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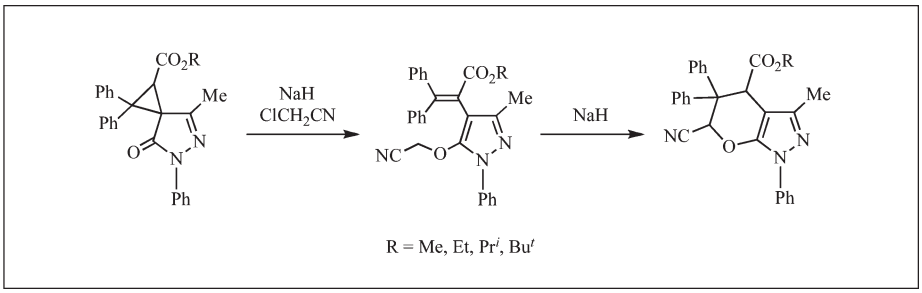

An approach to pyrano[2,3-*c*]pyrazoles starting from spirocyclopropanepyrazoles *via* a ring-opening/cyanomethylation and intramolecular cyclization is described. Reactions of spirocyclopropanepyrazoles **1a**-**d** with chloroacetonitrile in the presence of sodium hydride gave the corresponding cyanomethoxypyrazoles **4a**-**d**. Treatment of **4a**-**d** with sodium hydride at room temperature caused intramolecular Michael addition reaction to afford the corresponding pyrano[2,3-*c*]pyrazoles **5a**-**d**.

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INTRODUCTION

In many biologically active compounds, the pyrazole core is a privileged substructure. Compounds containing this ring system are known to display diverse pharmacological activities such as analgesic, antidepressant, antibacterial, plant growth regulatory, anti-inflammatory and antihyperglycemic activities [1–10]. In this context, the synthesis of pyrazole derivatives continues to attract attention and provides an interesting challenge [11–16]. In connection with our current research interests in this area, we have reported the synthesis of 1-acyl-1,2-dihydro-3*H*-pyrazol-3-ones through Lewis acid-mediated rearrangement of 3-acyloxypyrazoles [17]. More recently, we have also discussed the efficient method for the preparation of spirocyclopropanepyrazoles [18].

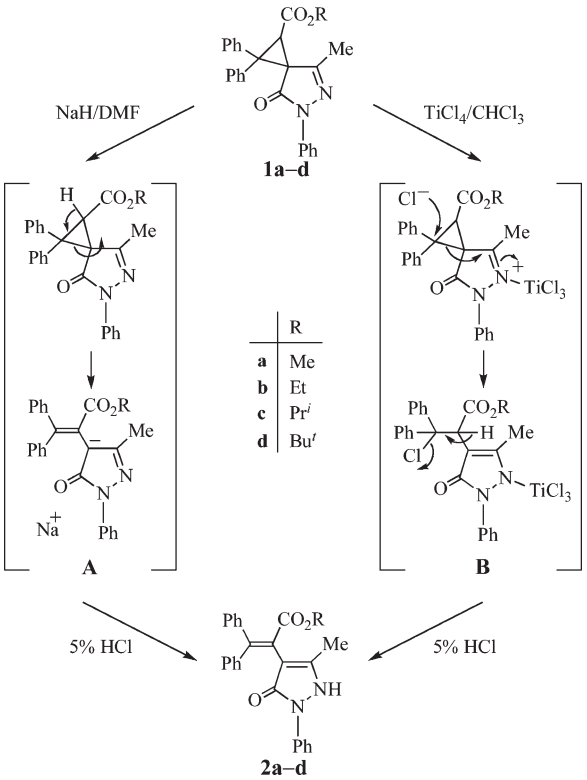
Some heterocyclic compounds containing condensed pyrazoles such as pyrano[2,3-*c*]pyrazoles possess a wide spectrum of pharmacological action, including analgesic, anti-inflammatory, vasodilating and antihypertensive activities [19–21]. Hence, the preparation and biological properties of new substituted pyrano[2,3-*c*]pyrazoles are of interest [22–36]. For these reasons, we focused our attention on the development of a new method for the preparation of pyrano[2,3-*c*]pyrazoles starting from spirocyclopropanepyrazoles and now report the results of our investigation, a ring-opening/cyanomethylation and intramolecular cyclization of them in the presence of a base such as sodium hydride.

RESULTS AND DISCUSSION

The starting materials, spiro compounds **1a**-**d**, were prepared by treatment of 2,4-dihydro-5-methyl-2-phenyl-4-(diphenylmethylene)-3*H*-pyrazol-3-one and α-chloro esters according to our previous investigation [18]. When a mixture of **1a**-**d** and sodium hydride in *N*,*N*-dimethylformamide was stirred at room temperature for 1 h, pyrazol-3-ones **2a**-**d** were obtained in excellent yields (Scheme 1 and Table 1). The IR spectra of **2a**-**d** display bands near 3100 cm^{-1} due to the secondary amino group and in the range of 1650–1690 cm^{-1} due to the two carbonyl groups. The ^1H NMR spectra of **2a**-**d** in deuteriochloroform exhibit a D_2O exchangeable signal near δ 10 attributable to the secondary amino proton. The ^{13}C NMR spectra of **2a**-**d** show two signals near δ 120 and 150 due to the olefin carbons, whereas those of **1a**-**d** show three signals near δ 50 due to the spirocyclopropane carbons. Elemental analyses and spectral data of **2a**-**d** are consistent with the proposed structures (see experimental section).

Fortunately, we found the reaction condition under which ring-opening products **2a**-**c** could be isolated in the presence of a Lewis acid. Titanium(IV) chloride-catalyzed ring-opening reactions have already been reported in the literature [37–39]. Subsequently, thermal treatment of **1a**-**c** with titanium(IV) chloride in chloroform caused ring opening of cyclopropane to give the corresponding pyrazol-3-ones **2a**-**c** in good yields. The

Scheme 1



melting points and IR spectra of these compounds **2a-c** coincided with those of samples prepared from **1a-c** and sodium hydride as described above. Interestingly, in the case of the reaction of **1d** as the substrate, the expected product **2d** could not be produced but instead the carboxylic acid **3** was obtained in 93% yield (Scheme 2 and see ''Experimental'' section). To confirm the structure of **3**, we carried out the hydrolysis of compound **2b**. Thus, thermal treatment of **2b** with potassium hydroxide in aqueous ethanol afforded the carboxylic acid **3** (73%), which was confirmed by direct comparison with an authentic sample prepared from **1d** and titanium(IV) chloride. Although the detailed mechanism for

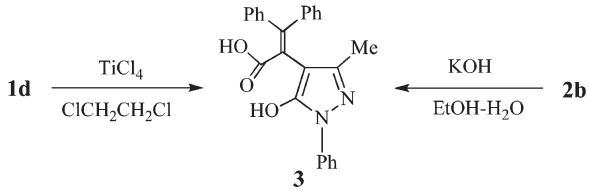
Table 1

Synthesis of compounds **2a-d** according to Scheme 1.

Entry	Substrate	Product	Yield (%)
1	**1a**	**2a**	99[a] 99[b]
2	**1b**	**2b**	99[a] 99[b]
3	**1c**	**2c**	99[a] 99[b]
4	**1d**	**2d**	86[a] 0[b]

[a] NaH/DMF, r.t., 1 h.
[b] $TiCl_4/CHCl_3$, reflux, 1h.

Scheme 2

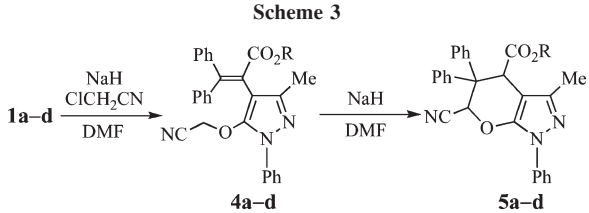


the formation of **3** is not clear at present, this is probably because the metal complex containing chelate ring coordinated by both carboxyl and hydroxyl groups would be easily formed as an intermediate in this reaction.

The formation of the pyrazole-3-ones **2** could be explained by possible mechanism presented in Scheme 1. Thus, the reaction of spiro compounds **1** with sodium hydride probably causes the ring opening of cyclopropane *via* deprotonation to give the sodium salts **A** of pyrazole, which could then undergo protonation of **A** to afford the pyrazoles **2**. On the other hand, treatment of **1** with titanium(IV) chloride probably causes ring opening reaction *via* an attack of chloride ion to cyclopropane ring, giving the intermediate chlorine-containing compound **B**. The pyrazol-3-ones **2** would then be produced easily from **B** through an elimination of hydrogen chloride.

Based on these results, we hypothesized if a cyanomethylation of sodium salts **A** of pyrazole could undergo readily under an appropriate reaction condition, the synthesis of cyanomethylated pyrazoles would be possible. Thus, we carried out the cyanomethylation of spiro compounds **1** with chloroacetonitrile by use of a sodium hydride/*N*,*N*-dimethylformamide system. Contrary to our expectation, when a mixture of **1a-d** and sodium hydride in *N*,*N*-dimethylformamide was stirred at room temperature for 1 h and then the reaction mixture was treated with chloroacetonitrile at 60°C for 1 h, the *O*-cyanomethylated pyrazoles **4a-d** were obtained in moderate to good yields (Scheme 3 and entries 1–4 in Table 2). By comparison of the NMR, mass spectra and elemental analyses of **4a-d** it seems that the structural assignments given to these compounds are correct. In this reaction, *C*- and/or *N*-cyanomethylated pyrazoles were not detected.

Scheme 3



a: R = Me, **b**: R = Et, **c**: R = Pr^i, **d**: R = Bu^t

Table 2

Synthesis of compounds **4a-d** and **5a-d** according to Scheme 3.

Entry	Substrate	Product	Yield (%)
1	**1a**	**4a**	67
2	**1b**	**4b**	58
3	**1c**	**4c**	76
4	**1d**	**4d**	85
5	**4a**	**5a**	35
6	**4b**	**5b**	61
7	**4c**	**5c**	56
8	**4d**	**5d**	58

To confirm the *O*-cyanomethylated pyrazoles **4**, we next examined the conversion of **4** into the fused pyrazole derivatives in the presence of a base. After some optimization, the best result was obtained when **4a-d** were treated with sodium hydride in *N,N*-dimethylformamide at room temperature, the expected pyrano[2,3-*c*]pyrazoles **5a-d** was isolated in moderate yields (Scheme 3 and entries 5–8 in Table 2). Although, we tested the reactions under the other conditions such as a potassium *tert*-butoxide/*N,N*-dimethylformamide and potassium *tert*-butoxide/*tert*-butyl alcohol system, those attempts were unacceptable with respect to yield. It makes us believe that the intramolecular Michael addition reaction of **4** can only be promoted by using a sodium hydride/*N,N*-dimethylformamide system.

The IR spectra of **5a-d** display bands near 2250 cm^{-1} due to a nonconjugated cyano group and near 1730 cm^{-1} due to a carbonyl group. The ^1H NMR spectra of **5a-d** in deuteriochloroform exhibit a signal near δ 5.0 attributable to the 4-methine proton and a signal near δ 6.0 attributable to the 6-methine proton. The ^{13}C NMR spectra of **5a-d** show a signal near δ 50 due to the 4-methine carbon, a signal near δ 60 due to the 5-quaternary carbon and a signal near δ 70 due to the 6-methine carbon, whereas those of **4a-d** show a signal near δ 40 due to the methylene carbon and two signals near δ 120 and 150 due to the olefin carbons. Elemental analyses and spectral data of **4** and **5** are consistent with the assigned structures (see experimental section). In addition, for products **5a-d**, a clear nuclear Overhauser effect was not observed between 4-methine proton and 6-methine proton of trans configuration. These results indicate that *trans*-pyrano[2,3-*c*]pyrazoles are more stable than *cis*-pyrano[2,3-*c*]pyrazoles.

Finally, on the basis of these results, we have tried to directly construct pyrano[2,3-*c*]pyrazoles **5** starting from sipro compounds **1** in a one-pot process. To optimize the yield of **5**, we carried out several further experiments on **1**, testing different reaction conditions, e.g. time, solvent and substrate/base molar ratio. The results are summarized in Table 3. After a mixture of 1.0 equivalent of **1a-d** and 1.0 equivalent of sodium hydride in *N,N*-dimethylformamide was stirred at room temperature for 1 h, the reaction mixture was treated with 1.0 equivalent of chloroacetonitrile at 60°C for 1 h and then with 0.5 equivalent of sodium hydride at room temperature, the corresponding pyrano[2,3-*c*]pyrazoles **5a-d** were obtained in moderate yields (Table 3).

In conclusion, we have developed a novel method for the construction of pyrano[2,3-*c*]pyrazole derivatives **5a-d**, proceeding by a ring-opening/cyanomethylation and intramolecular cyclization when spirocyclopropanepyrazoles **1a-d** are treated with chloroacetonitrile in the presence of sodium hydride. This methodology offers significant advantages with regard to the supply of pyrano[2,3-*c*]pyrazoles, which may exhibit biological activities such as analgesic, anti-inflammatory, vasodilating and antihypertensive activities. Functionalized pyrano[2,3-*c*]pyrazoles are important synthons in organic synthesis and for the preparation of biologically active compounds with interest in medicinal chemistry. Further studies on the synthesis of new substituted pyrano[2,3-*c*]pyrazoles are under way.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. The ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-A500 spectrometer at 500 and 125 MHz, respectively. The ^1H and ^{13}C chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane as internal standard. The positive FAB mass spectra were obtained on a JEOL JMS-700T spectrometer. The elemental analyses were performed on a YANACO MT-6 CHN analyzer.

General Procedure for the Preparation of Ring-Opening Products 2a-d from 1a-d. Procedure A. To an ice-cooled and stirred solution of **1a-d** [18] (1 mmole) in *N,N*-dimethylformamide (5 mL) was added 60% sodium hydride (0.04 g, 1 mmole). After the mixture was stirred at room temperature for 1 h, the solvent was removed *in vacuo*. A 5% hydrochloric acid solution (20 mL) was added to the residue with stirring and ice-cooling. The resulting mixture was extracted with chloroform (60 mL). The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with chloroform-acetone (4:1) as the eluent to afford **2a** (0.404 g, 99%),

Table 3

Synthesis of pyrano[2,3-*c*]pyrazoles **5a-d** starting from **1a-d**.

Entry	Substrate	Product	Yield (%)
1	**1a**	**5a**	28
2	**1b**	**5b**	47
3	**1c**	**5c**	44
4	**1d**	**5d**	59

2b (0.420 g, 99%), **2c** (0.436 g, 99%) and **2d** (0.388 g, 86%), respectively.

Procedure B. To an ice-cooled and stirred solution of **1a**-**c** (1 mmole) in chloroform (5 mL) was added titanium(IV) chloride (0.38 g, 2 mmoles). After the mixture was refluxed for 1 h, a 5% hydrochloric acid solution (20 mL) was added to the reaction mixture with stirring and ice-cooling. After work-up as described above, **2a** (0.406 g, 99%), **2b** (0.419 g, 99%) and **2c** (0.435 g, 99%) were obtained.

Methyl 2-(5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diphenylacrylate (2a). This compound was obtained as pale yellow needles, mp 141–143°C (chloroform-petroleum ether); IR (potassium bromide): ν 3060 (NH), 1714, 1685, 1656 cm^{-1} (C=O); ^{1}H NMR (deuteriochloroform): δ 1.32 (s, 3H, 5-Me), 3.37 (s, 3H, CO_2Me), 6.72 (d, J = 7.3 Hz, 2H, Ph-H), 6.99 (d, J = 3.7 Hz, 2H, Ph—H), 7.15–7.44 (m, 9H, Ph—H), 7.79 (d, J = 7.9 Hz, 2H, Ph—H), 10.33 ppm (s, 1H, NH); ^{13}C NMR (deuteriochloroform): δ 12.0 (5-Me), 52.3 (CO_2*Me*), 107.9 (C-4), 118.0, 121.6 (Ph—C), 122.2 (Ph_2C=*C*—CO_2Me), 124.6, 125.0, 127.9, 128.0, 128.1, 128.5, 128.7, 128.9, 129.1, 130.4, 137.1, 141.2, 142.4 (Ph—C), 149.1 (C-5), 150.2 (Ph_2*C*=C—CO_2Me), 162.7, 172.9 ppm (C=O); ms: m/z 411 $[M+H]^+$. *Anal*. Calcd. for $C_{26}H_{22}N_2O_3 \cdot 0.2H_2O$: C, 75.42; H, 5.45; N, 6.77. Found: C, 75.59; H, 5.45; N, 6.75.

Ethyl 2-(5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diphenylacrylate (2b). This compound was obtained as pale yellow needles, mp 149–151°C (chloroform-petroleum ether); IR (potassium bromide): ν 3110 (NH), 1711, 1680, 1656 cm^{-1} (C=O); ^{1}H NMR (deuteriochloroform): δ 0.69, 0.91 (t, J = 7.1 Hz, 3H, CO_2CH_2*Me*), 1.31, 1.62 (s, 3H, 5-Me), 3.90, 3.96 (q, J = 7.1 Hz, 2H, CO_2CH_2Me), 6.68 (d, J = 7.3 Hz, 2H, Ph—H), 6.97–7.45 (m, 11H, Ph—H), 7.70–7.83 (m, 2H, Ph—H), 8.43, 10.47 ppm (s, 1H, NH); ^{13}C NMR (deuteriochloroform): δ 12.0 (5-Me), 13.1, 13.3 (CO_2CH_2*Me*), 61.7 (CO_2*C*H_2Me), 108.0 (C-4), 117.9, 118.9, 121.5 (Ph—C), 122.4 (Ph_2C=*C*—CO_2CH_2Me), 124.4, 127.8, 128.0, 128.1, 128.5, 128.9, 129.0, 129.3, 130.4, 137.2, 141.3, 142.7 (Ph—C), 149.3 (C-5), 150.2 (Ph_2*C*=C—CO_2CH_2Me), 162.8, 172.5 ppm (C=O); ms: m/z 425 $[M+H]^+$. *Anal*. Calcd. for $C_{27}H_{24}N_2O_3$: C, 76.39; H, 5.70; N, 6.60. Found: C, 76.46; H, 5.78; N, 6.42.

Isopropyl 2-(5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diphenylacrylate (2c). This compound was obtained as pale yellow needles, mp 196–198°C (chloroform-petroleum ether); IR (potassium bromide): ν 3126 (NH), 1706, 1671, 1644 cm^{-1} (C=O); ^{1}H NMR (deuteriochloroform): δ 0.85, 0.91 (d, J = 6.4 Hz, 6H, CO_2CH*Me*$_2$), 1.32, 1.74 (s, 3H, 5-Me), 4.78, 4.84 (sep, J = 6.4 Hz, 1H, CO_2C*H*Me_2), 6.69 (d, J = 7.3 Hz, 1.2H, Ph—H), 6.97–6.99 (m, 1.2H, Ph—H), 7.13–7.46 (m, 10.6H, Ph—H), 7.73 (d, J = 7.6 Hz, 0.8H, Ph—H), 7.82 (d, J = 7.6 Hz, 1.2H, Ph—H), 8.74, 10.35 ppm (s, 1H, NH); ^{13}C NMR (deuteriochloroform): δ 12.7, 13.4 (5-Me), 20.9, 21.01, 21.09, 21.11 (CO_2CH*Me*$_2$), 69.5, 70.1 (CO_2*C*HMe_2), 108.3, 118.0 (C-4), 118.8, 121.5, 122.9 (Ph—C), 123.2, 124.4 (Ph_2C=*C*—CO_2CHMe_2), 124.8, 125.8, 127.6, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.6, 128.8, 128.9, 129.0, 129.4, 130.4, 137.3, 138.7, 141.2, 141.4, 142.7 (Ph—C), 146.3, 147.0 (C-5), 149.4, 149.7 (Ph_2*C*=C—CO_2CHMe_2), 162.8, 171.5, 171.8 ppm (C=O); ms: m/z 439 $[M+H]^+$. *Anal*. Calcd. for $C_{28}H_{26}N_2O_3$: C, 76.69; H, 5.98; N, 6.39. Found: C, 76.68; H, 6.03; N, 6.33.

tert-*Butyl 2-(5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diphenylacrylate (2d).* This compound was obtained as colorless needles, mp 175–177°C (chloroform-petroleum ether); IR (potassium bromide): ν 3106 (NH), 1706, 1683, 1656 cm^{-1} (C=O); ^{1}H NMR (deuteriochloroform): δ 1.14, 1.16 (s, 9H, CO_2CMe_3), 1.29, 1.69 (s, 3H, 5-Me), 6.65 (d, J = 7.3 Hz, 1.35H, Ph—H), 6.94–6.96 (m, 1.35H, Ph—H), 7.11–7.46 (m, 10.3H, Ph—H), 7.77 (d, J = 7.9 Hz, 0.65H, Ph—H), 7.85 (d, J = 7.9 Hz, 1.35H, Ph—H), 9.26, 10.74 ppm (s, 1H, NH); ^{13}C NMR (deuteriochloroform): δ 11.9, 13.4 (5-Me), 27.2, 27.4, 27.5 (CO_2C*Me*$_3$), 82.3, 83.8 (CO_2*C*Me_3), 97.6, 108.3 (C-4), 117.8, 118.8, 121.4 (Ph—C), 124.0 (Ph_2C=*C*—CO_2CMe_3), 124.1, 124.7, 125.7, 127.5, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.7, 128.8, 128.9, 129.3, 129.6, 129.7, 130.6, 137.5, 138.8, 140.4, 141.2, 141.6, 142.9, 145.4 (Ph—C), 146.0, 149.4 (C-5), 149.5, 150.4 (Ph_2*C*=C—CO_2CMe_3), 162.9, 171.3, 171.5, 176.3 ppm (C=O); ms: m/z 453 $[M+H]^+$. *Anal*. Calcd. for $C_{29}H_{28}N_2O_3 \cdot 0.5H_2O$: C, 75.47; H, 6.33; N, 6.07. Found: C, 75.51; H, 6.27; N, 6.06.

The Preparation of Carboxylic Acid Derivative 3 from 1d and/or 2b. Procedure A. To an ice-cooled and stirred solution of **1d** [18] (0.45 g, 1 mmole) in 1,2-dichloroethane (5 mL) was added titanium(IV) chloride (0.38 g, 2 mmoles). After the mixture was refluxed for 4 h, a 5% hydrochloric acid solution (20 mL) was added to the reaction mixture with stirring and ice-cooling. The precipitate was collected by filtration, washed with water, dried and recrystallized from chloroform-methanol to yield **2-(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-3,3-diphenylacrylic acid** (**3**) (0.37 g, 93%) as colorless needles, mp 277–279°C; IR (potassium bromide): ν 3448 (OH), 1676 cm^{-1} (C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 1.67 (s, 3H, 3-Me), 7.05–7.07 (m, 2H, Ph—H), 7.17–7.24 (m, 6H, Ph—H), 7.39–7.42 (m, 5H, Ph—H), 7.63–7.65 (m, 2H, Ph—H), 11.04, 12.21 ppm (s, 2H, 2×OH); ^{13}C NMR (dimethyl sulfoxide-d_6): δ 12.2 (3-Me), 118.3 (C-4), 124.3 (Ph_2C=*C*—CO_2H), 124.6, 127.4, 127.6, 127.7, 127.8, 128.8, 129.0, 129.6, 137.4, 141.8 (Ph—C), 142.2 (C-3), 147.1 (C-5), 147.5 (Ph_2*C*=C—CO_2H), 169.9 ppm (C=O); ms: m/z 397 $[M+H]^+$. *Anal*. Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.74; H, 5.09; N, 7.07. Found: C, 75.62; H, 5.13; N, 6.91.

Procedure B. After a mixture of **2b** (0.42 g, 1 mmole) and potassium hydroxide (0.56 g, 10 mmoles) in ethanol (5 mL) and water (2 mL) was refluxed for 8 h, the solvent was removed *in vacuo*. A 10% hydrochloric acid solution (20 mL) was added to the residue with stirring and ice-cooling. The precipitate was collected by filtration, washed with water, dried and recrystallized from chloroform-methanol to yield **3** (0.289 g, 73%).

General Procedure for the Preparation of Cyanomethoxypyrazoles 4a-d from 1a-d and chloroacetonitrile. To an ice-cooled and stirred solution of **1a**-**d** (5 mmoles) in *N*,*N*-dimethylformamide (15 mL) was added 60% sodium hydride (0.20 g, 5 mmoles). After the mixture was stirred at room temperature for 1 h, chloroacetonitrile (0.76 g, 10 mmoles) was added to the reaction mixture with stirring and then the resulting mixture was stirred at 60°C for 1 h. After the solvent was removed *in vacuo*, a 5% hydrochloric acid solution (20 mL) was added to the residue with stirring and ice-cooling. The resulting mixture was extracted with chloroform (60 mL). The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with chloroform as the eluent to afford **4a**-**d**.

Methyl 2-[5-(cyanomethoxy)-3-methyl-1-phenyl-1H-pyrazol-4-yl]-3,3-diphenylacrylate (4a). This compound was obtained as colorless prisms (1.51 g, 67%), mp 120–122°C (acetone-petroleum ether); IR (potassium bromide): ν 2251 (CN), 1712 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 2.05 (s, 3H, 3-Me), 3.55 (s, 3H, CO_2Me), 4.62 (s, 2H, OCH_2CN), 7.08–7.10 (m, 2H, Ph—H), 7.20–7.30 (m, 6H, Ph—H), 7.34–7.43 ppm (m, 7H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 13.3 (3-Me), 52.1 (CO_2Me), 57.9 (OCH_2CN), 105.1 (C-4), 114.0 (CN), 121.5 ($Ph_2C{=}C{-}CO_2Me$), 122.7, 127.3, 128.1, 128.4, 128.6, 129.1, 129.2, 137.6, 140.5, 141.5 (Ph—C), 148.3 (C-3), 148.4 (C-5), 150.8 ($Ph_2C{=}C{-}CO_2Me$), 170.2 ppm (C=O); ms: m/z 450 $[M+H]^+$. *Anal*. Calcd. for $C_{28}H_{23}N_3O_3$: C, 74.82; H, 5.16; N, 9.35. Found: C, 74.98; H, 5.22; N, 9.29.

Ethyl 2-[5-(cyanomethoxy)-3-methyl-1-phenyl-1H-pyrazol-4-yl]-3,3-diphenylacrylate (4b). This compound was obtained as colorless prisms (1.35 g, 58%), mp 98–100°C (acetone-petroleum ether); IR (potassium bromide): ν 2244 (CN), 1713 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 0.95 (t, J = 7.1 Hz, 3H, CO_2CH_2Me), 2.06 (s, 3H, 3-Me), 4.02 (q, J = 7.1 Hz, 2H, CO_2CH_2Me), 4.64 (s, 2H, OCH_2CN), 7.09–7.10 (m, 2H, Ph—H), 7.20–7.44 ppm (m, 13H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 13.4 (3-Me), 13.6 (CO_2CH_2Me), 57.9 (OCH_2CN), 61.2 (CO_2CH_2Me), 105.1 (C-4), 114.0 (CN), 121.9 ($Ph_2C{=}C{-}CO_2CH_2Me$), 122.7, 127.3, 128.1, 128.2, 128.4, 128.5, 129.2, 129.9, 137.6, 140.5, 141.7 (Ph—C), 148.36 (C-3), 148.43 (C-5), 150.5 ($Ph_2C{=}C{-}CO_2CH_2Me$), 169.8 ppm (C=O); ms: m/z 464 $[M+H]^+$. *Anal*. Calcd. for $C_{29}H_{25}N_3O_3$: C, 75.14; H, 5.44; N, 9.07. Found: C, 75.14; H, 5.52; N, 9.04.

Isopropyl 2-[5-(cyanomethoxy)-3-methyl-1-phenyl-1H-pyrazol-4-yl]-3,3-diphenylacrylate (4c). This compound was obtained as colorless needles (1.54 g, 65%), mp 143–145°C (acetone-petroleum ether); IR (potassium bromide): ν 2244 (CN), 1716 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 0.97 (d, J = 6.4 Hz, 6H, CO_2CHMe_2), 2.09 (s, 3H, 3-Me), 4.68 (s, 2H, OCH_2CN), 4.88 (sep, J = 6.4 Hz, 1H, CO_2CHMe_2), 7.19–7.23 (m, 2H, Ph—H), 7.25–7.30 (m, 6H, Ph—H), 7.33–7.35 (m, 3H, Ph—H), 7.37–7.43 ppm (m, 4H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 13.4 (3-Me), 21.2 (CO_2CHMe_2), 58.0 (OCH_2CN), 69.0 (CO_2CHMe_2), 105.0 (C-4), 114.0 (CN), 122.2 ($Ph_2C{=}C{-}CO_2CHMe_2$), 122.7, 127.3, 128.1, 128.3, 128.4, 129.1, 129.3, 129.9, 137.5, 140.5, 141.6 (Ph—C), 148.3 (C-3), 148.4 (C-5), 149.9 ($Ph_2C{=}C{-}CO_2CHMe_2$), 169.3 ppm (C=O); ms: m/z 478 $[M+H]^+$. *Anal*. Calcd. for $C_{30}H_{27}N_3O_3$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.43; H, 5.77; N, 8.75.

tert-*Butyl 2-[5-(cyanomethoxy)-3-methyl-1-phenyl-1H-pyrazol-4-yl]-3,3-diphenylacrylate (4d).* This compound was obtained as colorless needles (2.09 g, 85%), mp 85–87°C (diethyl ether-petroleum ether); IR (potassium bromide): ν 2251 (CN), 1711 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 1.24 (s, 9H, CO_2CMe_3), 2.13 (s, 3H, 3-Me), 4.70 (s, 2H, OCH_2CN), 7.06–7.08 (m, 2H, Ph—H), 7.19–7.21 (m, 3H, Ph—H), 7.25–7.29 (m, 3H, Ph—H), 7.34–7.42 ppm (m, 7H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 13.5 (3-Me), 27.6 (CO_2CMe_3), 58.0 (OCH_2CN), 81.9 (CO_2CMe_3), 105.1 (C-4), 114.1 (CN), 122.8 (Ph—C), 123.4 ($Ph_2C{=}C{-}CO_2CMe_3$), 127.2, 128.0, 128.2, 129.1, 129.4, 129.8, 137.7, 140.6, 141.7 (Ph—C), 148.4 (C-3), 148.5 (C-5), 149.5 ($Ph_2C{=}C{-}CO_2CMe_3$), 168.6 ppm (C=O); ms: m/z 492 $[M+H]^+$. *Anal*. Calcd. for $C_{31}H_{29}N_3O_3{\cdot}0.3CH_3CH_2OCH_2CH_3$: C, 75.27; H, 6.28; N, 8.18. Found: C, 75.26; H, 6.47; N, 8.01.

General Procedure for the Preparation of Pyrano[2,3-*c*]pyrazoles 5a-d from 4a-d. To an ice-cooled and stirred solution of **4a-d** (1 mmole) in *N*,*N*-dimethylformamide (5 mL) was added 60% sodium hydride (0.02 g, 0.5 mmole). After the mixture was stirred at room temperature for 48 h, a 5% hydrochloric acid solution (20 mL) was added to the reaction mixture with stirring and ice-cooling. The resulting mixture was extracted with chloroform (60 mL). The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with chloroform as the eluent to give **5a-d**.

Methyl 6-cyano-3-methyl-1,5,5-triphenyl-1,4,5,6-tetrahydropyrano[2,3-c]pyrazole-4-carboxylate (5a). This compound was obtained as colorless prisms (0.155 g, 35%), mp 218–220°C (chloroform-petroleum ether); IR (potassium bromide): ν 2255 (CN), 1740 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 2.28 (s, 3H, 3-Me), 3.26 (s, 3H, CO_2Me), 4.40 (s, 1H, 4-H), 6.54 (s, 1H, 6-H), 7.15–7.38 (m, 13H, Ph—H), 7.59–7.61 ppm (m, 2H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 12.6 (3-Me), 47.3 (C-4), 50.5 (C-5), 52.2 (CO_2Me), 71.2 (C-6), 96.3 (C-3a), 115.4 (CN), 120.4, 126.3, 128.0, 128.3, 129.1, 137.8, 139.4, 140.5, (Ph—C), 145.2 (C-3), 148.1 (C-7a), 171.8 ppm (C=O); ms: m/z 450 $[M+H]^+$. *Anal*. Calcd. for $C_{28}H_{23}N_3O_3$: C, 74.82; H, 5.16; N, 9.35. Found: C, 74.96; H, 5.26; N, 9.34.

Ethyl 6-cyano-3-methyl-1,5,5-triphenyl-1,4,5,6-tetrahydropyrano[2,3-c]pyrazole-4-carboxylate (5b). This compound was obtained as pale yellow prisms (0.282 g, 61%), mp 187–189°C (chloroform-petroleum ether); IR (potassium bromide): ν 2255 (CN), 1723 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 0.87 (t, J = 7.3 Hz, 3H, CO_2CH_2Me), 2.29 (s, 3H, 3-Me), 3.62–3.69 (m, 1H, CO_2CH_2Me), 3.75–3.82 (m, 1H, CO_2CH_2Me), 4.39 (s, 1H, 4-H), 6.59 (s, 1H, 6-H), 7.17–7.38 (m, 13H, Ph—H), 7.59–7.62 ppm (m, 2H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 12.7 (3-Me), 13.7 (CO_2CH_2Me), 47.2 (C-4), 50.5 (C-5), 61.3 (CO_2CH_2Me), 65.8 (C-6), 96.4 (C-3a), 115.5 (CN), 120.3, 126.2, 127.9, 128.2, 128.4, 129.1, 137.8, 139.6, 140.6 (Ph—C), 145.1 (C-3), 148.1 (C-7a), 171.5 ppm (C=O); ms: m/z 464 $[M+H]^+$. *Anal*. Calcd. for $C_{29}H_{25}N_3O_3{\cdot}0.5CH_3CH_2OCH_2CH_3$: C, 74.38; H, 6.04; N, 8.39. Found: C, 74.53; H, 6.03; N, 8.39.

Isopropyl 6-cyano-3-methyl-1,5,5-triphenyl-1,4,5,6-tetrahydropyrano[2,3-c]pyrazole-4-carboxylate (5c). This compound was obtained as colorless prisms (0.267 g, 56%), mp 188–189°C (chloroform-petroleum ether); IR (potassium bromide): ν 2254 (CN), 1718 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 0.62, 1.11 (d, J = 6.4 Hz, 6H, CO_2CHMe_2), 2.30 (s, 3H, 3-Me), 4.36 (s, 1H, 4-H), 4.58 (sep, J = 6.4 Hz, 1H, CO_2CHMe_2), 6.65 (s, 1H, 6-H), 7.17–7.38 (m, 13H, Ph—H), 7.59–7.61 ppm (m, 2H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 12.7 (3-Me), 21.0, 21.5 (CO_2CHMe_2), 47.1 (C-4), 50.3 (C-5), 69.0 (CO_2CHMe_2), 71.2 (C-6), 96.6 (C-3a), 115.5 (CN), 120.4, 126.2, 127.9, 128.2, 128.5, 129.1, 137.8, 139.7, 140.7 (Ph—C), 145.0 (C-3), 148.1 (C-7a), 171.1 ppm (C=O); ms: m/z 478 $[M+H]^+$. *Anal*. Calcd. for $C_{30}H_{27}N_3O_3$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.50; H, 5.84; N, 8.72.

tert-*Butyl 6-cyano-3-methyl-1,5,5-triphenyl-1,4,5,6-tetrahydropyrano[2,3-c]pyrazole-4-carboxylate (5d).* This compound was obtained as pale yellow prisms (0.287 g, 58%), mp 225–227°C (chloroform-petroleum ether); IR (potassium bromide): ν 2251 (CN), 1723 cm^{-1} (C=O); ^1H NMR (deuteriochloroform): δ 1.07 (s, 9H, CO_2CMe_3), 2.33 (s, 3H, 3-Me), 4.32 (s,

1H, 4-H), 6.61 (s, 1H, 6-H), 7.20–7.38 (m, 13H, Ph—H), 7.60–7.62 ppm (m, 2H, Ph—H); ^{13}C NMR (deuteriochloroform): δ 12.8 (3-Me), 27.5 (CO_2CMe_3), 47.6 (C-4), 50.4 (C-5), 71.2 (C-6), 82.1 (CO_2CMe_3), 96.9 (C-3a), 115.6 (CN), 120.3, 126.2, 127.8, 128.1, 128.2, 128.7, 129.1, 137.9, 140.0, 140.9 (Ph—C), 145.1 (C-3), 148.1 (C-7a), 170.6 ppm (C=O); ms: m/z 492 $[M+H]^+$. *Anal*. Calcd. for $C_{31}H_{29}N_3O_3$: C, 75.74; H, 5.95; N, 8.55. Found: C, 75.74; H, 6.03; N, 8.51.

General Procedure for the Preparation of Pyrano[2,3-*c*]pyrazoles 5a-d from 1a-d and Chloroacetonitrile. To an ice-cooled and stirred solution of **1a-d** (1 mmole) in *N,N*-dimethylformamide (5 mL) was added 60% sodium hydride (0.04 g, 1 mmole). After the mixture was stirred at room temperature for 1 h, chloroacetonitrile (0.075 g, 1 mmole) was added to the reaction mixture with stirring and then the resulting mixture was stirred at 60°C for 1 h. To an ice-cooled and stirred solution of the reaction mixture was added 60% sodium hydride (0.04 g, 1 mmole). After the mixture was stirred at room temperature for 48 h, a 5% hydrochloric acid solution (20 mL) was added to the reaction mixture with stirring and ice-cooling. The resulting mixture was extracted with chloroform (60 mL). The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with chloroform as the eluent to form **5a** (0.127 g, 28%), **5b** (0.219 g, 47%), **5c** (0.208 g, 44%), and **5d** (0.292 g, 59%), respectively.

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