Stereoselective Synthesis of Cyclopropane Rings under Phase-Transfer-Catalyzed Conditions

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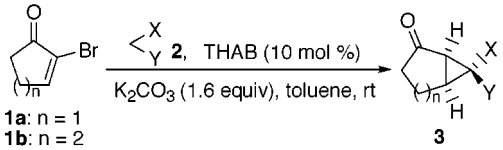
Cyclopropane and its derivatives are widely accepted as useful starting materials or intermediates for the synthesis of numerous natural products.[1] Traditionally, stereoselective construction of trisubstituted cyclopropane units has been accomplished by a cyclopropanation reaction using olefins as substrates with carbenoids, including transition metals[1b,2] such as the Simmons-Smith reaction[3] or by the addition−elimination sequence with α,β-unsaturated carbonyl compounds and carbon nucleophiles.[1a,4] Industry requires the development of useful carbon−carbon bond-forming reactions exhibiting high yields, high selectivities, low cost, safe, operational simplicity, mild reaction conditions, and environmental consciousness. It has been recognized that phase-transfer-catalyzed reactions can be a potential and efficient methodology to achieve these characteristics.[5,6] In this paper, we report a synthetic strategy to construct 1,2,3-trisubstituted cyclopropane rings including quaternary carbons with excellent yields in moderate-to-high diastereoselectivities under mild reaction conditions using phase-transfer catalysts (PTC).

Catalytic cyclopropanation reaction via intermolecular Michael addition and intramolecular alkylation processes can generate three stereocenters in each product. Initial work was focused on the catalytic cyclopropanation of easily prepared α-halocycloalkenone **1**[7] as a reactive olefin with a leaving group on the α-carbon and diisopropyl malonate **2a** as a soft carbon nucleophile using a catalytic amount of commercially available quaternary ammonium halide as the PTC in the presence of an inorganic base. We were pleased to find that α-bromocyclopentenone **1a** reacted smoothly with **2a** in toluene at room temperature for 6 h in the presence of a catalytic amount of tetrahexylammonium bromide (THAB) to give the desired product **3a** exclusively in 68% yield[8] (Table 1, entry 1). Interestingly, the corresponding α-iodoenone gave the cyclized product **3a** in lower yield. Likewise, α-bromocyclohexenone **1b** effectively reacted with dibenzyl malonate **2g** to give **3j** in 67% yield (entry 10). The quaternary ammonium bromide was more efficient than the corresponding chloride or iodide.[9] No reaction was observed in the absence of PTC, and it was recognized that the addition of a catalytic amount of PTC produced a dramatic increase in the reaction rate in this system.

To establish the generality of this phase-transfer-catalyzed cyclopropanation reaction, we turned our attention to the use of other nuculeophiles[10] involving an active methylene such as cyanoacetates and their derivatives. Thus, treatment of **1b** with **2b** or **2c** in the presence of THAB (10 mol %) in toluene at room temperature gave **3f** or **3i** in a stereoselective fashion in 91% and 93% yield, respectively, as a single isomer (Table 1, entries 6 and

Table 1. Catalytic Cyclopropanation under Phase-Transfer-Catalyzed Conditions



entry	enone	nucleophile	time (h)	yield of **3** (%)
1	**1a**	**2a**: X = Y = CO_2-*i*-Pr	6	**3a**: 68[a]
2	**1a**	**2b**: X = CO_2-*i*-Pr, Y = CN	41	**3b**: 77[b]
3	**1a**	**2c**: X = CO_2-*c*-Hex, Y = CN	2	**3c**: 79[c]
4	**1a**	**2d**: X = CO_2Bn, Y = CN	2	**3d**: 75[d]
5	**1a**	**2e**: X = CO_2-*c*-Oct, Y = CN	155	**3e**: 81
6	**1b**	**2b**: X = CO_2-*i*-Pr, Y = CN	15	**3f**: 91
7	**1b**	**2f**: X = CO_2-*n*-Bu, Y = COMe	14	**3g**: 83
8	**1b**	**2e**: X = CO_2-*c*-Oct, Y = CN	38	**3h**: 94
9	**1b**	**2c**: X = CO_2-*c*-Hex, Y = CN	37	**3i**: 93
10	**1b**	**2g**: X = Y = CO_2Bn	18	**3j**: 67
11	**1a**	**2h**: X = NO_2, Y = H	18	**3k**: 54[e]
12	**1b**	**2h**: X = NO_2, Y = H	9	**3l**: 51[e]

[a] Rb_2CO_3 (6.2 equiv) was used. [b] K_2CO_3 (2.2 equiv) was used. [c] Toluene-H_2O was used as solvent. [d] *o*-Xylene-H_2O was used as a solvent. [e] Nitromethane (15 equiv) was used in the presence of K_2CO_3 (3.0 equiv).

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(8) No other products except **3a** were detected on TLC in these reaction systems.

(9) Other PTCs involving an aromatic ring or a longer hydrophobic chain such as benzyltriethylammonium bromide (BTEB) or decyltrimethylammonium bromide (DTMB) are less effective in this reaction system.

(10) The reaction of α-substituted acetophenone derivatives with enones did not give cyclopropanes but the corresponding *cis*-fused furan derivatives as a sole product in modest yield.

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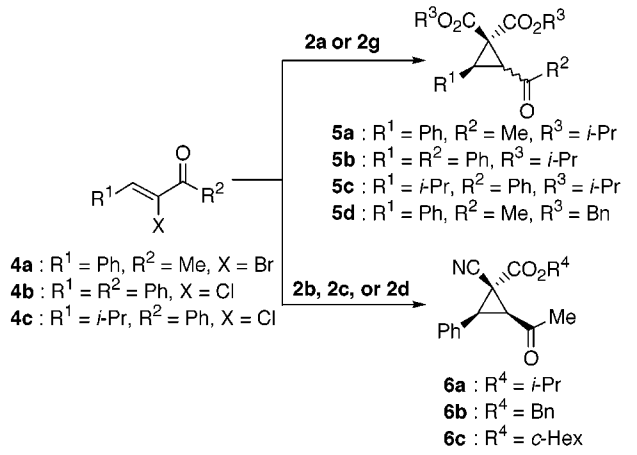
Table 2. Catalytic Cyclopropanation using Acyclic Enones with Various Nucleophiles[a]



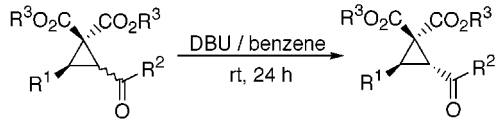
entry	enone	nucleophile	time (h)	yield (%)	cis:trans[b]
1	**4a**	**2a**	84	**5a**: 82	46:54[c]
2	**4b**	**2a**	58	**5b**: 88	trans only
3	**4c**	**2a**	38	**5c**: 100	33:67
4	**4a**	**2g**	60	**5d**: 86	45:55
5	**4a**	**2b**	15	**6a**: 91	one isomer[d]
6	**4a**	**2c**	67	**6b**: 84	one isomer[d]
7	**4a**	**2d**	33	**6c**: 90	one isomer[c]

[a] All reactions were performed in toluene with 10 mol % of THAB and K_2CO_3 (1.6 equiv) at rt. [b] Diastereomeric ratio of **5** was determined by ^{1}H NMR analysis. [c] BTF was used as a solvent. [d] The relative configuration of these products was assigned on the basis of an X-ray crystal structures of the cyclopropanes.[13]

9). In the nitromethane case, a substrate containing acidic protons, we were pleased that the corresponding nitrocyclopropanes were obtained as the sole product in moderate yield (Table 1, entries 11 and 12). The X-ray crystallographical and ^{1}H NMR[11] analysis revealed the stereochemistry of **3k** as exo, and the product **3l** was also suggested to have a similar configuration by comparison of the coupling constant on ^{1}H NMR spectra. As shown in Table 1, the reaction proceeded smoothly using mild reaction conditions to give the desired products in good-to-high yields using a variety of carbon nucleophiles. Thus, we have succeeded in establishing a synthetic route utilized with THAB for the preparation of substituted cyclopropane rings in a stereoselective fashion.

In general, it is more challenging to control the stereogenic centers in linear compounds compared with cyclic ones. Therefore, we aimed to obtain monocyclic cyclopropanated products by use of easily prepared acyclic α-haloenones **4**[7a,b] under phase-transfer-catalyzed conditions. Treatment of **4** with malonates or cyanoacetates under similar reaction conditions in toluene or benzotrifluoride (BTF[12]) afforded the corresponding cyclized products **5** or **6** in excellent yields, respectively. On the other hand, the reaction of **4** with malonate **2a** or **2g** proceeded smoothly to give **5** as a diastereoisomeric mixture (Table 2, entries 1, 3, and 4), though product **5b** was isolated as a single isomer (Table 2, entry 2). Encouraged by this result, we next examined the reaction of cyanoacetates instead of malonates with acyclic enones. Surprisingly, compounds **6** were obtained as sole dia-

Scheme 1. Isomerization of 5



5a : R^1 = Ph, R^2 = Me, R^3 = *i*-Pr
5c : R^1 = *i*-Pr, R^2 = Ph, R^3 = *i*-Pr
5d : R^1 = Ph, R^2 = Me, R^3 = Bn

7a : 74%
7b : 96%
7c : 68%

stereomers involving cis-orientation of both phenyl and acetyl groups and were obtained in excellent yields by the reaction of **4** with **2b**, **2c**, or **2d** (Table 2, entries 5 to 7).[13] To our knowledge, this is the first example of high stereoselectivity in the synthesis of cyclopropane rings with complete stereocontrol using linear compounds as substrates via a Michael addition, proton transfer, and then an intramolecular alkylation process. As depicted in Scheme 1, these compounds can be completely converted to the corresponding trans isomers with DBU in benzene in good-to-high yields.[14] These results are summarized in Table 2.

It seems that products **6** are not thermodynamic but kinetic ones. Thermodynamic calculation of the ground state of four possible diastereomers suggested that the product obtained, **6**, is not one of the most stable isomers.[15] The stereochemistry of each product in this reaction would be controlled by kinetic factors in the transition state of the cyclization process.

In conclusion, we have realized a catalytic cyclopropanation reaction using cyclic or acyclic α-haloenones under phase-transfer-catalyzed conditions. As shown above, a catalytic amount of THAB appears to act as a useful PTC to produce 1,2,3-trisubstituted cyclopropane rings in high-to-excellent yields in a stereoselective fashion under mild reaction conditions. The proposed mechanism of this catalytic cyclopropanation is both intermolecular Michael addition and intramolecular cyclization process. The stereochemistry of the cyclized products would be determined by the latter process. Although we have no correct explanation for the basis of these stereoselectivities in this reaction at the moment, the results described here will lead to further progress.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 270 and 67.8 MHz, respectively, using $CDCl_3$ with internal tetramethylsilane as the reference. Flash chromatography was performed on Cica-Merck Silica Gel 60 (230−400 mesh ASTM). Analytical TLC was carried out on precoated (0.25 mm) Merck silica gel F-254 plates. All solevents and reagents except α-haloenones were obtained from commercial sources and used as received without further purification.

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(13) The relative configuration of **3b**, **3k**, **6a**, and **6c** were determined by X-ray crystal structural analysis. See Supporting Information. According to comparison of the ^{1}H NMR analysis of the above-mentioned compounds, the stereochemistry of other cyclopropanated products were assigned.

(14) No isomerization occurred with compound **5b** under similar reaction conditions. Treatment of **6** with DBU resulted in decomposition of the starting materials.

(15) According to thermodynamic calculation for four possible diastereomers of cyclopropane derivatives using MOPAC 93 Rev.2-AM1, the isomer obtained was found not to be the most stable one, which has an energy gap of 1.92 kcal/mol relative to the most stable isomer. The reason for this unique stereoselectivity in this cyclopropanation reaction is not presently clear, though it seems that the stereocontrol in this reaction is not strongly dependent on the thermodynamic stability of the products but on kinetic factors during the cyclization step.

A general procedure for the catalytic cyclopropanation reaction under phase-transfer-catalyzed conditions is as follows:

Diisopropyl 2-oxobicyclo[3.1.0]hexane-6,6-dicarboxylate (3a). Diisopropyl malonate **2a** (0.19 mL, 1.0 mmol), THAB (21.8 mg, 0.05 mmol), and Rb_2CO_3 (716 mg, 3.1 mmol) were added to a solution of enone **1a** (80.5 mg, 0.5 mmol) in toluene (3.0 mL) at room temperature. After being stirred for 6 h, the reaction mixture was quenched with 1 N HCl and extracted with ethyl acetate (15 mL × 3). The combined organic layer was dried over Na_2SO_4. Removal of the solvent followed by flash column chromatography (silica gel, hexane:Et_2O = 2:1) gave the desired product **3a** (66.2 mg, 58%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.23−1.31 (m, 2H), 1.31−1.91 (m, 1H), 2.17−2.36 (m, 3H), 2.49 (d, J = 5.6 Hz, 1H), 2.72 (t, J = 5.6 Hz, 1H), 5.00−5.14 (m, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 20.6 (CH_2), 21.1 (CH_3), 21.6 (CH_3), 34.1 (CH_2), 34.8 (CH), 39.9 (4°), 40.7 (CH), 69.6 (O*C*HMe$_2$), 70.3 (O*C*HMe$_2$), 165.1 (*C*O$_2$-*i*-Pr), 167.1 (*C*O$_2$-*i*-Pr), 210.0 (C═O); IR (neat) 2361, 2257, 1740, 1728 cm^{-1}; MS *m*/*z* 268 (M$^+$), 128 (base peak); Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67: H, 7.51. Found: C, 62.31; H, 7.50.

Isopropyl 6-*endo*-cyano-2-oxobicyclo[3.1.0]hexane-6-*exo*-carboxylate (3b). Colorless crystals, mp 79 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.33 (d, J = 6.3 Hz, 6H), 2.30−2.55 (m, 4H), 2.75 (d, J = 5.6 Hz, 1H), 2.88 (t, J = 6.6 Hz, 1H), 5.05−5.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 20.9 (CH_2), 21.4 (CH_3), 25.2 (4°), 34.2 (CH_2), 36.7 (CH), 42.6 (CH), 72.0 (CH), 114.3 (CN), 164.1 (CO_2), 207.9 (C═O); IR (neat) ν 2988, 2893, 2251, 1755, 1717 cm^{-1}; MS *m*/*z* 207 (M$^+$), 165 (M$^+$-*i*-Pr, base peak); Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.76; H, 6.36; N, 6.64.

Cyclohexyl 6-*endo*-cyano-2-oxobicyclo[3.1.0]hexane-6-*exo*-carboxylate (3c). Yellow oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.21−1.55 (m, 6H), 1.76−1.82 (m, 4H), 2.31−2.55 (m, 4H), 2.76 (d, J = 5.6 Hz, 1H), 2.89 (t, J = 5.3 Hz, 1H), 4.83−4.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 20.9 (CH_2), 23.2 (CH_2 × 2), 25.0 (CH_2), 25.2 (4°), 31.0 (CH_2 × 2), 34.2 (CH_2), 36.7 (CH), 42.6 (CH_2), 76.4 (CH), 114.3 (CN), 164.0 (CO_2), 207.9 (C═O); IR (neat) ν 2939, 2863, 2244, 1738, 1732 cm^{-1}; MS *m*/*z* 247 (M$^+$), 165 (M$^+$-*c*-Hex), 83 (base peak); Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.06; H, 6.93; N, 5.66. Found: C, 68.00; H, 7.10; N, 5.74.

Benzyl 6-*endo*-cyano-2-oxobicyclo[3.1.0]hexane-6-*exo*-carboxylate (3d). Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.28−2.57 (m, 4H), 2.79 (d, J = 5.7 Hz), 2.91 (t, J = 5.7 Hz, 1H), 5.25 (s, 2H), 7.39 (br s, 5H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 20.9 (CH_2), 24.9 (4°), 34.1 (CH_2), 37.0 (CH), 42.8 (CH), 68.9 (CH_2), 114.0 (CN), 128.3, 128.5, 128.6, 128.8 (Ph, CH), 134.1 (Ph, 4°), 164.6 (CO_2), 207.5 (C═O); IR (neat) ν 3464, 3064, 2249, 1747, 1736 cm^{-1}; MS *m*/*z* 255 (M$^+$), 107, 91 (base peak); HRMS calcd for $C_{15}H_{13}NO_3$ 255.0894, found 255.0896.

Cyclooctyl 6-*endo*-cyano-2-oxobicyclo[3.1.0]hexane-6-*exo*-carboxylate (3e). Yellow oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.43-1.88 (m, 14H), 2.30−2.56 (m, 4H), 2.74 (d, J = 5.9 Hz, 1H), 2.87 (t, J = 5.9 Hz, 1H), 4.99−5.04 (m, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 20.9 (CH_2), 22.5 (CH_2), 22.5 (CH_2), 25.1 (CH_2), 25.2 (4°), 26.8 (CH_2 × 2), 31.0 (CH_2 × 2), 34.2 (CH_2), 34.2 (CH), 36.6 (CH), 79.3 (CH), 114.3 (CN), 163.9 (CO_2), 207.9 (C═O); IR (neat) ν 2928, 2859, 2244, 1788, 1732 cm^{-1}; MS *m*/*z* 275 (M$^+$), 169, 69 (base peak); Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.48; H, 7.83; N, 5.08.

Isopropyl 7-*endo*-cyano-2-oxobicyclo[4.1.0]heptane-7-*exo*-carboxylate (3f). Yellow oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.32 (d, J = 6.3 Hz, 6H), 1.86−2.11 (m, 3H), 2.34−2.46 (m, 3H), 2.52−2.61 (m, 2H), 5.00−5.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.1 (CH_2), 21.4 (CH_3), 22.8 (CH_2), 27.0 (4°), 30.0 (CH), 36.5 (CH), 38.3 (CH_2), 71.8 (CH), 115.0 (CN), 165.0 (MeCO$_2$), 201.6 (C═O); IR (neat) ν 2986, 2244, 1736, 1709 cm^{-1}; MS *m*/*z* 221 (M$^+$), 179 (M$^+$-*i*-Pr), 124 (base peak); Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.05; H, 6.85; N, 6.17.

***n*-Butyl 7-*endo*-acetyl-2-oxobicyclo[4.1.0]heptane-7-*exo*-carboxylate (3g)**. Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.95 (t, J = 7.3 Hz, 3H), 1.36−1.44 (m, 2H), 1.58−1.67 (m, 2H), 1.87−2.04 (m, 4H), 2.25 (s, 3H), 3.70−3.75 (m, 1H), 4.08−4.19 (m, 2H), 4.74 (d, J = 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 13.6 (CH_3), 14.1 (CH_3), 19.2 (CH_2), 20.2 (CH_2), 26.3 (CH_2), 30.7 (CH_2), 37.3 (CH_2), 44.9 (CH), 63.4 (CH_2), 83.9 (CH), 106.0 (4°), 165.2 (CO_2), 168.6 (MeC═O), 207.3 (C═O); IR (neat) ν 2959, 2874, 1725, 1720, 1698 cm^{-1}; MS *m*/*z* 252 (M$^+$), 151 (M$^+$-CO_2-*n*-Bu); HRMS calcd for $C_{14}H_{20}O_4$ 252.1360, found 252.1363.

Cyclooctyl 7-*endo*-cyano-2-oxobicyclo[4.1.0]heptane-7-*exo*-carboxylate (3h). Yellow oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.51−2.09 (m, 17H), 2.41−2.60 (m, 5H), 4.98−5.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.1 (CH_2), 22.5 (CH_2 × 2), 22.9 (CH_2), 25.1 (CH_2), 26.8 (CH_2 × 3), 27.1 (4°), 31.0 (CH_2 × 2), 32.0 (CH), 36.5 (CH), 38.3 (CH_2), 79.1 (CH), 115.0 (CN), 164.8 (CO_2), 201.6 (C═O); IR (neat) ν 2926, 2243, 1731, 1713 cm^{-1}; MS *m*/*z* 289 (M$^+$), 179 (M$^+$-*c*-Oct), 111, 64 (base peak); Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.26; H, 7.99; N, 4.64.

Cyclohexyl 7-*endo*-cyano-2-oxobicyclo[4.1.0]heptane-7-*exo*-carboxylate (3i). Yellow oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.18−1.51 (m, 6H), 1.75−2.11 (m, 5H), 2.35−2.46 (m, 4H), 2.52−2.62 (m, 3H), 4.80−4.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.6 (CH_2), 23.4 (CH_2 × 2), 23.7 (CH_2), 25.5 (CH_2), 27.6 (4°), 31.5 (CH_2 × 2), 32.6 (CH), 37.1 (CH), 38.8 (CH_2), 76.8 (CH), 115.6 (CN), 165.4 (CO_2), 202.2 (C═O); IR (neat) ν 2939, 2863, 2244, 1738, 1732 cm^{-1}; MS *m*/*z* 261 (M$^+$), 179 (M$^+$-*c*-Hex); HRMS calcd for $C_{15}H_{19}O_4$ 261.1364, found 261.1367.

Dibenzyl 2-oxobicyclo[4.1.0]heptane-7,7-dicarboxylate (3j). Colorless oil; ^{1}H NMR δ 1.18−1.39 (m, 1H), 1.54−1.65 (m, 1H), 2.01−2.17 (m, 4H), 2.35−2.43 (m, 2H), 5.05−5.19 (m, 4H), 7.29−7.34 (m, 10H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 18.5 (CH_2), 20.0 (CH_2), 29.0 (CH), 34.6 (CH), 37.8 (CH_2), 40.0 (4°), 67.8 (CH_2), 67.9 (CH_2), 127.9, 128.1, 128.3, 128.4, 128.6 (Ph, CH), 134.4, 134.8 (Ph, 4°), 165.3, 165.8 (C═O), 203.0 (C═O); IR (neat) ν 3034, 2957, 1740, 1709 cm^{-1}; MS *m*/*z* 378 (M$^+$), 287 (M$^+$-Bn), 91 (base peak); Anal. Calcd for $C_{23}H_{22}O_5$: C, 73.00; H, 5.86. Found: C, 72.78; H, 5.95.

6-*exo*-Nitro-2-oxobicyclo[3.1.0]hexane (3k). Colorless crystals, mp 64 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.94−2.02 (m, 1H), 2.21−2.40 (m, 3H), 2.82 (d, J = 6.7 Hz), 2.99 (dt, J = 6.7, 1.2 Hz, 1H), 4.41 (dd, J = 2.1, 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 22.4 (CH_2), 31.2 (CH), 32.9 (CH_2), 37.9 (CH), 62.2 (CH), 208.0 (C═O); IR (Nujol) ν 2953, 2855, 1732, 1539, 1311 cm^{-1}; MS *m*/*z* 141 (M$^+$), 95 (M$^+$-NO_2), 67 (base peak); HRMS calcd for $C_6H_7NO_3$ 141.0426, found 141.0248.

7-*exo*-Nitro-2-oxobicyclo[4.1.0]heptane (3l). Colorless crystals, mp 49 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.41−1.63 (m, 1H), 1.99−2.05 (m, 1H), 2.08−2.22 (m, 2H), 2.29−2.39 (m, 1H), 2.64−2.68 (m, 1H), 2.81 (dd, J = 8.2, 2.6 Hz, 1H), 4.67 (t, J = 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 18.1 (CH_2), 19.5 (CH_2), 26.8 (CH), 35.2 (CH), 37.1 (CH_2), 60.5 (CH), 201.3 (C═O); IR (Nujol) ν 2857, 1715, 1534, 1377 cm^{-1}; MS *m*/*z* 155 (M$^+$), 53 (base peak); HRMS calcd for $C_7H_9NO_3$ 155.0582, found 155.0576.

Diisopropyl 2-acetyl-3-phenylcyclopropane-1,1-dicarboxylate (5a). Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.92 (d, J = 6.3 Hz, 0.46 × 3H), 1.04 (d, J = 6.3 Hz, 0.54 × 3H), 1.13 (d, J = 2.3 Hz, 0.46 × 3H), 1.16 (d, J = 2.3 Hz, 0.54 × 3H), 2.37 (s, 0.46 × 3H), 2.43 (s, 0.54 × 3H), 3.09 (d, J = 7.6 Hz, 0.46 × 1H) 3.25 (d, J = 9.9 Hz, 0.46 × 1H), 3.45 (d, J = 7.6 Hz, 0.56 × 1H), 3.63 (d, J = 7.6 Hz, 0.56 × 1H), 4.76−4.81 (m, 0.46 × 1H), 4.98−5.15 (m, 0.54 × 1H), 7.22−7.26 (m, 0.46 × 5H), 7.26−7.30 (m, 0.56 × 5H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 21.2, 21.3, 21.4, 21.5 (CH_3), 31.4, 32.5, 36.1, 37.3, 37.5, 38.0 (CH), 41.7, 46.4 (4°), 68.6, 69.2, 69.6, 70.3 (CH), 127.0, 127.5, 128.1, 128.6, 130.6 (Ph, CH), 131.4, 133.2 (Ph, 4°), 200.7, 202.1 (C═O); IR (neat) ν 2982, 2938, 1713 cm^{-1}; MS *m*/*z* 284 (M$^+$-*i*-Pr), 115 (base peak); Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.59; H, 7.31.

Diisopropyl 2-benzoyl-3-phenylcyclopropane-1,1-dicarboxylate (5b). Colorless crystals, mp 60 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.88 (d, J = 6.3 Hz, 3H), 0.93 (d, J = 6.3 Hz, 3H), 1.10 (d, J = 6.3 Hz, 3H), 1.16 (d, J = 6.3 Hz, 3H), 3.88 (d, J = 7.9 Hz, 1H), 4.09 (d, J = 7.6 Hz, 1H), 4.81−5.03 (m, 2H), 7.24−7.31 (m, 5H), 7.47−7.63 (m, 3H), 8.11−8.14 (m, 2H), ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 21.2, 21.3, 21.4 (CH_3), 34.9, 35.1, (CH), 46.1 (4°), 69.3, 69.6 (CH), 127.5, 128.2 (CO_2), 193.3 (C═O), IR (Nujol) ν 2924, 1732, 1682 cm^{-1}, MS *m*/*z* 394 (M$^+$), 289, 105 (base peak); Anal. Calcd for $C_{24}H_{26}O_5$: C, 73.06; H, 6.65. Found: C, 72.83; H, 6.72.

Diisopropyl 2-benzoyl-3-isopropylcyclopropane-1,1-dicarboxylate (5c). Colorless crystals, mp 74 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.90 (d, J = 6.2 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H), 1.14 d, J = 6.2 Hz, 3H), 1.20 (d, J = 6.4 Hz, 3H), 1.23−1.30 (m, 3H), 1.43−1.58 (m, 1H), 1.81 (dd, J = 10.7, 9.5 Hz, 0.35 × 1H),

2.38 (dd, J = 10.6, 7.6 Hz, 0.65 × 1H), 3.45−3.51 (m, 1H), 4.88−5.20 (m, 1H), 7.45−7.60 (m, 2H), 7.97−8.05 (m, 2H), ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ, IR ($CHCl_3$) ν 3027, 2982, 1724, 1678 cm^{-1}, MS m/z, 360 (M^+), 317 (M^+-*i*-Pr, base peak); Anal. Calcd for $C_{21}H_{28}O_5$: C, 69.96; H, 7.83. Found: C, 70.04; H, 7.99.

Dibenzyl 2-acetyl-3-phenylcyclopropane-1,1-dicarboxylate (5d). Yellow oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.37 (s, 0.5 × 3H), 2.38 (s, 0.5 × 3H), 3.16 (d, J = 9.9 Hz, 0.5 × 1H), 3.33 (d J = 9.9 Hz 0.5 × 1H), 3.49 (d, J = 7.3 Hz, 0.5 × 1H), 3.70 (d, J = 7.3 Hz, 0.5 × 1H), 4.82−4.96 (m, 0.5 × 2H), 5.07−5.28 (m, 0.5 × 2H), 7.21−7.27 (m, 0.5 × 5H), 7.32−7.33 (m, 0.5 × 5H), ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 31.3 (CH_3), 32.5 (CH_3), 36.9 (CH_2), 37.6 (CH), 37.7 (CH), 38.4 (CH), 41.2 (4°), 45.9 (4°), 67.3, 67.4, 67.7, 67.87 (CH_2 × 4), 127.1, 127.5, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 130.5 (CH ×10), 130.5 (4°), 131.0, 132.8, 134.7, 137.9, 135.0 (CH × 5), 135.1 (4°), 164.3, 165.1, 165.5, 169.0 (C═O × 4), 200.8 (C═O) , IR (Nujol) ν 3034, 2953, 1736, 1713 cm^{-1}, MS, m/z, 428 (M^+), 385 (M^+-Ac), 294 (M^+-Bn), 91(base peak); Anal. Calcd for $C_{27}H_{24}O_5$: C, 75.68; H, 5.65. Found: C, 75.56; H, 5.83.

Isopropyl 2-acetyl-1-cyano-3-phenylcyclopropane-1-carboxylate (6a). Colorless crystals, mp 98 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.47 (d, J = 6.2 Hz, 6H), 2.44 (s, 3H), 3.30 (d, J = 10.5 Hz, 1H), 3.53 (d, J = 10.5 Hz, 1H), 5.21−5.35 (m, 1H), 7.36−7.49 (m, 5H), ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 21.5 (CH_3), 26.9 (4°), 32.1 (CH_3), 38.6, 40.3 (CH), 72.0 (CH), 128.3, 128.6, 128.7, 129.0, 129.3 (Ph, CH), 130.0 (Ph, 4°), 165.8 (CO_2), 198.1 (C═O), IR (Nujol) ν 2953, 2955, 2266, 1738, 1714 cm^{-1}, MS m/z 271 (M^+), 228 (M^+ - *i*-Pr), 169 (base peak); Anal. Calcd for $C_{16}H_{17}NO_2$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.60; H, 6.34; N, 5.19.

Benzyl 2-acetyl-1-cyano-3-phenylcyclopropane-1-carboxylate (6b). Colorless crystals, mp 76 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.35 (s, 3H), 3.23 (d, J = 10.5 Hz, 1H), 3.47 (d, J = 10.5 Hz, 1H), 5.32 (d, J = 2.3 Hz, 2H), 7.36−7.43 (m, 10 H), ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 26.8 (4°), 32.1 (CH_3), 38.9 (CH), 40.6 (CH), 69.0 (OCH_2), 113.2 (CN), 127.9, 128.1, 128.2, 128.4, 128.5, 128.7, 128.8, 129.1 (Ph, CH × 8), 129.8, 134.3 (Ph, 4° × 2), 166.4 (C═O), 197.9 (C═O), IR (neat) ν 3034, 2959, 2247, 1740, 1717 cm^{-1}, MS m/z 319 (M^+), 277 (M^+ -Ac), 91 (base peak); Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.21; H, 5.34; N, 4.39. Found: C, 75.25; H, 5.38; N, 4.43.

Cyclohexyl 2-acetyl-1-cyano-3-phenylcyclopropane-1-carboxylate (6c). Colorless crystals, mp 104 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.21−1.61 (m, 6H), 1.68−1.93 (m, 4H), 2.34 (s, 3H), 3.20 (d, J = 10.6 Hz, 1H), 3.43 (d, J = 10.6 Hz, 1H), 4.89−4.96 (m, 1H), 7.29−7.37 (m, 5H), ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 23.1 (CH_2 × 2), 25.0 (CH_2), 26.9 (4°), 31.0 (CH_2 × 2), 32.0 (CH_3), 38.6 (CH), 40.3 (CH), 76.4 (CH), 113.4 (CN), 128.0, 128.2, 128.4, 128.5, 129.0 (Ph, CH), 130.0 (Ph, 4°), 165.7 (CO_2), 198.1 (C═O), IR (neat) ν 3061, 3032, 2247, 1710, 1682 cm^{-1}, MS, m/z, 311 (M^+), 227 (M^+-*c*-Hex, base peak); Anal. Calcd for $C_{19}H_{21}NO_3$: C, 72.29; H, 6.80; N, 4.50. Found: C, 72.23; H, 6.74; N, 4.36.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for cyclopropanated products and X-ray data (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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