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Synthesis and Relative Stability of 3,5-Diacyl-4,5-dihydro-1*H*-pyrazoles Prepared by Dipolar Cycloaddition of Enones and α-Diazoketones

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An unusual reaction process that produced unexpected heterocyclic systems by a fragmentation−recombination mechanism is described. Thus treatment of the triketone, 3-acetyl-2,6-heptanedione, **1**, with methanesulfonyl azide gave, in addition to the expected α-diazo ketone **3a**, the dihydropyrazole **3c** and its oxidation product, the pyrazole **3d**. We propose that the initially formed α-diazo ketone **3a** fragments into the simple α-diazomethyl ketone and methyl vinyl ketone which then undergo an intermolecular [2,3]-dipolar cycloaddition. Analogous treatment of the trifluoromethyl trione **2** again afforded a pyrazole **4c**. Further experiments were carried out to lend evidence to our mechanistic hypothesis. Thus α-diazoacetophenone **5** and MVK underwent a [2,3]-dipolar cycloaddition under mild conditions to give the two regioisomeric dihydropyrazoles **6a** and **6b**. Interestingly these were formed in a 2:1 ratio, which suggested that **6a** was more stable than **6b**. The structures of **6a** and **6b** were optimized by using the B3LYP density functional method and the 6-31G* basis set and isomer **6a** was predicted to be 1.5 kcal/mol more stable than isomer **6b**. This energy difference could be rationalized by the greater capacity of the acetyl group than the benzoyl group to conjugate with the hydrazone. This difference in conjugation is reflected by key bond length differences. Thus we have discovered a novel fragmentation−cycloaddition process. We have also presented evidence for the mechanism of the formation of the dihydropyrazoles and carried out calculations to support these findings.

α-Diazocarbonyl compounds are an important class of intermediates for the preparation of structurally complex and diverse natural products.[1] In general, these are often used as synthetic precursors for certain transition metal-catalyzed reactions, such as ylide formation, cyclopropanation, and C−H insertion.[2] Recently, we investigated the construction of oxabicyclic ring structures using the rhodium-catalyzed cycloaddition of carbonyl ylide species prepared from diazo diketones. 3-Diazo-2,6-alkanediones are usually prepared by the diazo transfer reaction of the corresponding tricarbonyl compound, which is treated with a sulfonyl azide in the presence of base.[3] The mechanism involves formation of the triazoline intermediate, cleavage of the acyl group, and elimination of the sulfonamide (Scheme 1).[4] To facilitate the C−C bond cleavage, activating acyl groups, such as formyl, acetyl, benzoyl, and trifluoroacetyl, are generally employed as the leaving carbonyl unit. In this paper, we describe our unusual observations during the preparation of the 3-diazo-2,6-alkanediones using a diazo transfer reaction.

For the preparation of the necessary 3-diazo-2,6-alkanediones, an efficient procedure to synthesize the corresponding tricarbonyl compounds was needed (Scheme 2). It was reported that the transition metal-catalyzed Michael reaction of 1,3-dicarbonyl compounds with α,β-unsaturated ketones was particularly effective for the synthesis of tricarbonyl compounds since it used mild, neutral reaction conditions.[5] The Michael reaction of 2,4-pentanedione with methyl vinyl ketone in the presence of $FeCl_3 \cdot 6H_2O$ was carried out at room temperature to afford the 3-acetyl-2,6-heptanedione **1** in 74% yield. However, the tricarbonyl compound **2**, which would be converted to 1-phenyl-2-diazo-1,5-hexanedione, could not be generated with the same reaction conditions. Instead of Fe(III) as the transition metal, $Ni(acac)_2$ has been used to catalyze the Michael reaction although a high reaction

(1) For examples of the total synthesis of natural products with use of α-diazocarbonyl compounds, see: (a) Sawada, T.; Fuerst, D. E.; Wood, J. L. *Tetrahedron Lett.* **2003**, *44*, 4919. (b) Srikrishna, A.; Gharpure, S. J. *J. Org. Chem*. **2001**, *66*, 4379. (c) White, J. D.; Hrnciar, P.; Stappenbeck, F. *J. Org. Chem.* **1999**, *64*, 7871. (d) Padwa, A.; Precedo, L.; Semones, M. A. *J. Org. Chem.* **1999**, *64*, 4079. (e) Danheiser, R. L.; Casebier, D. S.; Loebach, J. L. *Tetrahedron Lett.* **1992**, *33*, 1149.

(2) For reviews of metal-catalyzed reactions of α-diazocarbonyl compounds, see: (a) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (b) Merlic, C. A.; Zechman, A. L. *Synthesis* **2003**, 1137. (c) Doyle, M. P.; Forbes, D. C. *Chem. Rev*. **1998**, *98*, 911. (d) Lebel, H.; Marcoux, J.; Molinaro, C.; Charette, A. B. *Chem. Rev.* 2003, 103, 977. (e) Doyle, M. P.; Protopopova, M. N. *Tetrahedron* **1998**, *54*, 7919. (f) Davies, H. M. L.; Beckwith, R. E. J. *Chem. Rev*. **2003**, *103*, 2861. (g) Taber, D. F.; Stiriba, S. *Chem.−Eur. J.* **1998**, *4*, 990.

(3) For methods for the synthesis of α-diazocarbonyl compounds, see: (a) Regitz, M.; Maas, G. *Diazo Compounds*, *Properties*, *and Synthesis*; Academic Press: New York, 1986. (b) Regitz, M. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978; Chapter 17. (c) Regitz, M. *Angew. Chem.*, *Int. Ed. Engl.* **1967**, *6*, 733. (d) Regitz, M. *Synthesis* **1980**, 368.

(4) Hendrickson, J. B.; Wolf, W. A. *J. Org. Chem.* **1968**, *33*, 3610.

(5) Christoffers, J. *J. Chem. Soc.*, *Perkin Trans. 1* **1997**, 3141.

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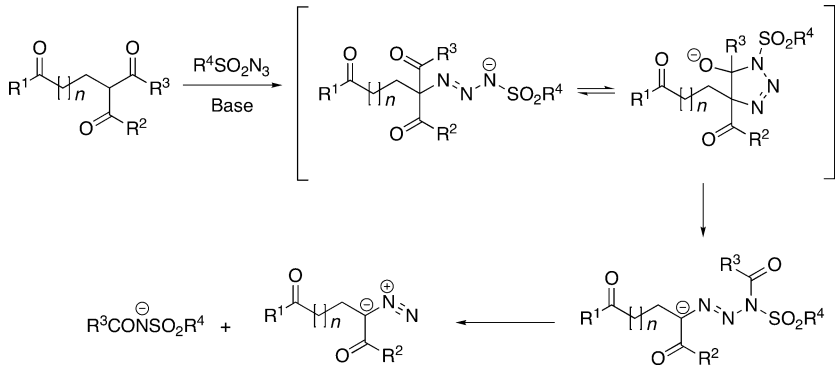
SCHEME 1. Deacylative Diazo Transfer Reaction



SCHEME 2. Michael Addition of 1,3-Diketone to Methyl Vinyl Ketone

temperature is required.[6] When the reaction was conducted in the presence of $Ni(acac)_2$ at 85 °C, the tricarbonyl compound **2** was obtained in 95% yield. An additional dehydration step (using P_2O_5 in a drying pistol) to remove the water of hydration after column chromatography was necessary to purify compound **2**.

Next, we attempted the diazo transfer reaction of the tricarbonyl compounds using methanesulfonyl azide and triethylamine in acetonitrile (Scheme 3). It has been reported that methanesulfonyl azide is more efficient for the diazo transfer than the generally used tosyl azide.[7] When the tricarbonyl compound **1** was treated with methanesulfonyl azide at room temperature, the corresponding 3-diazo-2,6-heptanedione **3a** and the hydroxytrione **3b**, a known product of the Michael addition of pentane-2,4-dione and MVK,[8] were generated in 39% and 11% yields, respectively. Much more interesting was the fact that the 4,5-dihydropyrazole **3c** and the pyrazole **3d** were unexpectedly produced in roughly 10% yield each in this reaction. Furthermore, the diazo transfer of the tricarbonyl compound **2** under the same reaction conditions provided only 13% of the desired diazoalkanedione **4a**, along with an inseparable mixture of the deacylated dione starting material **4b** (47%) and the pyrazole **4c** (15%). While examining several reaction procedures to improve the yield of the desired products, we learned that Danheiser had performed the diazo transfer reaction of α-trifluoroacetyl ketone in the presence of water.[7a] In addition, it was noted that dilute basic workup could cleanly remove the excess mesyl azide and byproducts.[7b] As a result, when 1 equiv of water was added to the reaction mixture and 10% aqueous sodium hydroxide was employed during workup, **4a** and **4b** were obtained in 38% and 30% yields, respectively, without any pyrazole **4c** being formed. The exact role of the water in this process is unclear since it is likely to hydrate the trifluoroacetyl group although perhaps some is still present to provide a good external nucleophile for cleavage of the trifluoroacetyl group. This would then favor the formation of the diazo ketone **4a** but it is not clear why the presence of water inhibits the formation of the pyrazole **4c**.

The proposed mechanism for the formation of both the dihydropyrazole (pyrazoline) and the pyrazole is shown in Scheme 4. As seen from thin-layer chromatography monitoring during the diazo transfer, it is clear that the diazoalkanedione is produced initially under these reaction conditions. The retro-Michael reaction of the resulting diazoalkanedione generates methyl vinyl ketone and an α-diazoketone. A 1,3-dipolar cycloaddition between these two intermediates then occurs to produce the 4,5-dihydro-3*H*-pyrazole **I**, which rapidly tautomerizes to the two conjugated 4,5-dihydro-1*H*-pyrazoles, e.g., when R = Me (**3c**). It is known that the cycloaddition of α-diazoketones to α,*β*-unsaturated carbonyl compounds leads to isomeric pyrazolines, which are easily oxidized to the corresponding pyrazoles.[9] Finally, further oxidation of the two isomers would produce the same pyrazole, e.g., **3d**, during the reaction. Although we cannot completely discount another possible mechanism, namely the direct insertion of the diazo moiety into the C−H bond α to the acetyl group, the fact that MVK is produced in this reaction (shown by the formation of **3b**, which requires free MVK) lends more evidence to the pathway proposed in Scheme 4.

To prove that the formation of the pyrazolines occurred by the proposed mechanism, we carried out the cycloaddition of α-diazoacetophenone to methyl vinyl ketone (Scheme 5).[10] α-Diazoacetophenone **5** was readily prepared by the reaction of benzoyl chloride with diazomethane. When α-diazoacetophenone **5** was treated with neat methyl vinyl ketone at 23 °C for 5 h, the pyrazoline **6a** was isolated as the major product in 45% yield and the regioisomeric pyrazoline **6b** as the minor product in 24% yield. The isomers were separated and each was fully characterized by ^{1}H NMR, ^{13}C NMR, and IR. One of the structural determinants was the position of the proton α to the acyl group, which appears at 5.23 ppm next to the benzoyl group in **6a** and at 4.45 ppm next to

(6) (a) Nelson, J. H.; Howells, P. N.; DeLullo, G. C.; Landen, G. L. *J. Org. Chem.* **1980**, *45*, 1246. (b) Padwa, A.; Zhang, Z. J.; Zhi, L. *J. Org. Chem.* **2000**, *65*, 5223.

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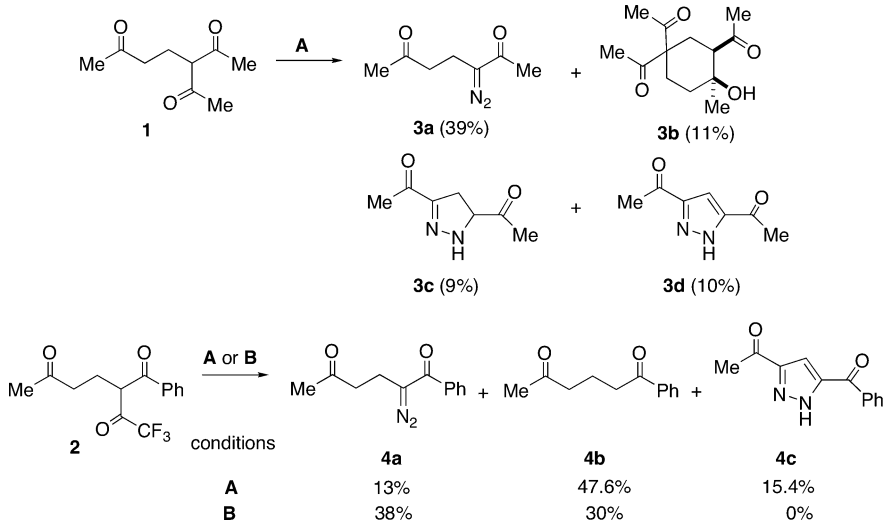
(8) Gomez-Bengoa, E.; Cuerva, J. M.; Mateo, C.; Echavarren, A. M. *J. Am. Chem. Soc.* **1996**, *118*, 8553.

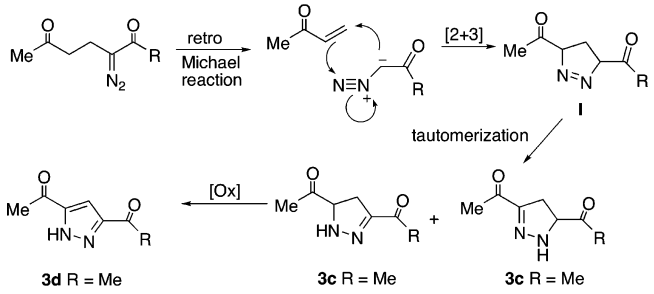
(9) Mancera, M.; Rodriguez, E.; Roffe, I.; Galbis, J. A. *Carbohydr. Res.* **1991**, *210*, 167.

SCHEME 3. Diazo Transfer Reaction[a]



[a] Reagents and conditions: (Method A) MsN_3, Et_3N, CH_3CN, 23 °C, 1.5 h; (Method B) MsN_3, Et_3N, H_2O, CH_3CN, 23 °C, 3 h, 10% aq NaOH.

SCHEME 4. Proposed Mechanism for the Formation of Dihydropyrazoles and Pyrazoles



the acetyl group in **6b**. However, the main piece of structural evidence was a comparison of the HMBC spectra of the two pyrazolines. In the spectrum of **6a** there was a correlation between the protons of the methyl group (δ 2.38) and the imine carbon (δ 150.3) while that correlation was absent in the spectrum of **6b**. Moreover there was a correlation in the spectrum of **6b** between the protons of the methyl group (δ 2.24) and the sp^3 carbon α to the nitrogen (δ 67.6). This implies that the acetyl group is attached to the imine carbon in **6a** and to the sp^3 carbon in **6b**. The pyrazoline **6b** seems to be less stable than **6a** and decomposes readily after column chromatography. As expected, oxidation of each isomer with DDQ in benzene furnished the same pyrazole, which was identical with the side product **4c** previously generated in the diazo transfer reaction. Consequently, we could confirm that the formation of the pyrazoline during the diazo transfer reaction resulted from a retro-Michael reaction followed by the dipolar cycloaddition reaction. The pyrazolines are fairly unstable compounds and are not easy to purify and handle. They are best isolated by a very rapid column chromatography since remaining on the column for an extended period of time produces some pyrazoles and decomposition products.[11] This instability of the pyrazolines probably contributes to the somewhat low yields in the oxidation of **6a** and **6b** to **4c**. These oxidations were carried out only to verify the structures of the pyrazolines and no attempts were made to optimize this process or to identify other reagents for this oxidation.

We explored computationally the relative energies and structures of the two isomeric pyrazolines in order to understand the greater stability of **6a**. The structures of pyrazolines **6a** and **6b** were optimized by using the B3LYP density functional method and the 6-31G* basis set. All calculations were done for the gas phase with Gaussian 98.[12] The optimized structures are shown in Figure 1. Isomer **6a** is predicted to be 1.5 kcal/mol more stable than isomer **6b**.

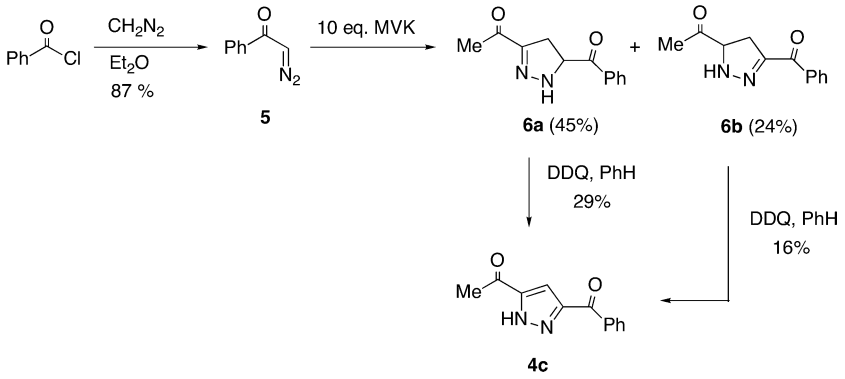
This energy difference can be rationalized by the greater capacity of the acetyl group than the benzoyl group to conjugate with the hydrazone. This increased conjugation is reflected in the decreased bond lengths for **6a** compared to **6b**. Figure 1 shows that the largest change in bond length occurs for the C−O and C−C bonds. The change in C−C bond length reflects greater conjugation of the hydrazone with the carbonyl group in **6a**, which rationalizes the greater stability of **6a**. The

(10) For some examples of the cycloaddition reaction of diazoalkanes, see: (a) Rispens, M. T.; Keller, E.; de Lange, B.; Zijlstra, R. W. J.; Feringa, B. L. *Tetrahedron*: *Asymmetry* **1994**, *5*, 607. (b) Guerra, F. M.; Mish, M. R.; Carreira, E. M. *Org. Lett*. **2000**, *2*, 4265. (c) Mish, M. R.; Guerra, F. M.; Carreira, E. M. *J. Am. Chem. Soc*. **1997**, *119*, 8379. (d) Gally, G.; Pätzel, M.; Jones, P. G. *Tetrahedron* **1995**, *51*, 1631.

(11) Depending on how the reactions are worked up and the length of time the compounds spend in the air on the column, one can get differing amounts of pyrazolines and pyrazoles. For example, rapid chromatography of the reaction mixture shown in Scheme 5 allows the isolation of only the pyrazolines **6a** and **6b** without any pyrazole **4c** being formed. In the reactions shown in Scheme 3, the compounds were left on the column for a longer period of time and therefore more of the pyrazoles were formed.

(12) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T. A.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*; Gaussian, Inc.: Pittsburgh, PA, 1998.

SCHEME 5. The Cycloaddition of α-Diazoacetophenone to Methyl Vinyl Ketone



phenyl group of the benzoyl is strongly conjugated with the carbonyl, which is reflected in the C−O bond length.

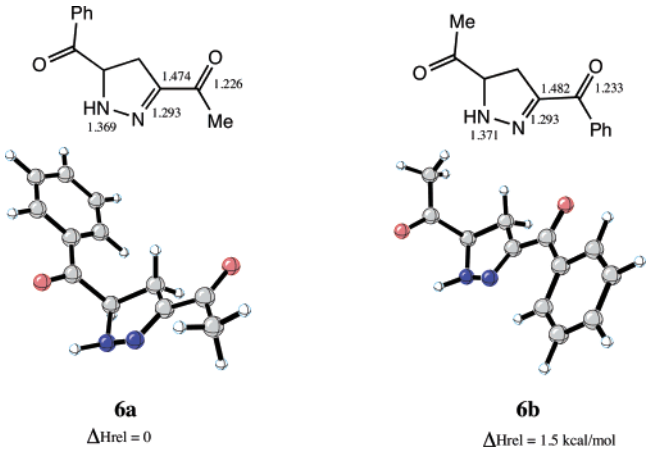


FIGURE 1. Bond lengths and relative energies of optimized pyrazolines.

In summary, we have described the unexpected formation of pyrazolines and/or pyrazoles during the diazo transfer reaction of tricarbonyl compounds with sulfonyl azides to produce 3-diazo-2,6-alkanediones. The mechanism presumably involves a retro-Michael reaction followed by cycloaddition of the α-diazo ketone with the enone generated in that step. Evidence for the validity of this mechanism was provided by the cycloaddition of α-diazoacetophenone with methyl vinyl ketone. In addition, density functional theory (DFT) calculations show that the thermodynamic energy difference between two isomers is consistent with the experimental results of the cycloaddition reaction, namely the isomer in which the acetyl group overlaps with the imine double bond is favored over that in which the benzoyl group is in conjugation with the imine.

Experimental Section

3-Acetyl-2,6-heptanedione (1). Methyl vinyl ketone (2.0 mL, 24.0 mmol) was added to a mixture of 1,3-pentanedione (2.40 g, 24.0 mmol) and $FeCl_3 \cdot H_2O$ (324 mg, 1.20 mmol) at 0 °C. The resulting mixture was stirred for 12 h at 23 °C and then purified by flash column chromatography on silica gel (2.5:1 to 1:1.5 hexane/ethyl acetate) to afford 3-acetyl-2,6-heptanedione **1** as an oil (3.00 g, 74%). The spectroscopic data of **1** were consistent with those reported in the literature.[5] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.66 (t, J = 7.0 Hz, 1H), 2.43 (t, J = 7.0 Hz, 1H), 2.18 (s, 6H), 2.11 (s, 3H), 2.06 (q, J = 7.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 207.4, 204.1, 66.8, 40.3, 29.9, 29.3, 21.4. IR (neat) 3003, 2939, 1715, 1601, 1421, 1360, 1156, 956, 720 cm^{-1}.

1-Phenyl-2-trifluoroacetyl-1,5-hexanedione (2). A mixture of 4,4,4-trifluoro-1-phenyl-1,3-butanedione (500 mg, 2.31 mmol), methyl vinyl ketone (0.23 mL, 2.76 mmol), and $Ni(acac)_2$ (6 mg, 0.02 mmol) in benzene (1 mL) was heated at 85 °C for 20 h. The solvent was removed under reduced pressure, and the resulting residue was purified on a silica gel column (1:1 hexane/ethyl acetate). Dehydration for 3−5 h by using a drying pistol with P_2O_5 and toluene at reflux gave the known 1-phenyl-2-trifluoroacetyl-1,5-hexanedione **2** (628 mg, 95%).[6b] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.11 (d, J = 7.6 Hz, 2H), 7.66 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.6 Hz, 2H), 5.14 (t, J = 6.9 Hz, 1H), 2.61 (dt, J = 18.8, 6.0 Hz, 1H), 2.56 (dt, J = 18.8, 6.7 Hz, 1H), 2.25 (dt, J = 6.6, 6.0 Hz, 1H), 2.24 (dt, J = 6.7, 6.6 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 207.6, 194.2, 187.8 (q, J = 35.8 Hz), 134.6, 134.5, 129.1, 129.0, 115.2 (q, J = 290.4 Hz), 53.9, 39.7, 29.9, 22.3. IR (neat) 3067, 2942, 1768, 1715, 1678, 1597, 1581, 1450, 1371, 1282, 1210, 1001, 928, 695 cm^{-1}. ^{19}F NMR ($CDCl_3$, 376 MHz) δ −78.6. HRMS (EI) m/z found for M^+ 286.0816, calcd for $C_{14}H_{13}F_3O_3$ 286.0817.

3-Diazo-2,6-heptanedione (3). To a solution of 3-acetyl-2,6-heptanedione **1** (200 mg, 1.18 mmol) in acetonitrile (1 mL) were added methanesulfonyl azide[7a] (0.15 mL, 1.82 mmol) and triethylamine (0.49 mL, 3.52 mmol) at 23 °C. The reaction mixture was stirred for 1.5 h, and the solvent was removed under reduced pressure. The crude residue was flash chromatographed on silica gel (2:1 to 1:1 hexane/ethyl acetate) to give 3-diazo-2,6-heptanedione **3a** (71 mg, 39%), the hydroxytrione **3b** (31 mg, 11%), 3,5-diacetyl-3,4-dihydro-*2H*-pyrazole **3c** (16 mg, 9%), and the known 3,5-diacetylpyrazole **3d**[13] (17 mg, 10%). The spectroscopic data for **3a**[6b] and **3b**[8] were identical with those reported in the literature. **3a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.71 (t, J = 6.2 Hz, 2H), 2.50 (t, J = 6.2 Hz, 2H), 2.17 (s, 3H), 2.15 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 207.7, 191.1, 67.2, 40.9, 29.7, 25.1, 17.8. IR (neat) 2928, 2081, 1715, 1633, 1420, 1371, 1330, 1163, 1016, 971 cm^{-1}. **3b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.88 (d, J = 2.5 Hz, 1H), 2.62 (dd, J = 13.0, 3.4 Hz, 1H), 2.36 (dd, J = 13.0, 2.6 Hz, 1H), 2.28 (s, 3H), 2.21 (m, 2H), 2.14 (s, 3H), 2.12 (s, 3H), 1.80 (dd, J = 13.0, 13.0 Hz, 1H), 1.70 (ddd, J = 14.2, 3.4, 3.4 Hz, 1H), 1.14 (s, 3H), 1.10 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 215.0, 206.7, 206.1, 68.6, 67.1, 52.6, 35.2, 31.2, 28.5, 27.9, 26.5, 25.8, 24.9. IR (neat) 3503, 2968, 2928, 1696, 1423, 1360, 1207, 1180, 961 cm^{-1}. **3c**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.81 (br s, 1H), 4.43 (dd, J = 13.3, 6.0 Hz, 1H), 3.20 (dd, J = 17.5, 13.3 Hz, 1H), 3.09 (dd, J = 17.5, 6.0 Hz, 1H), 2.40 (s, 3H), 2.20 (s, 3H). **3d**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 12.06 (br s, 1H), 7.33 (s, 1H),

(13) Kochetkov, N. K.; Ambrush, I.; Ambrush, T. I. *Zh. Obshch. Khim.* **1959**, *29*, 2964.

2.61 (s, 6H). IR (neat) 3297, 3124, 1686, 1667, 1467, 1355, 1237, 1012, 991, 946, 868 cm^{-1}.

1-Phenyl-2-diazo-1,5-hexanedione (4a). To a solution of 1-phenyl-2-trifluoroacetyl-1,5-hexanedione **2** (100 mg, 0.35 mmol) in acetonitrile (0.3 mL) were added methanesulfonyl azide[7a] (0.043 mL, 0.53 mmol) and triethylamine (0.15 mL, 1.08 mmol) at 23 °C. The reaction mixture was stirred for 1.5 h, and the solvent was removed under reduced pressure. The crude residue was flash chromatographed on silica gel (5:3 hexane/ethyl acetate) to give 1-phenyl-2-diazo-1,5-hexanedione **4a** (10 mg, 13%) and an inseparable mixture of 1-phenyl-1,6-hexanedione **4b** and the known 3-acetyl-5-benzoylpyrazole **4c**[13] (46 mg, 63% with 3.1:1 ratio). The spectroscopic data for **4a** and **4b** were identical with those reported in the literature.[6b,14] **4a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.54 (m, 2H), 7.47 (m, 1H), 7.41 (m, 2H), 2.84 (t, J = 6.2 Hz, 2H), 2.72 (t, J = 6.2 Hz, 2H), 2.18 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 207.7, 189.5, 137.5, 131.4, 128.5, 127.1, 66.9, 41.0, 29.8, 19.1. IR (neat) 3061, 2928, 2078, 1715, 1609, 1345, 1168, 705 cm^{-1}. **4b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.95 (m, 2H), 7.56 (m, 1H), 7.45 (m, 2H), 3.02 (t, J = 7.0 Hz, 2H), 2.57 (t, J = 7.0 Hz, 2H), 2.15 (s, 3H), 2.02 (quin, J = 7.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 208.4, 199.6, 136.6, 133.0, 128.5, 127.9, 42.5, 37.3, 29.8, 18.0.

α-Diazoacetophenone (5). To a solution of benzoyl chloride (0.521 g, 3.71 mmol) in diethyl ether (5 mL) was slowly added over a period of 3 h an ethereal solution of diazomethane, which was prepared by dropwise addition of a solution of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (3.81 g, 17.8 mmol, Diazald, Aldrich Company) in diethyl ether (40 mL) into a solution of potassium hydroxide (1.06 g, 18.9 mmol) in ethanol/water (7.5 mL/ 3 mL) at 60 °C. The resulting mixture was allowed to stand for an additional 3 h, and the solvent was removed under reduced pressure. The crude residue was purified by flash column chromatography on silica gel (4:1 hexane/ethyl acetate) to afford α-diazoacetophenone **5** (471 mg, 87%) as a yellow crystalline solid. The spectroscopic data for **5** were identical with those reported in the literature.[15] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.72 (d, J = 7.8 Hz, 2H), 7.48 (m, 1H), 7.38 (m, 2H), 5.94 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 186.3, 136.5, 132.6, 128.5, 126.6, 54.2. IR (neat) 3071, 2107, 1703, 1615, 1574, 1449, 1366, 1228, 870, 700 cm^{-1}.

3-Acetyl-5-benzoyl-4,5-dihydro-*1H*-pyrazole (6a) and 3-Acetyl-5-benzoyl-3,4-dihydro-*2H*-pyrazole (6b). α-Diazoacetophenone **5** (150 mg, 1.03 mmol) was treated with neat methyl vinyl ketone (0.43 mL, 5.17 mmol) at 23 °C. The reaction mixture was stirred for 5 h and the remaining methyl vinyl ketone was removed under reduced pressure. The crude residue was rapidly chromatographed on silica gel (2:1 hexane/ethyl acetate) to afford **6a** (101 mg, 45%) and **6b** (54 mg, 24%). **6a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.89 (m, 2H), 7.60 (m, 1H), 7.49 (m, 2H), 7.05 (br s, 1H), 5.23 (dd, J = 13.6, 5.4 Hz, 1H), 3.36 (dd, J = 17.5, 13.6 Hz, 1H), 3.15 (dd, J = 17.5, 5.4 Hz), 2.38 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 196.7, 194.1, 150.3, 134.1, 132.7, 128.9, 128.7, 64.4, 34.4, 25.4. IR (neat) 3335, 1687, 1660, 1597, 1552, 1449, 1415, 1227, 777, 695 cm^{-1}. HRMS (MALDI) *m/z* found for $(M + Na)^+$ 239.0796, calcd for $C_{12}H_{12}N_2O_2Na$ 239.0791. **6b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.11 (m, 2H), 7.53 (m, 1H), 7.43 (m, 2H), 7.02 (br s, 1H), 4.45 (dd, J = 13.3, 6.2 Hz, 1H), 3.43 (dd, J = 17.5, 13.3 Hz, 1H), 3.31 (dd, J = 17.5, 6.2 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 205.7, 187.4, 149.4, 136.5, 132.6, 130.0, 128.1, 67.6, 34.3, 25.4. IR (neat) 3334, 1721, 1688, 1634, 1598, 1576, 1542, 1448, 1417, 1235, 1179, 900, 864, 695 cm^{-1}. HRMS (MALDI) *m/z* found for $(M - H)^+$ 215.0816, calcd for $C_{12}H_{11}N_2O_2$ 214.0815. HMBC experiments: **6a**, correlation between protons at δ 2.38 and C at δ 150.3; **6b**, correlation between protons at δ 2.24 and C at δ 67.6.

3-Acetyl-5-benzoylpyrazole (4c). A solution of 3-acetyl-5-benzoyl-4,5-dihydro-*1H*-pyrazole **6a** (62 mg, 0.29 mmol) in benzene (2 mL) was treated with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ, 72 mg, 0.32 mmol) at 23 °C. The reaction mixture was stirred for 5 h. The solvent was removed under reduced pressure. The resulting mixture was triturated with chloroform, stirred with activated charcoal for 30 min, and filtered through Celite. The solvent was removed, again under reduced pressure, and the crude residue was chromatographed on silica gel (3:1 hexane/ethyl acetate) to afford the known 3-acetyl-5-benzoylpyrazole **4c**[13] (18 mg, 29%). 3-Acetyl-5-benzoylpyrazole **4c** was also produced from the pyrazoline **6b** by the same reaction procedure. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 12.02 (br s, 1H), 8.08 (d, J = 7.4 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.4 Hz, 2H), 7.41 (br s, 1H), 2.67 (s, 3H). IR (neat) 3250, 3069, 2923, 1687, 1651, 1599, 1449, 1241, 1180, 901, 731, 695 cm^{-1}. HRMS (EI) *m/z* found for M^+ 214.0737, calcd for $C_{12}H_{10}N_2O_2$ 214.0742.

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Supporting Information Available: Proton NMR spectra for all compounds and carbon NMR spectra for compounds **1**, **2**, **3ab**, **4b**, **5**, and **6ab** and a general Experimental Section. This material is available free of charge via the Internet at http://pubs.acs.org.

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