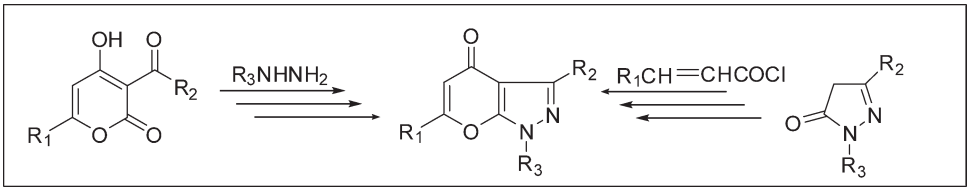
James W. Pavlik,[a]* Vuthichai Ervithayasuporn,[a] and Supawan Tantayanon[b]

[a]Department of Chemistry and Biochemistry, Worcester Polytechnic Institute, Worcester, Massachusetts 01609
[b]Department of Chemistry, Chulalongkorn University, Bangkok 10330, Thailand
*E-mail: jwpavlik@wpi.edu

Received December 16, 2009
DOI 10.1002/jhet.562
Published online 4 March 2011 in Wiley Online Library (wileyonlinelibrary.com).



Synthetic methods have been developed to prepare pyrano[2,3-*c*]pyrazoles with various substituents at ring positions 1, 3, and 6. The ^{1}H- and ^{13}C-NMR properties of these products and their precursors are presented and discussed.

J. Heterocyclic Chem., **48**, 710 (2011).

INTRODUCTION

Our interest in the mechanistic aspects of the photochemistry of the pyrano[2,3-*c*]pyrazole ring system [1] required the availability of a variety of these compounds bearing different substituents at ring positions 1, 3, and 6. This article describes the synthesis of these compounds.

RESULTS AND DISCUSSION

Gelin *et al*. [2] have described the synthesis of *N*-phenylpyrano[2,3-*c*]pyrazoles **4a–c** in three steps from dehydroacetic acid **1a** or from dehydroacetic acid derivatives **1b–1c** as shown in Scheme 1.

Following their three-step approach [2], 3,6-dimethyl-1-phenylpyrano[2,3-*c*]pyrazole-4(1*H*)-one **4a** was synthesized in our laboratory in an overall yield of 55%. As suggested, intermediates, **2a** and **3a**, were isolated and purified before proceeding to the next step. Work in our laboratory, however, revealed that the syntheses of **4a–c** can also be carried out in a ''one-pot'' procedure described in the Experimental Section. This approach led to the synthesis of **4a** in 74% which is substantially higher than the yield of 55% which was obtained when intermediates **2a** and **3a** were isolated and purified.

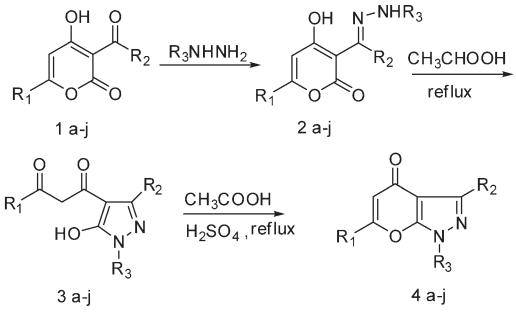
According to Scheme 1, the substituent on nitrogen in the pyranopyrazole is controlled by the hydrazine reagent used. Thus, to synthesize a series of *N*-methylpyranopyrazoles, we investigated using methylhydrazine in the synthetic procedure. In this respect, we have recently reported [1] that *N*-methylhydrazone **2e** [3], formed from reaction of **1e** with methylhydrazine [4], can be converted to 1,3,6-trimethylpyrano[2,3-*c*]pyrazole-4(1*H*)-one **4e** by the series of reactions shown in Scheme 1 or in a ''one-pot'' procedure described in the Experimental Section.

Inspection of Scheme 1 shows that the C3 substituent in pyranopyrazole **4** is determined by the R_2 group in the acyl side chain of **1**. To synthesize pyranopyrazoles with different R_2 substituents, dehydroacetic acid derivatives **1f** and **1g**, where R_2 = ethyl or propyl, were synthesized from commercially available 4-hydroxy-6-methyl-2-pyrone by acylation using propionic or butyric anhydride, respectively, using the method of Marcus *et al*. [5]. These known dehydroacetic acid derivatives **1f** and **1g** were converted to the previously unreported *N*-methylhydrazones **2f** and **2g** as shown in Scheme 2. In the case of the ethyl derivative, reaction of **1f** with methylhydrazine provided *N*-methylhydrazone **2f** in 56% yield and bipyrazole **5f** in 13% yield, which were separated by fractional crystallization from ethyl acetate. As a result of the similar solubilities of the analogous *n*-propyl derivatives, *N*-methylhydrazone **2g** was isolated in 45% by preparative layer chromatography. In this case, **5g** was not isolated.

Refluxing in acetic acid resulted in the isomerization of **2f** and **2g** to the previously unreported diketopyrazoles **3f** and **3g**. The ^{1}H- and ^{13}C-NMR spectra of these compounds, given in the Experimental Section, could be explained in terms of a mixture of keto and enol tautomers as shown in Scheme 3. Further isomerization of **3f** and **3g** by refluxing in acetic acid containing concentrated sulfuric acid provided pyranopyrazoles **4f** and **4g**. Their elemental analyses and spectral data are consistent with their proposed structures.

To utilize this approach to synthesize pyranopyrazole **4h** that is unsubstituted at position 3 of the pyrazole ring, the formylated dehydroacetic acid derivative **1h** was required. This was prepared in 71% yield by regiospecific formylation 4-hydroxy-6-methyl-2-pyrone

Scheme 1



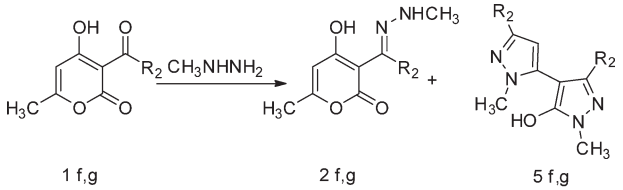
a) $R_1 = R_2 = CH_3$; R_3 = Ph
b) $R_1 = CH_3$; $R_2 = CH_2CH_3$; R_3 = Ph
c) $R_1 = CH_3$; $R_2 = R_3$ = Ph
d) $R_1 = R_3$ = Ph ; R_2 = H
e) $R_1 = R_2 = R_3 = CH_3$
f) $R_1 = R_3 = CH_3$; $R_2 = CH_2CH_3$
g) $R_1 = R_2 = CH_3$; $R_2 = CH_2CH_2CH_3$
h) $R_1 = CH_3$; R_2 = H ; R_3 = Ph
i) R_1 = Ph ; R_2 = H ; $R_3 = CH_3$
j) R_1 = Ph ; R_2 = H ; R_3 = Ph

using the procedure developed by Shimizu *et al*. [6]. This compound was then converted to the previously unreported *N*-phenylhydrazone **2h** in 81%. The ^{1}H- and ^{13}C-NMR spectra were consistent with the structure of **2h**. In particular, the protons of the C6 methyl group were observed as a 3H singlet at δ 2.20 while the C5 and amino protons appear as 1H singlets at δ 6.05 and 7.95, respectively. The ^{13}C-NMR spectrum showed the presence of 11 sets of carbon atoms of which five sets were confirmed by the DEPT-135 spectrum to be quaternary. The isomerization of **2h** to diketopyrazole **3h**, however, was not successful. Thus, refluxing **2h** in acetic acid for 1 h led only to the recovery of starting material whereas more prolonged refluxing led only to the decomposition of the *N*-phenylhydrazone **2h** without formation of any distinguishable product.

Because of the failure of the above synthetic procedure, a different approach to the synthesis of **4i** and **4j** was explored. Colatta *et al*. [7] have reported that 1,3-disubstituted pyrazolones are useful starting materials for the synthesis of pyranopyrazoles substituted at C3 of the pyrazole ring. Although it has not been demonstrated that this approach can also be used to synthesize pyranopyrazoles unsubstituted at C3 of the pyrazole ring, this possibility was explored.

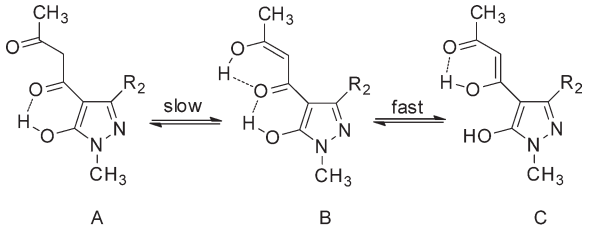
The required *N*-methyl- and *N*-phenylpyrazolones **6i** and **6j** were synthesized by condensation of *N*-methyl- or *N*-phenylhydrazine with commercially available dimethyl methoxymethylenemalonate followed by saponification and decarboxylation of the resulting esters according to the procedure reported by Tietze *et al*. [8] and Claisen and Haase [9], respectively.

Scheme 2



(f : $R_2= CH_2CH_3$, g : $R_2 = CH_2CH_2CH_3$)

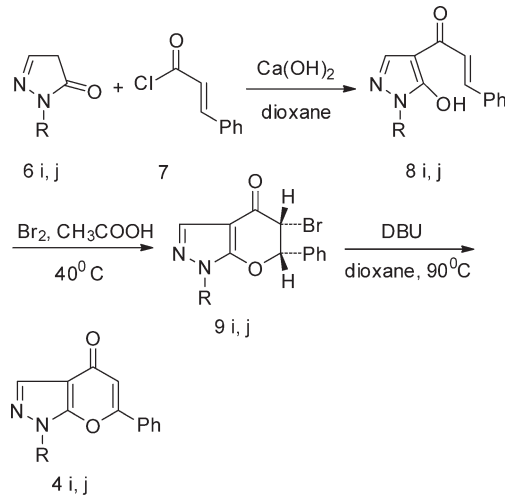
Scheme 3



(R_2 = Et or nPR)

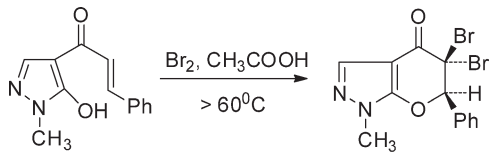
Based on the synthetic approach developed by Heinish *et al*. [10], pyrazolones **6i** and **6h** were then converted to *N*-methyl- and *N*-phenylpyranopyrazoles **4i** and **4j** by the sequence of reactions shown in Scheme 4. Thus, C-acylation of pyrazolones **6i** or **6j** with cinnamoyl chloride **7** in a slurry of $Ca(OH)_2$ in dioxane gave the α,β-unsaturated ketones **8i** or **8j**. Bromination using bromine in acetic acid at 40°C gave previously unreported monobromo products **9i** or **9j**, which were assigned the cis-sterochemistry based on ^{1}H-NMR analysis. Thus, in the case of **9i**, the protons at C5 and C6 appeared as a pair of doublets (J = 11.7 Hz) at δ 5.49 and 5.26. Based on the Karplus equation, the magnitude of the coupling constant indicated a very small dihedral angle (θ − 0°) and the assigned cis-stereochemistry. Interestingly, when the bromination of *N*-methyl **8i** was carried out at temperatures above 60°C, the unexpected 5,5-dibromo-1-methyl-6-phenyl-5,6-dihydropyran[2,3-*c*] pyrazol-4(1*H*)-one **10** (Scheme 5) was obtained in 33%

Scheme 4



(i = CH_3 ; j = Ph)

Scheme 5



8 i 10

yield. Dehydrobromination of **9j** or **9i** with DBU in refluxing dioxane resulted in the formation of pyranopyrazoles **4j** or the previously unreported **4i**, respectively. The approach shown in Scheme 5 thus provides a pathway for the synthesis of pyranopyrazoles unsubstituted in the pyrazole ring. Presumably, the use of other α,β-unsaturated acyl chlorides would also allow control of the substituents in the 4-pyrone ring.

EXPERIMENTAL

Melting points were determined using a MEL-TEMP apparatus and are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded at 400.1 and 100.6 MHz, respectively, in deuteriochloroform on a Brucker FTNMR system. ^{1}H- and ^{13}C-NMR chemical shifts were measured relative to internal tetramethylsilane and chloroform, respectively. All ^{13}C-NMR spectra are proton decoupled. Mass spectra were recorded on a Waters Micromass model ZMD spectrometer using electrospray ionization and 1:1 acetonitrile:water solvent flow.

3,6-Dimethyl-1-phenylpyrano[2,3-*c*]pyrazole-4(1*H*)-one (4a) "one-pot approach." Phenylhydrazine (1.1 g, 1.0 mL, 10.2 mmol) was added dropwise to a hot (80°) solution of dehydroacetic acid **1a** (1.66 g, 10.0 mmol) in ethanol (50 mL). After several minutes, a yellow solid precipitated that was filtered to give yellow crystals (2.51 g). Without further purification the crystals were dissolved in glacial acetic acid (50 mL) and refluxed for 1 h. Concentrated sulfuric acid (1.0 mL) was added dropwise and the resulting solution was refluxed for 1 additional hour, cooled to room temperature, and poured into cold water (100 mL). The resulting precipitate was filtered, washed with 5% aqueous sodium carbonate, water, and dried to furnish crude **4a** (2.31 g), which was recrystallized from actonitrile to give **4a** as colorless crystals: mp 148–149°C (lit. [2], 150°C), yield, 1.75 g (7.35 mmol, 74%).

1,3,6-Trimethylpyrano-[2,3-*c*]pyrazole-4(1*H*)-one (4e) "one-pot approach." *N*-methylhydrazone **3e** (1.00 g, 5.10 mmol) in glacial acetic acid (20 mL) was refluxed for 1 h. Concentrated sulfuric acid (1.0 mL) was added dropwise and the resulting mixture was refluxed for 1 additional hour. The resulting mixture was allowed to cool to room temperature, neutralized with a saturated aqueous solution of sodium carbonate, and extracted with dichloromethane (40 mL). The organic phase was dried (anhydrous sodium sulfate) and evaporated to give **4e** (0.71 g), which was recrystallized from ethyl acetate to give **4e** as a white crystalline product: mp 154–155°C (lit. [1] 154–155°C); yield 0.49 g (2.78 mmol; 55%).

3-Ethyl-1,6-dimethylpyrano[2,3-*c*]pyrazole-4(1*H*)-one (4f). ***4-Hydroxy-6-methyl-3-[1-(2-methylhydrazano)propyl]-3,4-dihydro-2H-pyran-2-one (2f).*** A solution of methylhydrazine (0.25 g, 0.29 mL, 5.50 mmol) and ethanol (5 mL) was added dropwise to a solution of 4-hydroxy-6-methyl-3-propionyl-2H-pyran-2-one **1f** [5] (1.00 g, 5.49 mmol) in ethanol at room temperature during a period of 10 min. After complete addition, the solution was stirred at room temperature for 2 h. Evaporation of the solvent gave a crude mixture of **2f** and 5-hydroxy-3-ethyl-1-methyl-4-(1,3-dimethylpyrazol-5-yl) pyrazole **5f**. The mixture was dissolved in hot ethyl acetate (20 mL) and allowed to cool to give **2f** (0.20 g), which was recrystallized from ethyl acetate to give colorless crystals of **2f**: mp 162–163°C; yield 0.16 g (0.734 mmol, 13%); ^{1}H-NMR (deuteriochloroform) δ 5.75 (s, 1H), 3.63 (s, 3H), 3.49 (s, 3H), 2.36 (q, J = 7.6 Hz, 2H), 2.04 (s, 3H), 1.02 (t, J = 7.8 Hz, 3H); ^{13}C-NMR (deuteriochloroform) δ 151.9, 151.4, 148.4, 137.6, 107.5, 89.2, 36.4, 33.4, 21.2, 13.8, 13.5; MS (ESI): $(M + Na)^+$ = 242.7. Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 59.98; H, 7.32; N, 25.44. Found: C, 60.21; H, 7:19, N, 25.41.

Evaporation of the mother liquor gave **5f** (1.12 g), which was recrystallized from toluene and hexane to give **5f** (1.12 g), which was recrystallized from toluene and hexane to give **5f** as a white crystalline solid: mp 97–98°C; yield 0.65 g (3.10 mmol; 56%); ^{1}H-NMR (deuteriochloroform) δ 15.2 (s, 1H), 5.68 (s, 1H), 4.03 (br, NH), 3.26 (q, J = 6.1 Hz, 2H), 2.82 (d, J = 5.5 Hz, 3H), 2.11 (s, 3H), 1.21 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (deuteriochloroform) δ 184.2, 178.6, 162.7, 162.6, 106.8, 93.9, 39.0, 22.0, 19.8, 11.5; MS (ESI): $(M + Na)^+$ = 233.0. Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 57.13; H, 6.71; N, 13.83. Found: C, 57.26; H, 6.71; N, 13.24.

1-(3-Ethyl-5-hydroxy-1-methyl-1H-pyrazol-4-yl)butane-1,3-dione (3f). A solution of **2f** (1.23 g, 5.86 mmol) in glacial acetic acid (15 mL) was refluxed for 1 h. Evaporation of the solvent gave **3f** (1.31 g), which was recrystallized from acetonitrile to give **3f** as white crystals: mp 123–124°C; yield 0.86 g (4.10 mmol, 70%); ^{1}H-NMR (deuteriochloroform) enol (major), δ 15.0 (s, 1H), 11.5 (br, OH), 5.59 (s, 1H), 3.57 (s, 3H), 2.78 (q, J = 7.6 Hz, 2H), 2.06 (s, 3H), 1.32 (t, J = 7.3 Hz, 3H); keto (minor) δ 11.5 (br, OH), 3.80 (s, 2H), 3.57 (s, 3H), 2.78 (q, J = 7.6 Hz, 2H), 2.30 (s, 3H), 1.32 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (deuteriochloroform) enol (major), δ 188.1, 180.9, 158.8, 151.3, 98.6, 96.7, 32.5, 22.7, 22.5, 12.6; keto (minor), δ 188.6, 180.9, 158.8, 151.3, 98.6, 55.2, 32.5, 30.8, 22.4, 12.5; MS (ESI): $(M + Na)^+$ = 232.9; Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 57.13; H, 6.71; N, 13.33. Found: C, 57.13; H, 7.04; N, 13.17.

3-Ethyl-1,6-dimethylpyrano [2,3-c] pyrazole-4(1H)-one (4f). Concentrated sulfuric acid (0.20 mL) was added dropwise to a solution of **3f** (0.35 g, 1.67 mmol) in glacial acetic acid (10 mL) and the resulting mixture was heated at reflux for 1 h. The solution was allowed to cool to room temperature, neutralized with aqueous sodium carbonate, and extracted with dichloromethane (30 mL). The organic layer was dried (anhydrous sodium sulfate) and evaporated to yield crude **4f** (0.29 g), which was recrystallized from cyclohexane to give **4f** as white crystalline product; mp 99–100°C; yield 0.26 g (1.33 mmol, 79%); ^{1}H-NMR (deuteriochloroform) δ 5.92 (s, 1H), 3.79 (s, 3H), 2.91 (q, J = 7.6 Hz, 2H), 2.32 (s, 3H), 1.29 (t, J = 7.8 Hz, DH); ^{13}C-NMR (deuteriochloroform) δ 175.9, 161.3, 154.9, 151.4, 112.5, 104.9, 34.1, 22.3, 19.8, 13.4; MS (ESI): $(M + Na)^+$ = 214.9; Anal. Calcd for $C_{10}H_{20}N_2O_2$: C, 62.49; H, 6.29; N, 14.57. Found: C, 62.63; H, 6.34; N, 14.78.

3-Ethyl-1,6-dimethylpyrano[2,3-*c*]pyrazole-4(1*H*)-one (4f) "one-pot approach." A solution of *N*-methylhydrazone **2f** (0.30 g, 1.43 mmol) in glacial acetic acid (10 mL) was heated

at reflux for 1 h. Concentrated sulfuric acid (0.20 mL) was added dropwise and the resulting mixture was refluxed for 1 additional hour. After cooling, the mixture was neutralized with aqueous saturated sodium carbonate and extracted with dichloromethane (30 mL). The organic layer was dried (anhydrous sodium sulfate) and evaporated to provide crude **4f** (0.26 g), which was recrystallized from cyclohexane to give **4f** as a white crystalline product: mp 99–100°C; yield 0.18 g (0.94 mmol, 66%).

1,6-Dimethyl-3-propylpyrano[2,3-*c*]pyrazole-4(1*H*)-one (4g). ***4-Hydroxy-6-methyl-3-[1-(2-methylhydrazano)butryl]-3,4-dihydro-2H-pyran-2-one (2g).*** A solution of methylhydrazine (0.95 mL, 0.83 g, 18.1 mmol) in ethanol (10 mL) was added dropwise to a solution of 3-butyryl-4-hydroxy-6-methyl-2*H*-pyran-2-one **1g** [5] (3.38 g, 17.2 mmol) in ethanol (40 mL) at room temperature over a period of 10 min and the resulting mixture was stirred at room temperature for 2 h. Evaporation of the solvent gave the crude product (4.15 g), which was purified by preparative layer chromatography: silica gel, dichloromethane (10): ethanol (1). The band at Rf = 0.30 gave a solid which was recrystallized from toluene–hexane to give **2g** as white crystals: mp 70–71°C; yield 1.73 g (7.72 mmol, 45%): ^{1}H-NMR (deuteriochloroform) δ 15.3 (s, 1H), 5.67 (s, 1H), 4.02 (q, J = 5.1 Hz, NH), 3.21 (t, J = 7.6 Hz, 2H), 2.80 (d, J = 5.8 Hz, 3H), 2.10 (s, 3H), 1.57 (sextet, J = 7.8 Hz, 2H), 1.04 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (deuteriochloroform) δ 184.6, 177.7, 163.1, 163.2, 107.2, 39.3, 30.6, 21.4, 20.2, 14.8; MS (ESI): (M + Na)$^+$ = 247.1; Anal. Calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19; N, 12.49. Found: C, 58.94; H, 6.97; N, 12.46.

1-(3-Ethyl-5-hydroxyl-1-methyl-1H-pyrazole-4-yl)butane-1,3-dione (3g). A solution of **2g** (0.18 g, 0.80 mmol) in glacial acetic acid (5 mL) was heated at reflux for 1 h. Evaporation of the solvent gave **3g** (0.19 g), which was recrystallized from ethyl acetate–hexane to give **3g** as a white crystalline solid: mp 96–97°C; yield 0.11 g (0.49 mmol, 61%); ^{1}H-NMR (deuteriochloroform) enol (major) δ 15.0 (s, 1H), 11.5 (br OH), 5.57 (s, 1H), 3.56 (s, 3H), 2.63 (t, J = 7.6 Hz, 2H), 2.06 (s, 3H), 1.67 (sextet, J = 7.8 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H); keto (minor) δ 11.5 (br, OH), 3.80 (s, 2H), 3.57 (s, 3H), 2.63 (t, J = 7.6 Hz, 2H), 2.29 (s, 3H), 1.67 (sextet, J = 7.8 Hz, 2H), 0.98 (t = 7.3 Hz, 3H); ^{13}C-NMR (deuteriochloroform) enol (major) δ 188.6, 181.3, 159.2, 150.5, 99.2, 97.1, 33.0, 31.7, 22.9, 22.2, 14.4: keto (minor) δ 188.6, 181.3, 159.2, 150.5, 102.9, 55.6, 31.4, 31.2, 22.4, 14.4; MS (ESI): (M + Na)$^+$ = 242.0; Anal. Calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19; N, 12.49. Found: C, 58.60, H, 6.93; N, 12.30.

1,6-Dimethyl-3-propylpyrano[2,3-c]pyrazole-4-(1H)-one (4g). Concentrated sulfuric acid (0.10 mL) was added dropwise to a solution of **3g** (0.12 g, 0.54 mmol) in glacial acetic acid (5 mL), the mixture was refluxed for 1 h, neutralized with aqueous sodium carbonate, and extracted with dichloromethane (20 mL). The organic layer was dried and evaporated to give crude **4g** (0.10 g), which was recrystallized from cyclohexane to give **4g** as white crystals: mp 61–62°C; yield 0.082 g (0.398 mmol, 74%); ^{1}H-NMR (deuteriochloroform) δ 5.92 (s, 1H), 3.79 (s, 3H), 2.82 (t, J = 7.6 Hz, 2H), 2.32 (s, 3H), 1.76 (sextet, J = 7.6 Hz, 2H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (deuteriochloroform) δ 175.9, 161.3, 154.9, 150.2, 112.6, 105.1, 34.1, 30.8, 30.8, 22.3, 19.7, 14.2; MS (ESI): (M + H)$^+$ = 207.1. Anal. Calcd for $C_{11}H1_4N_2O_2$: C, 64.06; H, 6.84; N, 13.58. Found: C, 63.86; H 6.58; N, 13.53.

4-Hydroxy-6-methyl-3-[1-(2-phenylhydrazazono)methyl]-2H-pyran-2-one (2h). Phenylhydrazine (0.26 mL, 0.29 g, 2.70 mmol) was added to a hot (80°C) solution of 4-hydroxy-6-methyl-2-oxo-2H-pyran-3-carbaldehyde **1h** (0.34 g, 2.70 mmol) in ethanol (20 mL). After several minutes of heating, the solution turned yellow. It was allowed to cool to room temperature and then placed in a refrigerator overnight. Suction filtration gave yellow crystals (0.151 g), which were recrystallized from ethanol to give **2h** as yellow crystals: mp 212–213°C; yield 0.47 g (1.93 mmol, 71%); ^{1}H-NMR (dimethylsulfoxide-d_6) δ 13.2 (s, 1H), 10.2 (s, 1H), 7.95 (s, 1H), 7.12 (t, J = 8.1 Hz, 2H), 6.67 (m, 3H), 2.30 (s, 3H); ^{13}C-NMR (dimethylsulfoxide-d_6) δ 171.5, 163.6, 162.4, 144.4, 141.6, 129.5, 119, 9, 111.9, 102.0, 95.9, 19.6: (ESI): (M + Na)$^+$ = 267.1; Anal. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.93; H, 4.95; N, 11.47. Found: C, 64.05; H, 4.81, N, 11.47.

1-Methyl-6-phenylpyrano[2,3-*c*]pyrazole-4(1*H*)-one (4i). ***5-Bromo-1-methyl-6-phenyl-5,6-dihydropyrano[2,3-c]pyrazole-4(1H)-one (9i).*** A solution of bromine (0.10 mL, 0.31 g, 2.0 mmol) in glacial acetic acid (10 mL) was added dropwise during a period of 1 h to a stirred solution of (*E*)-1-(5-hydroxy-1-methyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-ene-1-one **8i** [11] (0.41 g, 1.80 mmol) in glacial acetic acid (30 mL) at 40°C. Stirring was continued for 2 additional hours after which the solution was cooled, treated with water (50 mL), neutralized with saturated aqueous sodium carbonate, and extracted with dichloromethane (20 mL). The organic phase was dried (anhydrous sodium sulfate) and evaporated to give crude **9i** (0.55 g), which was recrystallized from acetonitrile to give **9i** as a white solid: mp 177–178°C; yield 0.44 g (1.59 mmol), 88%; ^{1}H-NMR (deuteriochloroform) δ 7.77 (s, 1H), 7.42 (m, 2H), 7.37 (m, 3H), 5.49 (d, J = 11.7 Hz, 1H) 5.26 (d, J = 11.7 Hz, 1H) 3.69 (s, 3H); ^{13}C-NMR (deuteriochloroform) δ 188.1, 158.3, 137.9, 137.2, 129.4, 128.9, 128.2, 101.9, 49.0, 48.6, 33.3; MS (ESI): (M + Na)$^+$ = 331.2. Anal. Calcd for $C_{13}H_{11}N_2O_2Br$: C, 50.84; H, 3.61; N, 9.12. Found: C, 50.86; H, 3.62; N, 9.18.

1-Methyl-6-phenylpyrano[2,3-c]pyrazole-4-(1H)-one (4i). 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.06 mL, 0.06 g, 0.40 mmol) was added to a solution of **9i** (0.10 g, 0.326 mmol) in dioxane (10 mL) and the solution was stirred for 1 h at 90°C. After cooling, water (15 mL) was added and stirring was continued for 30 min. The solution was extracted with dichloromethane (30 mL) and the organic phase was washed with 2*N* hydrochloric acid (10 mL), dried (anhydrous sodium sulfate), and evaporated to give **4i** (0.091 g), which was recrystallized from ethyl acetate to give **4i** as white crystals: mp 147–148°C; yield 0.051 g (0.226 mmol, 69%); ^{1}H-NMR (deuteriochloroform) δ 7.95 (s, 1H), 7.77 (m, 2H), 7.52 (m, 3H), 6.64 (s, 1H), 3.99 (s, 3H); ^{13}C-NMR (deuteriochloroform) δ 175.3, 160.4, 154.4, 134.8, 131.9, 131.2, 129.6, 126.5, 109.9, 107.9, 34.8; MS (ESI); (M + Na)$^+$ = 249.2; Anal. Calcd for $C_{13}H_{10}N_2O_2$: C, 69.00; H, 4.46; N, 12.39. Found: C, 68.79; H, 4.77; N, 12.43.

1,6-Diphenylpyrano[2,3-*c*]pyrazole-4(1*H*)-one (4i). ***5-Bromo-1,6-diphenyl-5,6-dihydropyrano[2,3-c]pyrazole-4(1H)-one (9j).*** A solution of bromine (0.13 mL, 0.40 g, 2.54 mmol) in glacial acetic acid (15 mL) was added dropwise during 1 h to a stirred solution of (*E*)-1-(5-hydroxy-1-phenyl-1*H*)-pyrazole-4-yl)-3-phenylprop-2-ene-1-one **8j** [11] (0.37 g, 1.27 mmol) in glacial acetic (30 mL) at 60°C and the reaction mixture was stirred for 2 additional hours. After cooling to room temperature and addition of water (50 mL), filtration gave crude **9j** (0.37 g).

The crude material was dissolved in dichloromethane (20 mL), treated with decolorizing carbon, and evaporated to give crude **9j** (0.35 g), which was recrystallized from acetonitrile to give **9j** as white crystals: mp 195–196°C; yield 0.22 g (0.60 mmol, 47%); ^{1}H-NMR (deuteriochloroform) δ 7.96 (s, 1H), 7.81 (d, J = 7.8 Hz, 2H), 7.46 (m, 2 H), 7.37 (m, 3H), 7.35 (m, 1H), 5.53 (d, J = 11.4 Hz, 1H), 5.09 (d, J = 11.4 Hz, 1H); ^{13}C-NMR (deuteriochloroform) δ 189.1, 158.8, 138.5, 138.3, 137.3, 129.9, 129.7, 129.4, 128.7, 128.1, 121.8, 103.2, 49.3, 49.1; MS (ESI); $(M + Na)^+ = 393.3$. Anal. Calcd for $C_{18}H_{13}N_2O_2Br$: C, 58.26; H, 3.53; N, 7.59. Found: C, 58.34; H, 3.63; N, 7.30.

REFERENCES AND NOTES

[1] Pavlik, J. W.; Ervithayasuporn, V.; MacDonald, J. C.; Tantayanon, S. Arkivoc 2009, 8, 57.

[2] Gelin, S.; Chantegrel, B.; Nadi, A. I. J Org Chem 1983, 48, 4078.

[3] Cantos, A.; de March, P.; Moreno-Manas, M.; Pla, A.; Sanchez-Fernando, F.; Virgili, A. Bull Chem Soc Jpn 1987, 60, 4425.

[4] Reaction of methylhydrazine with dehydroacetic acid **1** led to a mixture of *N*-methylhydrazone **2e** and 5-hydroxy-1,3-dimethyl-4-(1,3-dimethylpyrazol-5yl)pyrazole which were separated on the basis of their very different solubilities in ethyl acetate.

[5] Marcus, E.; Stephen, J. F.; Chan, J. K. J Org Chem 1969, 34, 2527.

[6] Shimizu, T.; Hiranuma, S.; Watanabe, T.; Kirihara, M. Heterocycles 1994, 38, 243.

[7] Colatta, V.; Catarzi, D.; Varano, F.; Filacchioni, G.; Cecci, L.; Trincavelli, L.; Martini, C.; Lucacchini, A. Il Farmaco 1998, 53, 189.

[8] Tietze, L. F.; Brumby, T.; Pretor, M.; Remberg, G. J Org Chem 1988, 53, 810.

[9] Claisen, L.; Haase, E. Chem Ber 1889, 28, 35.

[10] Heinish, G.; Hellub, D.; Holzer, W. J Heterocyclic Chem 1991, 28, 1047.

[11] Holzer, W.; Krca, I. Heterocycles 2003, 60, 2323.