An Efficient Procedure for the Synthesis of α,β-Unsaturated Ketones and Its Application to Heterocyclic Systems

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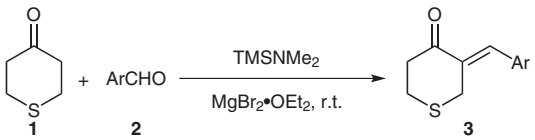
Abstract: An efficient and room-temperature procedure is developed for high yield synthesis of novel α,β-unsaturated derivatives of thiopyran **3** directly from ketone **1** and various aldehydes in the presence of catalytic quantities of $TMSNMe_2$ and $MgBr_2{\cdot}OEt_2$ under solvent-free conditions. The main advantage of the procedure is that the formation of the undesired bis by-products is minimized. In addition, the procedure is applicable to other enolizable carbocyclic and acyclic ketones.

Key words: α,β-unsaturated ketones, thiopyran-4-one, magnesium bromide etherate, aldol condensation

α,β-Unsaturated ketones are of great importance in synthetic organic chemistry since they are found as key components in many natural and biologically active structures.[1] In addition, they could serve as convenient precursors for other nucleophilic synthetic transformations.[2] Several strategies are reported so far for the preparation of these compounds.[3] However, many of them usually incorporate more than one-step reaction or require the use of commercially unavailable starting materials.

A routine method for the synthesis of these compounds is the aldol condensation of ketones with aldehydes,[4] which often involves the use of strong bases and is accompanied by competitive formation of the respective bis by-products. To overcome this limitation, two recent improved approaches were introduced based on the use of dimethylammonium dimethyl carbonate and a pyrrolidine imide catalyst,[5] respectively. However, in these methods either prolonged high temperature treatment of the reactants were needed, workup had to be performed under an atmosphere of CO_2, use of a solvent or a large excess of the reactants was required, or the yields were low or moderate in many cases. Thus, the development of efficient methods capable of producing the title compounds under milder conditions has yet remained a great challenge. Nevertheless, in both of the investigations a catalytic cycle involving transient iminium species was suggested, facilitating the formation of the desired products. This mechanism and the fact that silylated amines ease the formation of the intermediate iminium salts,[6] encouraged us to study the effect of silylated amines in direct synthesis of α,β-unsaturated ketones.

We have an ongoing program on the synthesis of bisarylmethylidenes of various homo- and heterocyclic ketones.[7] As part of this program, we decided to extend our experience to the synthesis of the monoarylidene counterparts. Based on our previous studies on thiopyran system,[8] we envisaged that ketone **1** could be an appropriate probe for evaluating possible synthesis of products **3** using silylated amines.[9] A search in the literature showed very rare previous successful examples on the preparation of products **3**. Nyberg et al., who studied the aldol reactions of various ketones, observed no formation of **3** for proline-catalyzed reactions of **1** under aqueous conditions.[10] In two other independent attempts and under harsher conditions, only low yields of a single product of type **3** were obtained in each case.[11] As a result of our investigation, here we would like to report on a novel and high yield room temperature procedure for the synthesis of α,β-unsaturated derivatives of **3** (Scheme 1). The procedure is applicable to the reactions of both homo- and heterocyclic ketones with various aldehydes.



Scheme 1 Reaction of ketone **1** with aldehydes **2**

First, **1** was subjected to react with benzaldehyde under various conditions. In most of the experiments, formation of **3a** along with other competitive by-products was observed. Better results were obtained when magnesium based Lewis acids were used in the presence of silylated amines leading to the formation of **3a** in moderate yields. The results were further optimized when an equimolar solvent-free mixture of the two reactants came into contact with $TMSNMe_2$ and $MgBr_2{\cdot}OEt_2$ leading to the formation of the respective product **3a** in high yield (Table 1) and lowering the amounts of the side-products to minimum quantities. Experiments showed that 7 mol% of $MgBr_2{\cdot}OEt_2$ is enough for the reaction to complete within 6 hours (Table 1, entry 1). Control experiments in the absence of either $MgBr_2{\cdot}OEt_2$ or $TMSNMe_2$ led to no significant process. Under optimized conditions, other

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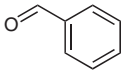
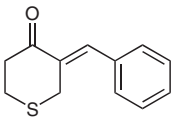
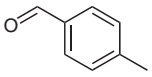
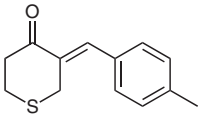
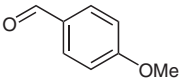
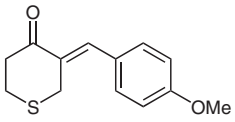
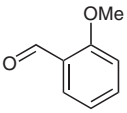
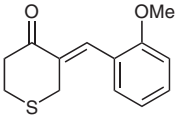
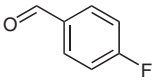
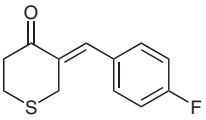
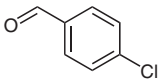
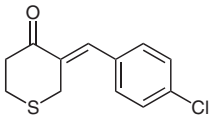
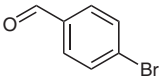
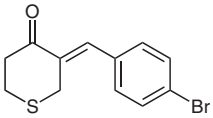
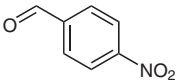
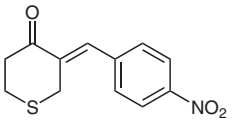
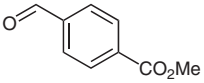
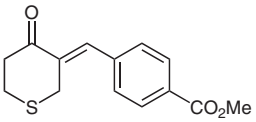
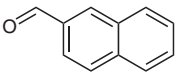
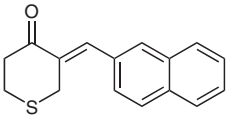
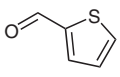
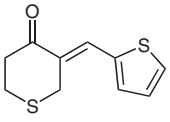
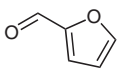
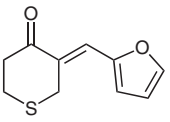
aldehydes bearing various substituents behaved similarly to produce compounds **3b–l** within 3–8 hours (entries 2–12) showing the generality of the method.

In all cases, reactions proceeded rapidly at room temperature and complete disappearance of the starting materials was observed within the time periods indicated in the

Table 1 Solvent-Free Synthesis of **3** Using $MgBr_2 \cdot OEt_2$ and $TMSNMe_2$

Entry	Aldehyde		Product		Time (h)	Yield (%)[a]
1	**2a**		**3a**		6	70
2	**2b**		**3b**		8	66
3	**2c**		**3c**		8	65
4	**2d**		**3d**		8	65
5	**2e**		**3e**		3	80
6	**2f**		**3f**		4	76
7	**2g**		**3g**		4	77
8	**2h**		**3h**		3	77
9	**2i**		**3i**		4	72
10	**2j**		**3j**		8	68
11	**2k**		**3k**		3	80
12	**2l**		**3l**		3	80

[a] Isolated yields.

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Table 1. Analysis of the reaction mixtures by ^{1}H NMR spectroscopy showed the formation of a single monoarylidene isomer with *Z*-stereochemistry as the major product in each reaction. The structure of the products was assigned based on their spectroscopic analyses. The proposed *Z*-geometry was confirmed by X-ray crystallography[12] of product **3i** (Figure 1).

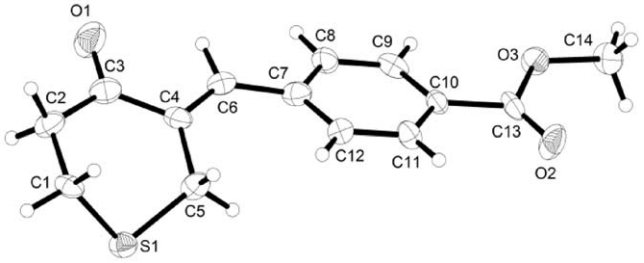
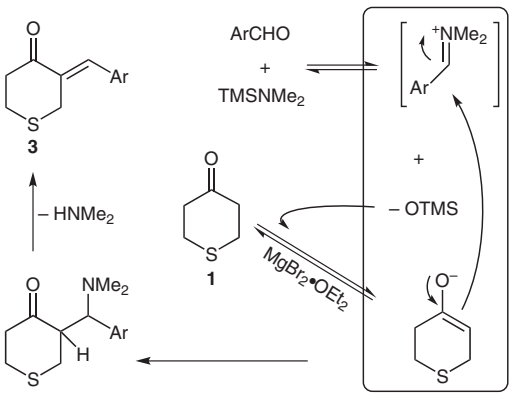


Figure 1 Crystal structure of **3i**; displacement ellipsoids at 50% probability level

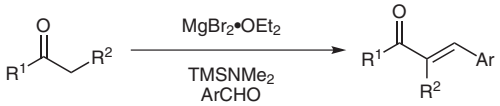
Based on the results, a mechanistic pathway could be proposed, as depicted in Scheme 2. Initially, in the presence of the $TMSNMe_2$, the starting aldehyde is converted to its respective iminium salt. Then, the trimethylsilanolate anion, resulting from this conversion, facilitates the $MgBr_2{\cdot}OEt_2$-catalyzed enolization of the ketone **1**. Finally, addition of the enol to the iminium ion results in the formation of **3**. Similar mechanisms involving iminium ions in aldol condensations have also been offered by others.[5]



Scheme 2 Proposed mechanism for the synthesis of **3**

With these results in hand, we were encouraged to extend the procedure to the synthesis of α,β-unsaturated derivatives of homocyclic and acyclic systems as well. The classical approach for the synthesis of these compounds involves the use of aldol condensation of ketones with aldehydes.[4] However, the method suffers from the use of relatively strong bases and is limited by competitive formation of side products. Alternative methods such as dehydration of β-hydroxy ketone products of Mukaiyama reaction,[13] tandem ring expansion–aldol condensation of *tert*-trihalomethyl carbinols,[3f] coupling of alkenyl trichloroacetates with aldehydes,[1c] and organocatalyzed aldol condensation procedures[14] have been introduced in recent years to improve the synthesis of α,β-unsaturated ketones and aldehydes. However, some of the methods still require more than one step reaction or employ reagents which are not commercially available. Therefore, there is still a demand for the development of more efficient procedures for selective and high-yield preparation of these compounds under milder conditions. Table 2 shows the successful application of our method to the reactions of three model cyclic and acyclic ketones with various aldehydes.

Table 2 Application of the Present Method to Other Ketones



R^1, R^2	Ar	Time (h)	Yield (%)
-$(CH_2)_4$-	Ph	16	93
-$(CH_2)_4$-	4-ClC_6H_4	14	85
-$(CH_2)_4$-	4-$MeOC_6H_4$	18	94
-$(CH_2)_3$-	Ph	5	90
-$(CH_2)_3$-	4-ClC_6H_4	4	82
-$(CH_2)_3$-	4-$MeOC_6H_4$	7	92
Ph, H	Ph	16	80
Ph, H	4-$O_2NC_6H_4$	14	64
Ph, H	4-$MeOC_6H_4$	24	71

In conclusion, we have presented a convenient and efficient protocol for the synthesis of monoarylidenes of various cyclic ketones. Products are prepared in one pot, the method involves mild reaction conditions, and the workup is easy. More importantly, the procedure is applicable to both homo- and heterocyclic ketones, the use of expensive and commercially unavailable reagents is avoided, and reactions are conducted with equimolar quantities of the starting materials. We can reach at a better conclusion by the comparison of the present method with some selected recent reports, as summarized in Table 3 for the synthesis of monoarylidenes of cyclohexanone. The same comparisons can be made for other cyclic and acyclic systems, which would end up with similar conclusions.[3,15]

We are currently working on the reactions involving the use of aliphatic aldehydes and other similar heterocyclic systems, for which the products shown in Figure 2 are already synthesized in our laboratory. Utilization of the products in other synthetic reactions is also under investigation.

Melting points are uncorrected. IR spectra were recorded using KBr disks on a Bruker Vector-22 IR spectrometer. NMR spectra were obtained on a FT-NMR Bruker Ultra Shield™ (500 MHz) as $CDCl_3$

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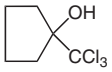
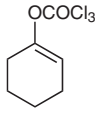
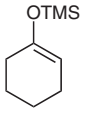
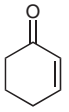
Table 3 Comparison of the Present Method with Related Procedures for the Synthesis of Monoarylidenes of Cyclohexanone

Conditions	Substrate	Reference
$TMSNMe_2$, $MgBr_2{\cdot}OEt_2$[a]	ketones	present work
$Me_2NCO_2H{\cdot}Me_2NH$,[b] 50 °C	ketones	Kreher et al.[5a]
$CrCl_2$,[b] THF, HMPA		Falck et al.[3f]
$Bu_2Sn(OMe)_2$,[a] THF, MeOH		Yanagisawa et al.[1c]
$SnCl_2$,[a] AcCl,[b] CH_2Cl_2		Oriyama et al.[16a]
n-Bu_3SnH, AIBN, toluene, 80 °C		Enholm et al.[16b]

[a] Catalytic.
[b] Excess.

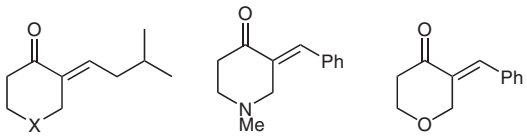


Figure 2 Additional compounds prepared using aliphatic aldehydes and other systems

solutions using TMS as internal standard reference. Elemental analyses were performed using a Thermo Finnigan Flash EA 1112 instrument. MS spectra were obtained on a Fisons 8000 Trio instrument at ionization potential of 70 eV. TLC experiments were carried out on precoated silica gel plates using PE–EtOAc (4:1) as the eluent. Compound **1**[17] and $MgBr_2{\cdot}OEt_2$[18] were prepared according to known methods. $TMSNMe_2$, solvents, and all other starting materials were purchased from commercial sources. Aldehydes were redistilled or recrystallized before being used. Petroleum ether (PE) refers to the fraction boiling in the range 40–60 °C.

α,β-Unsaturated Ketones 3; General Procedure

A mixture of an aldehyde **2** (3 mmol), ketone **1** (348 mg, 3.00 mmol), $MgBr_2{\cdot}OEt_2$ (7 mol%, 54 mg), and $TMSNMe_2$ (176 mg, 237 μL, 1.5 mmol) was stirred at r.t. under inert atmosphere for the given period of time (Table 1). The progress of the reaction was monitored by TLC (eluent: PE–EtOAc, 4:1). At the end, H_2O (5 mL) was added to the mixture and the product was extracted with Et_2O (2×5 mL). The combined organic layers were dried (Na_2SO_4). Evaporation of the solvent led to a residue, which was purified by column chromatography using silica gel and PE–EtOAc (4:1) as the eluent. Isolated yields of products were 60–80% (Table 1). The structure of the new products was determined by their physical and spectroscopic specifications and their purity was confirmed by elemental analyses.

(*Z*)-3-Benzylidenedihydro-2*H*-thiopyran-4(3*H*)-one (3a)

Yield: 70%; cream-colored solid; mp 63–64 °C.

IR (KBr): 1717, 1668, 1587 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.94–2.98 (m, 2 H), 3.06–3.08 (m, 2 H), 3.87 (s, 2 H), 7.38–7.40 (m, 3 H), 7.43–7.46 (m, 2 H), 7.57 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 29.1, 41.8, 129.0, 129.3, 130.2, 134.8, 135.2, 136.2, 199.2.

MS (70 eV): *m*/*z* = 204 (M^+), 147, 115, 89.

Anal. Calcd for $C_{12}H_{12}OS$: C, 70.55; H, 5.92. Found: C, 70.43; H, 6.00.

(*Z*)-3-(4-Methylbenzylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3b

Yield: 66%; yellow solid; mp 103–105 °C.

IR (KBr): 1710, 1511 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.40 (s, 3 H), 2.92–2.95 (m, 2 H), 3.03–3.05 (m, 2 H), 3.86 (s, 2 H), 7.23 (d, *J* = 7.5 Hz, 2 H), 7.28 (d, *J* = 7.5 Hz, 2 H), 7.54 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 21.8, 26.4, 29.2, 41.7, 129.8, 130.4, 132.3, 134.0, 136.5, 139.7, 199.1.

MS (70 eV): *m*/*z* = 218 (M^+), 145, 119, 91.

Anal. Calcd for $C_{13}H_{14}OS$: C, 71.52; H, 6.46. Found: C, 71.12; H, 6.53.

(*Z*)-3-(4-Methoxybenzylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3c)

Yield: 65%; yellow solid; mp 83–85 °C.

IR (KBr) 1684, 1601, 1511 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.90–2.92 (m, 2 H), 3.02–3.03 (m, 2 H), 3.85 (s, 3 H), 3.87 (s, 2 H), 6.95 (d, *J* = 7.0 Hz, 2 H), 7.35 (d, *J* = 7.0 Hz, 2 H), 7.53 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.3, 29.2, 41.6, 55.7, 114.5, 127.6, 132.3, 132.8, 136.4, 160.7, 198.9.

MS (70 eV): *m*/*z* = 234 (M^+), 134, 55, 43.

Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 67.03; H, 6.10.

(*Z*)-3-(2-Methoxybenzylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3d)

Yield: 65%; yellow solid; mp 92–94 °C.

IR (KBr): 1679, 1599, 1487 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.92–2.95 (m, 2 H), 3.03–3.06 (m, 2 H), 3.77 (s, 2 H), 3.88 (s, 3 H), 6.90 (d, *J* = 8.0 Hz, 1 H), 6.98 (dd, *J* = 6.5, 7.5 Hz, 1 H), 7.22 (dd, *J* = 1.5, 7.5 Hz, 1 H), 7.35 (ddd, *J* = 1.5, 7.5, 8.0 Hz, 1 H), 7.69 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.5, 29.3, 42.0, 55.9, 111.2, 120.6, 124.2, 130.0, 130.7, 131.0, 132.5, 158.6, 199.2.

MS (70 eV): *m*/*z* = 234 (M^+), 173, 131, 116.

Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 66.92; H, 6.12.

(*Z*)-3-(4-Fluorobenzylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3e)

Yield: 80%; cream colored solid; mp 55–56 °C.

IR (KBr): 1697, 1594, 1517 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.93–2.96 (m, 2 H), 3.05–3.07 (m, 2 H), 3.83 (s, 2 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 7.36 (dd, *J* = 5.5, 8.0 Hz, 2 H), 7.51 (s, 1 H).

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^{13}C NMR ($CDCl_3$): δ = 26.3, 28.9, 41.7, 116.1, 116.3, 131.2, 131.3, 132.2, 132.3, 134.6, 135.1, 163.2, 164.3, 199.0.

MS (70 eV): *m*/*z* = 222 (M^+), 133, 82.

Anal. Calcd for $C_{12}H_{11}FOS$: C, 64.84; H, 4.99. Found: C, 64.73; H, 4.89.

(*Z*)-3-(4-Chlorobenzylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3f)
Yield: 76%; oil.

IR (KBr): 1707, 1604, 1488 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.93–2.95 (m, 2 H), 3.04–3.08 (m, 2 H), 3.81 (s, 2 H), 7.30 (d, *J* = 8.5 Hz, 2 H), 7.41 (d, *J* = 8.5 Hz, 2 H), 7.48 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 29.0, 41.8, 129.3, 131.5, 133.6, 134.8, 135.2, 135.3, 198.9.

MS (70 eV): *m*/*z* = 238 (M^+), 181, 147, 115, 91.

(*Z*)-3-(4-Bromobenzylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3g)
Yield: 77%; brown solid; mp 112–114 °C.

IR (KBr): 1712, 1485, 1421 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.98–3.00 (m, 2 H), 3.04–3.07 (m, 2 H), 3.80 (s, 2 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 7.45 (s, 1 H), 7.56 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 29.0, 41.8, 123.6, 131.7, 132.3, 134.0, 134.8, 135.4, 198.9.

MS (70 eV): *m*/*z* = 281 (M^+), 194, 115, 45.

Anal. Calcd for $C_{12}H_{11}BrOS$: C, 50.90; H, 3.92. Found: C, 50.59; H, 3.99.

(*Z*)-3-(4-Nitrobenzylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3h)
Yield: 77%; brown solid; mp 112–114 °C.

IR (KBr): 1697, 1594, 1517 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.98–3.00 (m, 2 H), 3.08–3.11 (m, 2 H), 3.79 (s, 2 H), 7.51 (s, 1 H), 7.53 (d, *J* = 8.5 Hz, 2 H), 8.31 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 29.0, 41.9, 124.3, 130.8, 132.8, 137.7, 141.8, 147.9, 198.7.

MS (70 eV): *m*/*z* = 249 (M^+), 147, 115, 60.

Anal. Calcd for $C_{12}H_{11}NO_3S$: C, 57.82; H, 4.45. Found: C, 57.62; H, 4.32.

Methyl (*Z*)-4-[(4-oxo-2*H*-thiopyran-3(4*H*,5*H*,6*H*)-ylidene)methyl]benzoate (3i)
Yield: 72%; brown solid; mp 96–98 °C.

IR (KBr): 1714, 1608, 1434 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.96–2.98 (m, 2 H), 3.07–3.10 (m, 2 H), 3.83 (s, 2 H), 3.97 (s, 3 H), 7.41 (d, *J* = 8.0 Hz, 2 H), 7.54 (s, 1 H), 8.11 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 30.5, 41.9, 52.7, 130.0, 130.2, 130.6, 134.6, 136.4, 139.7, 166.9, 198.9.

MS (70 eV): *m*/*z* = 262 (M^+), 247, 204, 147, 115.

Anal. Calcd for $C_{14}H_{14}O_3S$: C, 64.10; H, 5.38. Found: C, 63.73; H, 5.26.

(*Z*)-3-(Naphthalen-2-ylmethylene)dihydro-2*H*-thiopyran-4(3*H*)-one (3j)
Yield: 68%; yellow solid; mp 82–84 °C.

IR (KBr): 1717, 1601, 1468 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.97–2.99 (m, 2 H), 3.08–3.10 (m, 2 H), 3.96 (s, 2 H), 7.48 (dd, *J* = 1.5, 8.5 Hz, 1 H), 7.54–7.58 (m, 2 H), 7.72 (s, 1 H), 7.86–7.90 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 26.4, 29.2, 41.8, 127.1, 127.4, 127.5, 128.2, 128.7, 128.8, 130.1, 132.7, 133.4, 133.6, 135.0, 136.4, 199.2.

MS (70 eV): *m*/*z* = 254 (M^+), 197, 165, 135.

Anal. Calcd for $C_{16}H_{14}OS$: C, 75.55; H, 5.55. Found: C, 75.30; H, 5.62.

(*Z*)-3-(Thiophen-2-ylmethylene)dihydro-2*H*-thiopyran-4(3*H*)-one (3k)
Yield: 80%; yellow solid; mp 94–96 °C.

IR (KBr): 1717, 1668, 1587 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.92–2.96 (m, 2 H), 3.00–3.05 (m, 2 H), 3.98 (s, 2 H), 7.17–7.20 (m, 1 H), 7.38 (d, *J* = 5.0 Hz, 1 H), 7.58 (d, *J* = 5.0 Hz, 1 H), 7.83 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.3, 29.4, 41.4, 128.25, 129.7, 130.3, 130.6, 134.3, 138.4, 197.9.

MS (70 eV): *m*/*z* = 210 (M^+), 118, 116, 88.

Anal. Calcd for $C_{10}H_{10}OS_2$: C, 57.11; H, 4.79. Found: C, 57.43; H, 4.70.

(*Z*)-3-(Furan-2-ylmethylene)dihydro-2*H*-thiopyran-4(3*H*)-one (3l)
Yield: 80%; oil (80%).

IR (KBr): 1711, 1607 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.90–2.93 (m, 2 H), 3.03–3.06 (m, 2 H), 4.15 (s, 2 H), 6.55 (dd, *J* = 1.5, 3.5 Hz, 1 H), 6.72 (d, *J* = 3.5 Hz, 1 H), 7.33 (s, 1 H), 7.60 (d, *J* = 1.5 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.2, 29.3, 39.2, 112.7, 118.3, 122.4, 130.1, 145.2, 151.9, 198.3.

MS (70 eV): *m*/*z* = 194 (M^+), 165, 107, 97.

(*Z*)-3-(3-Methylbutylidene)dihydro-2*H*-thiopyran-4(3*H*)-one (3m)
Yield: 60%; yellow solid, mp 76–78 °C.

IR (KBr): 1710, 1424 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.96 (d, *J* = 6.5 Hz, 6 H), 1.80–1.84 (m, 1 H), 2.06–2.09 (m, 2 H), 2.82–2.85 (m, 2 H), 2.98 (t, *J* = 6.0 Hz, 2 H), 3.56 (s, 2 H), 6.68–6.71 (m, 1 H).

^{13}C NMR ($CDCl_3$): δ = 23.0, 26.3, 27.6, 28.7, 37.3, 41.8, 135.3, 139.1, 198.7.

MS (70 eV): *m*/*z* = 184 (M^+), 129, 115.

Anal. Calcd for $C_{10}H_{16}OS$: C, 65.17; H, 8.75. Found: C, 64.77; H, 8.73.

(*E*)-3-Benzylidenedihydro-2*H*-pyran-4(3*H*)-one (7a)
Yield: 79%; yellow solid; mp 103–104 °C.

IR (KBr): 1678, 1450, 983 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.61 (t, *J* = 6.0 Hz, 2 H), 4.00 (t, *J* = 6.0 Hz, 2 H), 4.77 (d, *J* = 2.0 Hz, 2 H), 7.19–7.21 (m, 2 H), 7.27–7.35 (m, 3 H), 7.55 (t, *J* = 2.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 40.1, 65.9, 69.1, 129.1, 129.8, 130.9, 133.7, 134.7, 136.4, 196.5.

MS (70 eV): *m*/*z* = 188 (M^+), 159, 131, 115.

Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.12; H, 6.54.

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References

(1) (a) Hallgas, B.; Dobos, Z.; Agócs, A.; Idei, M.; Kéri, G.; Loránd, T.; Mészáros, G. *J. Chromatogr., B* **2007**, *856*, 148. (b) Das, U.; Doroudi, A.; Das, S.; Bandy, B.; Balzarini, J.; De Clercq, E.; Dimmock, J. R. *Bioorg. Med. Chem.* **2008**, *16*, 6261. (c) Yanagisawa, A.; Goudu, R.; Arai, T. *Org. Lett.* **2004**, *6*, 4281. (d) Rao, Y. K.; Fang, S. H.; Tzeng, Y. M. *Bioorg. Med. Chem.* **2004**, *12*, 2679. (e) Thanigaimalai, P.; Lee, K. C.; Sharma, V. K.; Rao, E. V.; Roh, E.; Kim, Y.; Jung, S. H. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 1922.

(2) (a) Caruana, P. A.; Frontier, A. J. *Tetrahedron* **2007**, *63*, 10646. (b) Haunert, F.; Bolli, M. H.; Hinzen, B.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2235. (c) Subramaniyan, G.; Raghunathan, R. *Synth. Commun.* **2004**, *34*, 1825. (d) Huang, X. G.; Zhang, L. M. *J. Am. Chem. Soc.* **2007**, *129*, 6398. (e) Olsen, R. J.; Minniear, J. C.; Overton, W. M.; Sherrick, J. M. *J. Org. Chem.* **1991**, *56*, 989. (f) Chebanov, V. A.; Desenko, S. M.; Gurley, T. W. *Azaheterocycles Based on α,β-Unsaturated Carbonyls*; Springer: Berlin, **2008**.

(3) (a) Das, B.; Banerjee, J.; Chowdhury, N.; Majhi, A.; Holla, H. *Synlett* **2006**, 1879. (b) Raju, S. V. N.; Ponrathnam, S.; Rajan, C. R.; Srinivasan, K. V. *Synlett* **1996**, 239. (c) Zhu, J. L.; Ko, Y. C.; Kuo, C. W.; Shia, K. S. *Synlett* **2007**, 1274. (d) Chen, J. M.; Huang, X. *Synthesis* **2004**, 2459. (e) Sydnes, L. K.; Pedersen, G. S.; Holmelid, B.; Sandberg, M. *Synthesis* **2007**, 3692. (f) Falck, J. R.; He, A.; Reddy, L. M.; Kundu, A.; Barma, D. K.; Bandyopadhyay, A.; Kamila, S.; Akella, R.; Bejot, R.; Mioskowski, C. *Org. Lett.* **2006**, *8*, 4645. (g) Takeishi, K.; Sugishima, K.; Sasaki, K.; Tanaka, K. *Chem. Eur. J.* **2004**, *10*, 5681.

(4) (a) Yang, S. D.; Wu, L. Y.; Yan, Z. Y.; Pan, Z. L.; Liang, Y. M. *J. Mol. Catal. A: Chem.* **2007**, *268*, 107. (b) Wang, J. F.; Lei, M.; Li, Q.; Ge, Z. M.; Wang, X.; Li, R. T. *Tetrahedron* **2009**, *65*, 4826. (c) Qiu, R.; Qiu, Y.; Yin, S.; Xu, X.; Luo, S.; Au, C.-T.; Wong, W.-Y.; Shimada, S. *Adv. Synth. Catal.* **2010**, *352*, 153. (d) Qiu, R.; Qiu, Y.; Yin, S.; Song, X.; Meng, Z.; Xu, X.; Zhang, X.; Luo, S.; Au, C.-T.; Wong, W.-Y. *Green Chem.* **2010**, *12*, 1767.

(5) (a) Kreher, U. P.; Rosamilia, A. E.; Raston, C. L.; Scott, J. L.; Strauss, C. R. *Org. Lett.* **2003**, *5*, 3107. (b) Wang, W.; Mei, Y.; Li, H.; Wang, J. *Org. Lett.* **2005**, *7*, 601.

(6) (a) Erkkilä, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416. (b) Levin, V. V.; Kozlov, M. A.; Song, Y.-H.; Dilman, A. D.; Belyakov, P. A.; Struchkova, M. I.; Tartakovsky, V. A. *Tetrahedron Lett.* **2008**, *49*, 3108.

(7) (a) Abaee, M. S.; Mojtahedi, M. M.; Hamidi, V.; Mesbah, A. W.; Massa, W. *Synthesis* **2008**, 2122. (b) Abaee, M. S.; Mojtahedi, M. M.; Zahedi, M. M. *Synlett* **2005**, 2317. (c) Abaee, M. S.; Mojtahedi, M. M.; Zahedi, M. M.; Mesbah, A. W.; Mohaddes Ghandchi, N.; Massa, W. *Phosphorus Sulfur Silicon Relat. Elem.* **2007**, *182*, 2891. (d) Abaee, M. S.; Mojtahedi, M. M.; Zahedi, M. M.; Sharifi, R.; Mesbah, A. W.; Massa, W. *Synth. Commun.* **2007**, *37*, 2949.

(8) (a) Abaee, M. S.; Mojtahedi, M. M.; Zahedi, M. M.; Sharifi, R.; Khavasi, H. *Synthesis* **2007**, 3339. (b) Abaee, M. S.; Mojtahedi, M. M.; Zahedi, M. M.; Sharifi, R. *Heteroat. Chem.* **2007**, *18*, 44. (c) Abaee, M. S.; Mojtahedi, M. M.; Akbari, M.; Mehraki, E.; Mesbah, A. W.; Harms, K. *J. Heterocycl. Chem.* **2011**, in press. (d) Abaee, M. S.; Mojtahedi, M. M.; Pasha, G. F.; Akbarzadeh, E.; Shockravi, A.; Mesbah, A. W.; Massa, W. *Org. Lett.* **2011**, *13*, 5282.

(9) For other synthetic utilities of thiopyrans, see: (a) Beye, G. E.; Ward, D. E. *J. Am. Chem. Soc.* **2010**, *132*, 7210. (b) Li, D.; Xu, X.; Liu, Q.; Dong, S. *Synthesis* **2008**, 1895. (c) Margaretha, P.; Schmidt, K.; Kopf, J.; Sinnwell, V. *Synthesis* **2007**, 1426. (d) Rosiak, A.; Frey, W.; Christoffers, J. *Eur. J. Org. Chem.* **2006**, 4044.

(10) Nyberg, A. I.; Usano, A.; Pihko, P. M. *Synlett* **2004**, 1891.

(11) (a) Liotta, F.; Lu, H.; Xia, M.; Wachter, M. P. US Patent 223798, **2006**; *Chem. Abstr.* **2006**, *145*, 397511. (b) Kato, H.; Nagata, O.; Iwabuchi, Y.; Sato, T.; Uda, J.; Inoue, T.; Nakamura, H.; Kawasaki, N.; Tanaka, I.; Kurita, N.; Ishikawa, T. European Patent Appl. EP2062884, **2009**; *Chem. Abstr.* **2008**, *148*, 379476.

(12) Crystallographic data for **3i** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-846075. Copies of these data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk or via www.ccdc.cam.ac.uk/conts/retrieving.html].

(13) (a) Ishihara, K.; Kurihara, H.; Yamamoto, H. *Synlett* **1997**, 597. (b) Taju, S. V. N.; Ponrathnam, S.; Rajan, C. R.; Sirinivasan, K. V. *Synlett* **1996**, 239.

(14) (a) Zumbansen, K.; Döhring, A.; List, B. *Adv. Synth. Catal.* **2010**, *352*, 1135. (b) Arnold, A.; Markert, M.; Mahrwald, R. *Synthesis* **2006**, 1099. (c) Markert, M.; Mahrwald, R. *Synthesis* **2004**, 1429.

(15) (a) Yatluk, Y. G.; Sosnovskikh, V. Y.; Suvorov, A. L. *Russ. J. Org. Chem.* **2004**, *40*, 763. (b) Yi, W.-B.; Cai, C. *J. Fluorine Chem.* **2009**, *130*, 484. (c) Zhu, Y.-W.; Yi, W.-B.; Cai, C. *J. Fluorine Chem.* **2011**, *132*, 71. (d) Chen, X.; Liu, B.-K.; Kang, H.; Lin, X.-F. *J. Mol. Catal. B: Enzym.* **2011**, *68*, 71. (e) Tanaka, K.; Sasaki, K.; Takeishi, K.; Hirano, M. *Eur. J. Org. Chem.* **2007**, 5675.

(16) (a) Oriyama, T.; Iwanami, K.; Miyauchi, Y.; Koga, G. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3716. (b) Enholm, E. J.; Whitley, P. E. *Tetrahedron Lett.* **1995**, *36*, 9157.

(17) Ward, D. E.; Rasheed, M. A.; Gillis, H. M.; Beye, G. E.; Jheengut, V.; Achonduh, G. T. *Synthesis* **2007**, 1584.

(18) Pohmakotr, N.; Geiss, J. H.; Seebach, D. *Chem. Ber.* **1979**, *112*, 1420.

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