27 (d, $J=10.3$ Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.8, 157.7, 146.0, 143.0, 135.5, 135.1, 130.1, 129.8, 128.8, 128.6, 126.5, 122.6, 121.9, 116.9, 114.0, 86.0, 66.5, 53.9; IR (film) ν_{max} : 3069, 2957, 1747, 1592, 1481, 1434, 1385, 1243, 1083, 1017, 871, 824, 764, 738, 691, 661, 550 cm^{-1} ; HRMS (ESI) calcd for

$\text{C}_{20}\text{H}_{16}\text{ClN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 383.0794, found 383.0793.

Methyl 1-(4-chlorophenyl)-5-oxo-3-phenyl-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3u**): Yellow solid (91 mg, 79% yield). m.p. 133~136 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 8.02~7.86 (m, 2H), 7.53~7.37 (m, 3H), 7.37~7.23 (m, 2H), 7.23~7.08 (m, 2H), 6.90 (d, $J=10.3$ Hz, 1H), 6.42 (s, 1H), 6.24 (d, $J=10.3$ Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.8, 157.8, 145.9, 140.6, 135.7, 129.7, 129.1, 128.9, 128.6, 128.2, 126.4, 121.9, 118.3, 86.0, 66.8, 53.8; IR (film) ν_{max} : 3065, 2957, 1746, 1594, 1493, 1448, 1435, 1386, 1242, 1118, 1083, 1007, 927, 824, 762, 738, 691, 549, 502 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{ClN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 383.0794, found 383.0795.

Methyl 1-(3-bromophenyl)-5-oxo-3-phenyl-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3v**): Yellow solid (103 mg, 80% yield). m.p. 130~133 $^{\circ}\text{C}$; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ : 7.95~7.92 (m, 2H), 7.62~7.36 (m, 4H), 7.24~7.20 (m, 2H), 7.05~7.01 (m, 1H), 6.96 (d, $J=10.3$ Hz, 1H), 6.41 (s, 1H), 6.26 (d, $J=10.3$ Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.8, 157.7, 146.0, 143.1, 135.5, 130.3, 129.8, 128.8, 128.6, 126.5, 125.6, 123.1, 121.9, 119.8, 114.4, 86.0, 66.5, 53.9; IR (film) ν_{max} : 3068, 2956, 1745, 1589, 1479, 1448, 1434, 1385, 1242, 1120, 1064, 1017, 873, 823, 764, 691, 548 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{BrN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 427.0288, found 427.0290.

Methyl 1-(4-bromophenyl)-5-oxo-3-phenyl-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3w**): Yellow solid (104 mg, 81% yield). m.p. 171~173 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 8.06~7.86 (m, 2H), 7.48~7.43 (dm, 5H), 7.16~7.00 (m, 2H), 6.91 (d, $J=10.3$ Hz, 1H), 6.42 (s, 1H), 6.25 (d, $J=10.3$ Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.8, 157.8, 145.9, 141.0, 135.6, 132.1, 129.7, 128.8, 128.6, 126.4, 121.9, 118.4, 115.6, 86.0, 66.6, 53.8; IR (film) ν_{max} : 2921, 2346, 1743, 1588, 1489, 1448, 1385, 1259, 1118, 1074, 874, 822, 763, 749, 691, 659, 547, 498 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{BrN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 427.0288, found 427.0292.

Methyl 5-oxo-3-phenyl-1-(*o*-tolyl)-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3x**): Yellow solid (103 mg, 95% yield). m.p. 100~103 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 7.99~7.88 (m, 2H), 7.50~7.35 (m, 3H), 7.35~7.18 (m, 3H), 7.04~7.01 (m, 1H), 6.62~6.59 (m, 2H), 6.17 (d, $J=10.3$ Hz, 1H), 3.85 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 168.4, 158.4, 146.5, 140.2, 136.9, 135.3, 131.4, 129.4, 129.2, 128.5, 127.5, 127.2, 126.3, 126.2, 121.0, 85.3, 68.4, 53.3, 18.1; IR (film) ν_{max} : 3063, 2956, 1739, 1583, 1492, 1447, 1383, 1240, 1123, 1062, 940, 874, 827, 799, 764, 693, 663, 551 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 363.1339, found 363.1338.

Methyl 5-oxo-3-phenyl-1-(*m*-tolyl)-1,3a-dihydro-*pyrano*[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3y**): Yellow solid (104 mg, 96% yield). m.p. 95~99 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 7.98~7.94 (m, 2H), 7.58~7.36 (m, 3H), 7.36~7.17 (m, 1H), 7.10 (s, 1H), 7.01~6.86 (m, 3H),

6.43 (s, 1H), 6.23 (d, $J=10.3$ Hz, 1H), 3.90 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.2, 158.1, 145.2, 141.9, 139.2, 136.2, 129.4, 129.2, 128.9, 128.5, 126.3, 124.1, 121.5, 118.2, 114.1, 86.1, 66.9, 53.7, 21.4; IR (film) ν_{max} : 2922, 2346, 1743, 1606, 1586, 1491, 1447, 1385, 1258, 1188, 1119, 1065, 874, 827, 764, 691, 660, 485 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 363.1339, found 363.1339.

Methyl 5-oxo-3-phenyl-1-(*p*-tolyl)-1,3a-dihydropyrano[3,2-*c*]pyrazole-7a(5*H*)-carboxylate (**3z**): Brown solid (101 mg, 93% yield). m.p. 110~113 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 7.99~7.90 (m, 2H), 7.51~7.37 (m, 3H), 7.19~7.16 (m, 2H), 7.11~7.08 (m, 2H), 6.85 (d, $J=10.3$ Hz, 1H), 6.44 (s, 1H), 6.21 (d, $J=10.3$ Hz, 1H), 3.90 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 169.2, 158.2, 145.3, 139.7, 136.3, 133.3, 129.6, 129.30, 129.27, 128.5, 126.3, 121.5, 118.1, 86.0, 67.3, 53.6, 20.4; IR (film) ν_{max} : 2956, 2924, 1746, 1614, 1563, 1514, 1448, 1385, 1241, 1119, 1068, 1017, 929, 890, 821, 762, 741, 692, 660, 509 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 363.1339, found 363.1337.

7a-Benzoyl-1,3-diphenyl-3a,7a-dihydropyrano[3,2-*c*]pyrazol-5(1*H*)-one (**3zc**): Yellow solid (27 mg, 68% yield). m.p. 71~72 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ : 8.16~8.09 (m, 2H), 8.05~7.99 (m, 2H), 7.67~7.58 (m, 1H), 7.52~7.42 (m, 5H), 7.34~7.27 (m, 2H), 7.22~7.15 (m, 2H), 7.11~6.98 (m, 1H), 6.78 (dd, $J=10.3$, 1.2 Hz, 1H), 6.58 (d, $J=1.2$ Hz, 1H), 6.24 (d, $J=10.3$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 195.5, 158.3, 145.9, 141.7, 137.8, 134.3, 132.6, 129.7, 129.4, 129.2, 129.0, 128.9, 128.6, 126.6, 123.1, 120.9, 116.7, 86.0, 72.0; IR (film) ν_{max} : 1743, 1673, 1595, 1492, 1447, 1383, 1272, 1231, 1082, 1063, 1013, 884, 822, 758, 689, 651, 547, 517 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{19}\text{N}_2\text{O}_3$ $[\text{M} + \text{H}]^+$ 395.1390, found 395.1379.

Supporting Information Copies of ^1H NMR and ^{13}C NMR spectra of all products and X-ray data of **3w**. The Supporting Information is available free of charge via the Internet at <http://sioc-journal.cn>.

References

- [1] For selected reviews, see: (a) Yoshida, H.; Yanai, H.; Namiki, Y.; Fukatsu-Sasaki, K.; Furutani, N.; Tada, N. *CNS Drug Rev.* **2006**, *12*, 9.
(b) Bhutani, R.; Pathak, D. P.; Husain, A.; Kapoor, G.; Kant, R. *Int. J. Pharm. Sci. Res.* **2015**, *6*, 4113.
(c) Marella, A.; Ali, M. R.; Alam, M. T.; Saha, R.; Tanwar, O.; Akhter, M.; Shaquiquzzaman, M.; Alam, M. M. *Mini-Rev. Med. Chem.* **2013**, *13*, 921.
For selected examples, see: (d) Li, Z.; Zhang, Z.; Zhang, W.; Liu, Q.; Liu, T.; Zhang, G. *Synlett* **2013**, *24*, 2735.
(e) Rui, J.; Yang, J.; Huang, J.; Wang, J.; Xu, X.; Xu, H.; Wang, S. *Chin. J. Org. Chem.* **2016**, *36*, 2183 (in Chinese).
(芮坚, 杨金来, 黄建峰, 王佳瑜, 徐徐, 徐海军, 王石发, 有机化学, **2016**, *36*, 2183.)
(f) Shi, Y.; Li, Y.; Fang, Y.; Ye, L.; Chen, J.; Dai, H. *Chin. J. Org. Chem.* **2016**, *36*, 1431 (in Chinese).
(石玉军, 李阳, 方源, 叶林玉, 陈佳, 戴红, 有机化学, **2016**, *36*, 1431.)
(g) Li, F.; Wang, X.; Yu, H. *Chin. J. Org. Chem.* **2016**, *36*, 1127 (in Chinese).
(李福卫, 王小龙, 于海涛, 有机化学, **2016**, *36*, 1127.)
(h) Li, Z.; Chen, F.; Wang, D.; Huang, X.; Li, Y. *Chin. J. Org. Chem.* **2016**, *36*, 838 (in Chinese).
(李志鹏, 陈斐然, 王东阳, 黄杏甜, 李毅群, 有机化学, **2016**, *36*, 838.)
(i) Feng, J.; Abulajiang, K.; Ma, X.; Li, W.; Obul, M. *Chin. J. Org. Chem.* **2016**, *36*, 222 (in Chinese).
(冯俊, 阿布拉江·克依木, 马夏冰, 李文博, 麦麦提艾力·奥布力, 有机化学, **2016**, *36*, 222.)
(j) Dai, H.; Li, H.; Jin, Z.; Liu, W.; Xiao, Y.; He, H.; Wang, Q.; Shi, Y. *Chin. J. Org. Chem.* **2016**, *36*, 185 (in Chinese).
(戴红, 李宏, 金智超, 刘文永, 肖瑶, 何海兵, 汪清民, 石玉军, 有机化学, **2016**, *36*, 185.)
(k) Hong, Y.; Dai, H.; Ye, L.; Zhong, S.; Cao, X.; Shi, Y.; Li, C.; Shi, J.; Shi, L. *Chin. J. Org. Chem.* **2017**, *37*, 3006 (in Chinese).
(洪宇, 戴红, 叶林玉, 仲苏林, 曹雄飞, 石玉军, 李春建, 石健, 有机化学, **2017**, *37*, 3006.)
(l) Sun, N.; Shen, Z.; Zhai, Z.; Han, L.; Weng, J.; Tan, C.; Liu, X. *Chin. J. Org. Chem.* **2017**, *37*, 2705 (in Chinese).
(孙娜波, 沈钟华, 翟志文, 韩亮, 翁建全, 谭成侠, 刘幸海, 有机化学, **2017**, *37*, 2705.)
(m) Dai, H.; Yao, W.; Ye, L.; Fang, Y.; Shi, Y.; Song, C.; Li, C.; Shi, J. *Chin. J. Org. Chem.* **2017**, *37*, 2165 (in Chinese).
(戴红, 姚炜, 叶林玉, 方源, 石玉军, 宋婵, 李春建, 石健, 有机化学, **2017**, *37*, 2165.)
(n) Shi, J.; Ren, G.; Wu, N.; Liu, X.; Xu, T.; Tan, C. *Chin. J. Org. Chem.* **2017**, *37*, 2131 (in Chinese).
(史建俊, 任贵华, 吴宁捷, 刘幸海, 许天明, 谭成侠, 有机化学, **2017**, *37*, 2131.)
(o) Sun, N.; Shen, Z.; Zhai, Z.; Wu, H.; Weng, J.; Tan, C.; Liu, X. *Chin. J. Org. Chem.* **2017**, *37*, 2044 (in Chinese).
(孙娜波, 沈钟华, 翟志文, 武宏科, 翁建全, 谭成侠, 刘幸海, 有机化学, **2017**, *37*, 2044.)
(p) Shi, Y.; Ye, L.; Zhong, S.; Cao, X.; Dai, H.; Hong, Y.; Li, C.; Shi, J.; Wu, J. *Chin. J. Org. Chem.* **2017**, *37*, 1844 (in Chinese).
(石玉军, 叶林玉, 仲苏林, 曹雄飞, 戴红, 洪宇, 李春建, 石健, 吴锦明, 有机化学, **2017**, *37*, 1844.)
(q) Dai, H.; Chen, J.; Hong, Y.; Yuan, B.; Fan, C.; Ma, R.; Liang, Z.; Shi, J. *Chin. J. Org. Chem.* **2017**, *37*, 1542 (in Chinese).
(戴红, 陈佳, 洪宇, 袁斌颖, 范崇光, 马瑞媛, 梁志鹏, 石健, 有机化学, **2017**, *37*, 1542.)
(r) Dai, H.; Ye, L.; Li, Y.; Fang, Y.; Shi, Y.; Liang, Z.; Shi, J. *Chin. J. Org. Chem.* **2017**, *37*, 1020 (in Chinese).
(戴红, 叶林玉, 李阳, 方源, 石玉军, 梁志鹏, 石健, 有机化学, **2017**, *37*, 1020.)
(s) Zhang, C.; Sun, X.; Pu, Y.; Li, C.; Sun, L.; Wang, J.; Li, Y. *Chin. J. Org. Chem.* **2017**, *37*, 440 (in Chinese).
(张成路, 孙晓娜, 蒲雨昕, 李传银, 孙丽杰, 王静, 李益政, 有机化学, **2017**, *37*, 440.)
(t) Zhai, Z.; Wang, Q.; Shen, Z.; Tan, C.; Weng, J.; Liu, X. *Chin. J. Org. Chem.* **2017**, *37*, 232 (in Chinese).
(翟志文, 汪乔, 沈钟华, 谭成侠, 翁建全, 刘幸海, 有机化学, **2017**, *37*, 232.)
(u) Rui, J.; Zhang, Q.; Wang, X.; Xu, X.; Xu, H.; Rao, W.; Wang, S. *Chin. J. Org. Chem.* **2017**, *37*, 218 (in Chinese).
(芮坚, 张齐, 王欣, 徐徐, 徐海军, 饶卫东, 王石发, 有机化学, **2017**, *37*, 218.)
- [2] (a) Buchanan, J. G.; Edgar, A. R.; Hutchison, R. J.; Stobie, A.; Wightman, R. H. *J. Chem. Soc., Chem. Commun.* **1980**, 237.
(b) Lima, J. L. F. C.; Oliveira Sá, S. M.; Santos, J. L. M.; Zagatto, E. A. G. *J. Pharm. Biomed. Anal.* **2003**, *32*, 1011.
(c) Chande, M. S.; Barve, P. A.; Suryanarayan, V. *J. Heterocycl. Chem.* **2007**, *44*, 49.
(d) Wube, A. A.; Wenzig, E.-M.; Gibbons, S.; Asres, K.; Bauer, R.; Bucar, F. *Phytochemistry* **2008**, *69*, 982.

- (e) Fujimori, Y.; Katsuno, K.; Nakashima, I.; Ishikawa-Takemura, Y.; Fujikura, H.; Isaji, M. *J. Pharmacol. Exp. Ther.* **2008**, 327, 268.
- [3] (a) Coldham, I.; Hufton, R. *Chem. Rev.* **2005**, 105, 2765.
 (b) Yu, J.; Shi, F.; Gong, L.-Z. *Acc. Chem. Res.* **2011**, 44, 1156.
 (c) Adrio, J.; Carretero, J. C. *Chem. Commun.* **2011**, 47, 6784.
 (d) Adrio, J.; Carretero, J. C. *Chem. Commun.* **2014**, 50, 12434.
 (e) Najera, C.; Sansano, J. M.; Yus, M. *Org. Biomol. Chem.* **2015**, 13, 8596.
- [4] For selected examples, see: (a) Kanemasa, S.; Kobayashi, S. *Bull. Chem. Soc. Jpn.* **1993**, 66, 2685.
 (b) Feddoui, A.; Ait Itto, M. Y.; Hasnaoui, A.; Villemain, D.; Jaffres, P.-A.; Sopkova-De Oliveira Santos, I.; Riahi, A.; Huet, F.; Daran, J.-C. *J. Heterocycl. Chem.* **2004**, 41, 731.
 (c) Lauria, A.; Guarcello, A.; Dattolo, G.; Almerico, A. M. *Tetrahedron Lett.* **2008**, 49, 1847.
 (d) Yavari, I.; Khalili, G.; Mirzaei, A. *Helv. Chim. Acta* **2010**, 93, 277.
 (e) Wang, G.; Liu, X.; Huang, T.; Kuang, Y.; Lin, L.; Feng, X. *Org. Lett.* **2013**, 15, 76.
 (f) Liu, H.; Jia, H.; Wang, B.; Xiao, Y.; Guo, H. *Org. Lett.* **2017**, 19, 4714.
 (g) Guo, Z. Y.; Jia, H.; Liu, H. L.; Wang, Q. J.; Huang, J. X.; Guo, H. *Org. Lett.* **2018**, 20, 2939.
 (h) Zeng, Y.; Zhou, L.; Gao, X.; Wu, Y.; Wang, Q.; Guo, Z.; Huang, J.; Guo, H. *J. Heterocyclic Chem.* **2018**, 55, 2781.
- [5] Huisgen, R.; Grashey, R.; Seidel, M.; Wallbillich, G.; Knupfer, H.; Schmidt, R. *Justus Liebigs Ann. Chem.* **1962**, 653, 105.
- [6] For selected recent examples, see: (a) Chen, C.-H.; Liao, C.-C. *Org. Lett.* **2000**, 2, 2049.
 (b) Gutekunst, W. R.; Baran, P. S. *J. Am. Chem. Soc.* **2011**, 133, 19076.
 (c) Kraus, G. A.; Riley, S.; Cordes, T. *Green Chem.* **2011**, 13, 2734.
 (d) Gutekunst, W. R.; Gianatassio, R.; Baran, P. S. *Angew. Chem., Int. Ed.* **2012**, 51, 7507.
 (e) Smith, M. W.; Snyder, S. A. *J. Am. Chem. Soc.* **2013**, 135, 12964.
 (f) Guney, T.; Lee, J. J.; Kraus, G. A. *Org. Lett.* **2014**, 16, 1124.
 (g) Lee, J. J.; Kraus, G. A. *Green Chem.* **2014**, 16, 2111.
 (h) Plevová, K.; Chang, L.; Martin, E.; Llopis, Q.; Dechoux, L.; Thorimbert, S. *Adv. Synth. Catal.* **2016**, 358, 3293.
 (i) Liu, Q.; Zu, L. *Angew. Chem., Int. Ed.* **2018**, 57, 9505.
- [7] For selected examples reacting as olefins, see: (a) Imagawa, T.; Sueda, N.; Kawanisi, M. *Tetrahedron* **1974**, 30, 2227.
 (b) White, J. D.; Matsui, T.; Thomas, J. A. *J. Org. Chem.* **1981**, 46, 3376.
 (c) Brown, B. A.; Colvin, E. W. *J. Chem. Soc., Chem. Commun.* **1984**, 1514.
 (d) Matsui, T.; Kitajima, S.; Nakayama, M. *Bull. Chem. Soc. Jpn.* **1988**, 61, 316.
- [8] For selected examples reacting as diene, see: (a) Corey, E. J.; Watt, D. S. *J. Am. Chem. Soc.* **1973**, 95, 2303.
 (b) Posner, G. H.; Wettlaufer, D. G. *J. Am. Chem. Soc.* **1986**, 108, 7373.
 (c) Jung, M. E.; Street, L. J.; Usui, Y. *J. Am. Chem. Soc.* **1986**, 108, 6810.
 (d) Jung, M. E.; Hagenah, J. A. *J. Org. Chem.* **1987**, 52, 1889.
 (e) Lee, J. J.; Kraus, G. A. *Tetrahedron Lett.* **2013**, 54, 2366.
 (f) Kraus, G. A.; Wang, S. *RSC Adv.* **2017**, 7, 56760.
- [9] (a) Shimo, T.; Iwakiri, T.; Somekawa, K.; Suishu, T. *J. Heterocyclic Chem.* **1992**, 29, 199.
 (b) Gutekunst, W. R.; Baran, P. S. *J. Org. Chem.* **2014**, 79, 2430.
- [10] Trost, B. M.; Schneider, S. *Angew. Chem., Int. Ed. Engl.* **1989**, 28, 213.
- [11] Zheng, S.; Lu, X. *Org. Lett.* **2009**, 11, 3978.
- [12] Liu, K.; Teng, H.-L.; Wang, C.-J. *Org. Lett.* **2014**, 16, 4508.
- [13] Usachev, S. A.; Popova, N. V.; Moshkin, V. S.; Sosnovskikh, V. Y. *Chem. Heterocycl. Compd.* **2015**, 51, 913.
- [14] (a) Na, R.; Jing, C.; Xu, Q.; Jiang, H.; Wu, X.; Shi, Y.; Zhong, J.; Wang, M.; Benitez, D.; Tkatchouk, E.; Goddard III, W. A.; Guo, H.; Kwon, O. *J. Am. Chem. Soc.* **2011**, 133, 13337.
 (b) Wu, X.; Na, R.; Liu, H.; Liu, J.; Wang, M.; Zhong, J.; Guo, H. *Tetrahedron Lett.* **2012**, 53, 342.
 (c) Guo, H.; Liu, H.; Zhu, F.-L.; Na, R.; Jiang, H.; Wu, Y.; Zhang, L.; Li, Z.; Yu, H.; Wang, B.; Xiao, Y.; Hu, X.-P.; Wang, M. *Angew. Chem., Int. Ed.* **2013**, 52, 12641.
 (d) Zhang, L.; Yu, H.; Yang, Z.; Liu, H.; Li, Z.; Guo, J.; Xiao, Y.; Guo, H. *Org. Biomol. Chem.* **2013**, 11, 8235.
 (e) Liu, H.; Wu, Y.; Zhao, Y.; Li, Z.; Zhang, L.; Yang, W.; Jiang, H.; Jing, C.; Yu, H.; Wang, B.; Xiao, Y.; Guo, H. *J. Am. Chem. Soc.* **2014**, 136, 2625.
 (f) Zhang, L.; Liu, H.; Qiao, G.; Hou, Z.; Liu, Y.; Xiao, Y.; Guo, H. *J. Am. Chem. Soc.* **2015**, 137, 4316.
 (g) Liu, H.; Yuan, C.; Wu, Y.; Xiao, Y.; Guo, H. *Org. Lett.* **2015**, 17, 4220.
 (h) Gao, Z.; Wang, C.; Yuan, C.; Zhou, L.; Xiao, Y.; Guo, H. *Chem. Commun.* **2015**, 51, 12653.
 (i) Yang, W.; Zhang, Y.; Qiu, S.; Zhao, C.; Zhang, L.; Liu, H.; Zhou, L.; Xiao, Y.; Guo, H. *RSC Adv.* **2015**, 5, 62343.
 (j) Liu, Y.; Yang, W.; Wu, Y.; Mao, B.; Gao, X.; Liu, H.; Sun, Z.; Xiao, Y.; Guo, H. *Adv. Synth. Catal.* **2016**, 358, 2867.
 (k) Wang, C.; Gao, Z.; Zhou, L.; Yuan, C.; Sun, Z.; Xiao, Y.; Guo, H. *Org. Lett.* **2016**, 18, 3418.
 (l) Yuan, C.; Zhou, L.; Xia, M.; Sun, Z.; Wang, D.; Guo, H. *Org. Lett.* **2016**, 18, 5644.
 (m) Li, Z.; Yu, H.; Liu, Y.; Zhou, L.; Sun, Z.; Guo, H. *Adv. Synth. Catal.* **2016**, 358, 1880.
 (n) Wang, C.; Jia, H.; Zhang, C.; Gao, Z.; Zhou, L.; Yuan, C.; Xiao, Y.; Guo, H. *J. Org. Chem.* **2017**, 82, 633.
 (o) Yang, W.; Sun, W.; Zhang, C.; Wang, Q.; Guo, Z.; Mao, B.; Liao, J.; Guo, H. *ACS Catal.* **2017**, 7, 3142.
 (p) Zhou, L.; Yuan, C.; Zhang, C.; Zhang, L.; Gao, Z.; Wang, C.; Liu, H.; Wu, Y.; Guo, H. *Adv. Synth. Catal.* **2017**, 359, 2316.
 (q) Wang, B.; Liu, H.; Wang, Q.; Yuan, C.; Jia, H.; Liu, C.; Guo, H. *Tetrahedron* **2017**, 73, 5926.
 (r) Liu, H.; Zhao, Y.; Li, Z.; Jia, H.; Zhang, C.; Xiao, Y.; Guo, H. *RSC Adv.* **2017**, 7, 29515.
 (s) Gao, Z.; Wang, C.; Zhou, L.; Yuan, C.; Xiao, Y.; Guo, H. *Org. Lett.* **2018**, 20, 4302.
 (t) Zhou, L.; Yuan, C.; Zeng, Y.; Liu, H.; Wang, C.; Gao, X.; Wang, Q.; Zhang, C.; Guo, H. *Chem. Sci.* **2018**, 9, 1831.
 (u) Yuan, C.; Wu, Y.; Wang, D.; Zhang, Z.; Wang, C.; Zhou, L.; Zhang, C.; Song, B.; Guo, H. *Adv. Synth. Catal.* **2018**, 360, 652.
 (v) Jia, H.; Guo, Z.; Liu, H.; Mao, B.; Shi, X.; Guo, H. *Chem. Commun.* **2018**, 54, 7050.
- [15] Crystallographic data for **3w** has been deposited with the Cambridge Crystallographic Data Centre as deposition number CCDC 1849068.

(Lu, Y.)