Novel Photochemical Hydrolysis of *o*-Acetylphenylacetonitriles to Amides

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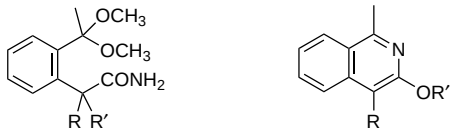
Received December 4, 1995[⊗]

Irradiation of *o*-acetylphenylacetonitriles **1a**,**b** in methanol (λ >280 nm) leads to essentially quantitative photohydrolysis with formation of the corresponding ketal amides **3a**,**b**. The mechanism proposed for this novel reaction is supported by the qualitatively different photochemical behavior of **1c** and by a labeling experiment with **1a-L** that confirms transfer of the carbonyl oxygen atom of **1a** to the amide oxygen atom of **3a**.

In the course of another study we had occasion to irradiate *o*-acetylphenylacetonitrile (**1a**) in methanol and were surprised to isolate after chromoatographic purification a good yield of the corresponding amide **2a**. We

1 **2**



3 **4**

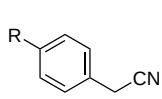
a, R = R′ = H; **b**, R = CH_3, R′ = H; **c**, R = R′ = CH_3

have now investigated the mechanism of this unexpected hydrolysis and report our findings for **1a** and the related nitriles **1b**,**c** below.[1] Photochemical results are discussed first, followed by presentation of the straightforward synthesis of necessary compounds.

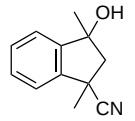
Photochemical Experiments. The first indication of how hydrolysis of **1a** occurs came with the observation that **2a** is not the direct product of the photochemical reaction. If the reaction mixture is worked up after irradiation without chromatography or use of acid, the product obtained in essentially quantitative yield is dimethyl ketal **3a**. This ketal undergoes smooth hydrolysis to **2a** on chromatography over silica gel or on very mild treatment with acid. Further acid treatment of **2a** leads to the yellow 3-hydroxy-1-methylisoquinoline (**4a**),[2] which was sometimes observed in minor amounts on acid workup of the photochemical reaction.[3]

Isolation of **3a** as the reaction product solves the initial puzzle of how hydrolysis of a nitrile takes place in methanol; more specifically, it suggests that conversion of **1a** into **3a** follows the path shown in Scheme 1. Thus, irradiation of **1a** leads through unexceptional γ-hydrogen abstraction[4] to biradical **5a**, which relaxes to **6a**.[5] The stereochemistry of the hydroxyl and cyano groups of **6a** permits cyclization to the corresponding iminolactone **7a**, which then rearomatizes to **8a** on 1,4 addition of methanol. The aromatic iminolactone **8a** can add another molecule of methanol, probably by way of the highly stabilized carbocation **9a** formed on protonation and heterolytic cleavage, finally furnishing the isolated ketal amide **3a**.

Several experiments support this mechanistic scheme. As the mechanism permits, the methyl-substituted nitrile **1b** behaves in an analogous fashion, furnishing ketal **3b** on irradiation and workup in the absence of acid and ketone **2b**, along with small amounts of isoquinoline **4b** and the related methyl ether **4c**, in the presence of acid. Intermediates **5b**−**9b** readily account for this behavior. As the mechanism also requires, neither phenylacetonitrile (**10**) nor *p*-acetylphenylacetonitrile (**11**) undergoes hydrolysis under these conditions. Each is recovered unchanged from the irradiation conditions.



10, R = H
11, R = CH_3CO



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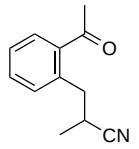

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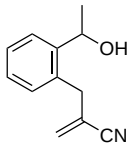

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The mechanism in the scheme also implies that dimethyl-substituted nitrile **1c** cannot react as **1a**,**b** do. In fact, we found that **1c** behaves quite differently under these conditions. Irradiation of **1c** furnished a crude reaction mixture whose infrared spectrum showed no sign of amide absorption. Workup led to four isomeric photochemical products, all of which retain the nitrile functionality. Two of these products are the two diastereomeric hydroxy nitriles **12**, which are formed in the ratio 83:17. The major isomer of **12** could be obtained pure and has been fully characterized. The other two products

[⊗] Abstract published in *Advance ACS Abstracts,* May 1, 1996.

(1) A preliminary communication has appeared: Lu, Q.; Bovonsombat, P.; Agosta, W. C. *Tetrahedron Lett.* **1995**, *36*, 8941.

(2) This compound has been previously reported: Alpha, B.; Anklam, E.; Deschenaux, R.; Lehn, J.-M. *Helv. Chim. Acta* **1988**, *71*, 1042. The ^{1}H NMR spectrum of our sample of **4a** was compatible with that on record.

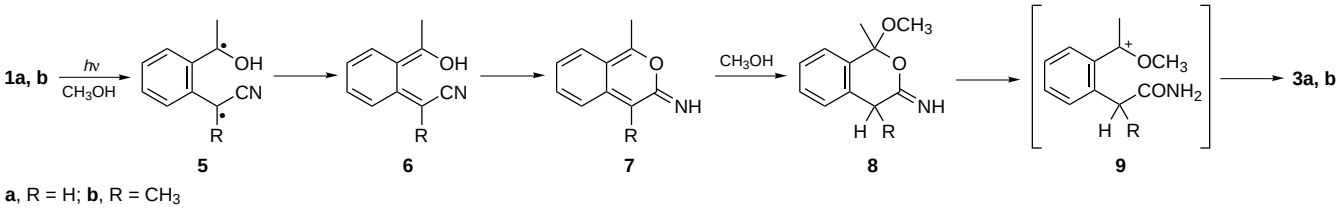
(3) Related cyclizations to 3-hydroxyisoquinolines have been studied: Jones, D. W. *J. Chem. Soc. C* **1969**, 1729. For a relevant review, see: Hazai, L. *Adv. Heterocycl. Chem.* **1991**, *52*, 155.

(4) Wagner, P. J. *Pure Appl. Chem.* **1977**, *49*, 259.

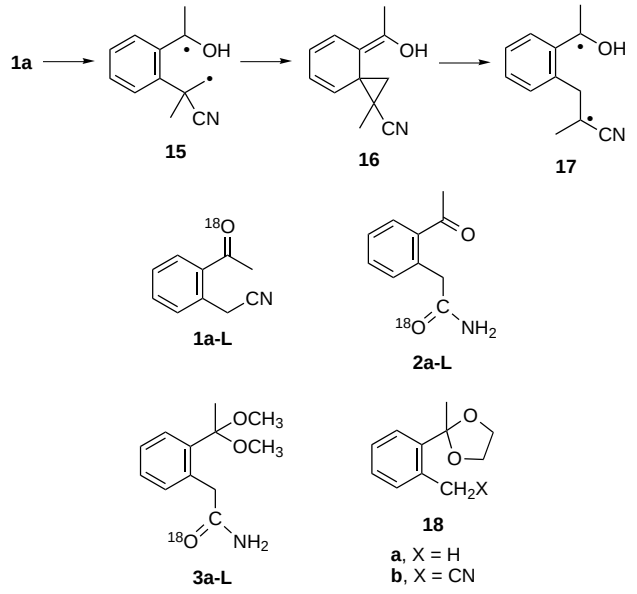
(5) Biradical **5a** presumably also relaxes to geometric isomers of **6a**, and these then revert to **1a**. For information on the distribution of enol isomers on γ-hydrogen abstraction in simple *o*-methylphenones, see: Haag, R.; Wirz, J.; Wagner, P. J. *Helv. Chem. Acta* **1977**, *60*, 2595.

S0022-3263(95)02147-5 CCC: $12.00

Scheme 1



Scheme 2



are the rearranged keto nitrile **13** and the isomeric unsaturated hydroxy nitrile **14**. All of these photorearrangements of **1c** can be accounted for by way of abstraction of δ-hydrogen[6] to yield **15**. This biradical can collapse to **12** or close to **16**, as shown (Scheme 2). After **16** reopens to **17**, both **13** and **14** can be formed through appropriate 1,6 hydrogen transfers. Precedents for each of these steps are available from earlier studies of δ abstraction from the ortho position in aromatic ketones.[6] For our present purposes, the behavior of **1c** underscores the necessity of a γ-hydrogen for hydrolysis of the nitrile.

Finally the mechanistic scheme requires that the oxygen atom of the carbonyl group of **1a**,**b** becomes the carbonyl oxygen of the product amide and that in methanol as solvent this transfer of oxygen be clean and complete. We investigated this prediction using **1a-L** containing 55% ^{18}O in the carbonyl group, as indicated by its mass spectrum. Irradiation of **1a-L** under the conditions used for **1a** furnished **2a-L** and **3a-L,** the NMR and mass spectra of which were examined. Earlier work has shown that ^{18}O-substitution induces a small upfield shift in the carbonyl carbon signal in ^{13}C-NMR spectra.[7] This effect was apparent in **1a-L**, which showed ^{13}C-NMR signals at δ 200.255 for the ^{18}O-carbonyl carbon and δ 200.300 for the ^{16}O-carbonyl carbon. The NMR spectrum of **2a-L** had two amide carbonyl signals of essentially equal size, one at δ 171.809 and the other at δ 171.781, and a single ketone carbonyl signal at δ 201.847. Mass spectra of both **2a-L** and **3a-L** showed each to contain 53−55% of one atom of ^{18}O; fragmentation patterns confirmed in each case that this ^{18}O atom is located at the amide carbonyl group. These results thus fully support the mechanistic requirement that the carbonyl oxygen of **1a** becomes the amide carbonyl oxygen of **2a** and **3a**. We also measured the quantum yields for reaction of **1a**,**b** using the concomitant formation of acetophenone from γ-chlorobutyrophenone[8] as an actinometer and found them to be 0.1 (4.8% conversion) for disappearance of **1a** and 0.03 (1.5% conversion) for **1b**.[9]

Preparative Experiments. Cyano ketone **1a**[10] was prepared from the ethylene ketal of *o*-methylacetophenone (**18a**) through benzylic bromination with *N*-bromosuccinimide,[11] followed by reaction with sodium cyanide[12] and then deketalization of **18b**. The para isomer **11**[13] was prepared in the same manner from *p*-methylacetophenone. For **1b**, ketal **18b** was methylated using sodium hydride and methyl iodide in dimethyl sulfoxide.[14] The ketal of **1b** was deketalized by treatment with aqueous HCl in acetone. Dimethyl nitrile **1c** was available through deprotonation of either **18b** or the ketal of **1b** with lithium diisopropylamide in tetrahydrofuran containing hexamethylphosphoramide and treatment with methyl iodide.[15] Deketalization of the ketal of **1c** was most satisfactory using a three-phase system consisting of aqueous oxalic acid, silica gel, and methylene chloride.[16] Labeled ketone **1a-L** was also synthesized from **18b** through treatment with $H_2{}^{18}O$ in the presence of camphorsulfonic acid in hot tetrahydrofuran.[7] Mass spectral analysis of the product **1a-L** showed it to contain 55% of one atom of ^{18}O.

Experimental Section

Material and Equipment. Analytical GLC was carried out on a HP-5890 temperature-programmable gas chromatograph using a capillary (30 m × 0.25 mm) column with a film thickness of 0.25 μm. All NMR spectra were recorded at 300 MHz and are reported in ppm downfield from TMS employed as an internal standard (δ). All spinning-disk chromatographic separations were carried out on a Chromatotron (Harrison Model-7924 T) using silica gel coated (1, 2, or 4 mm thick) glass rotors. All reactions sensitive to moisture and air were performed under argon. All organic solutions obtained by workup of the reaction mixture were washed with brine and dried over anhydrous $MgSO_4$ prior to removal of solvent.

(6) Wagner, P. J. *Acc. Chem. Res.* **1989**, *22*, 83, and references cited therein.

(7) Risley, J. M.; DeFrees, S. A.; Van Etten, R. L. *Org. Magn. Reson.* **1983**, *21*, 28 and references cited therein.

(8) For type II reaction of γ-chlorobutyrophenone, Φ is reported to be 0.09: Wagner, P. J. *Acc. Chem. Res.* **1971**, *4*, 168.

(9) For a discussion of the factors that control hydrogen abstraction and its reversion in *o*-alkylphenones, see: Wagner, P. J.; Chen, C-P. *J. Am. Chem. Soc.* **1976**, *98*, 239. An additional limitation on the efficiency of reaction of **1a,b** is the requirement that enol **6a,b** be formed.

(10) Freerksen, R. W.; Pabst, W. E.; Raggio, M. L.; Sherman, S. A.; Wroble, R. R.; Watt, D. S. *J. Am. Chem. Soc.* **1977**, *99*, 1536.

(11) Anzalone, L.; Hirsch, J. A. *J. Org. Chem.* **1985**, *50*, 2128.

(12) Friedman, L.; Schechter, H. *J. Org. Chem.* **1960**, *25*, 877.

(13) Kluiber, R. W. *J. Org. Chem.* **1966**, *31*, 1298.

(14) Bloomfield, J. J. *J. Org. Chem.* **1961**, *26*, 4112.

(15) MacPhee, J.-A.; Dubois, J.-E. *Tetrahedron* **1980**, *36*, 775.

(16) Huet, F.; Lechevallier, A.; Pellet, M.; Conia, J. M. *Synthesis* **1978**, 63.

Preparation of *o*-Acetylphenylacetonitrile (1a). *o*-Acetylphenylacetonitrile was prepared from *o*-methylacetophenone through the formation of the ethylene ketal, followed by bromination with NBS, and reaction with NaCN to give ketal **18b**. The ketal **18b** obtained in this way was used in preparation of **1a-L** and **1b** after purification. Deketalization of **18b** with dilute HCl yielded **1a**. Spectral data (^{1}H NMR, IR, MS) were identical with those reported:[10] ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.3, 135.3, 132.9, 130.9, 130.7, 130.6, 128.4, 118.0, 28.7, 23.1.

Preparation of 2-(*o*-Acetylphenyl)propionitrile (1b). To a stirred suspension of NaH (140 mg, 80% dispersion in mineral oil) in DMSO (3 mL) was added a solution of ethylene ketal **18b** (580 mg, 2.8 mmol) and methyl iodide (513 mg, 3.6 mmol) in dry ether (3 mL). The reaction mixture was stirred at rt for 2.25 h and then cooled in ice water. 2-Propanol (0.2 mL) was added dropwise, followed by the addition of water (5 mL). The aqueous layer was extracted three times with ether. The combined ethereal layers were washed with dilute HCl, water, and brine, then dried, and concentrated in vacuo. After purification, the ketal obtained in this way was used in the preparation of **1c** described below. The crude reaction mixture was then dissolved in acetone (7.5 mL), treated with HCl (6 N, 1.5 mL), and stirred at rt for 1.25 h. After removal of solvent, the aqueous layer was extracted three times with ether. The combined ethereal layer was washed with dilute Na_2CO_3, water, and brine, then dried, and concentrated in vacuo. The residue was purified by chromatography to give **1b** (320 mg, 66%) as a colorless liquid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83 (dd, 1 H, J = 7.5, 1.5 Hz), 7.71 (dd, 1 H, J = 7.8, 1.2 Hz), 7.58 (td, 1 H, J = 7.5, 1.2 Hz), 7.46 (td, 1 H, J = 7.5, 1.2 Hz), 4.96 (q, 1 H, J = 6.9 Hz), 2.63 (s, 3 H), 1.61 (d, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.8, 137.7, 135.1, 132.8, 130.4, 128.9, 127.9, 122.2, 29.2, 28.0, 21.6; IR (neat) 2241, 1684, 1600 cm^{-1}; MS m/z 174.0925 [(M + H)$^+$, calcd for $C_{11}H_{12}NO$ 174.0919].

Preparation of 2-(*o*-Acetylphenyl)-2-methylpropionitrile (1c). To a stirred solution of LDA (2.0 M, 1.0 mL, 2.0 mmol) in dry THF (1 mL) was added the ethylene ketal of **1b** (200 mg, 0.92 mmol) in THF (1 mL) slowly, followed by HMPA (720 mg) at 0−2 °C. The reaction mixture was stirred at this temperature for 0.5 h, and methyl iodide (230 mg, 3.7 mmol) was then added. After being stirred for 0.5 h, the mixture was allowed to warm to rt followed by pouring onto ice water. The aqueous layer was extracted three times with ether. The combined ethereal layer was washed with water and brine and then dried and concentrated in vacuo. The residue was purified by chromatography to give a mixture of ketal dimethyl nitrile and unreacted starting material. The mixture in CH_2Cl_2 (1.0 mL) was then added at rt to a stirred suspension of silica gel (680 mg), aqueous oxalic acid (10%, 68 mg), and CH_2Cl_2 (3.5 mL).[16] The reaction was monitored by GC. After the reaction was complete, Na_2CO_3 was added and the mixture was stirred for 5 min. The mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography to give **1c** (76 mg, 44%) as a white solid: mp 88−89 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48−7.39 (m, 4 H), 2.70 (s, 3 H), 1.86 (s, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.7 140.8, 138.7, 130.6, 127.5, 126.0, 124.6, 36.5, 31.1, 29.5; IR ($CHCl_3$) 2237, 1696, 1598, cm^{-1}; HRMS m/z 188.1072 [(MH)$^+$, calcd for $C_{12}H_{14}NO$ 188.1075].

Preparation of *p*-Acetylphenylacetonitrile (11). *p*-Acetylphenylacetonitrile was prepared from *p*-methylacetophenone as described for **1a**. Its spectral data (^{1}H NMR, IR) are identical with those reported:[13] ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.3, 136.7, 135.1, 129.0, 128.1, 117.2, 26.6, 23.5.

Preparation of [^{18}O]-*o*-Acetylphenylacetonitrile (1a-L). A mixture of ethylene ketal **18b** (306 mg, 1.5 mmol), 10-camphorsulfonic acid (34 mg, 0.15 mmol), and $H_2{}^{18}O$ (54 mg, 3 mmol) in dry THF (3 mL) was heated under reflux for 4 h, following a known procedure.[7] The mixture was allowed to cool to rt and concentrated in vacuo. The residue was purified by chromatography to give **1a-L** (188 mg, 79%): ^{13}C NMR ($CDCl_3$, 75 MHz) showed a signal at δ 200.255 for C=^{18}O and a signal at δ 200.300 for C=^{16}O. Mass spectral analysis showed it to contain 55% of one atom of ^{18}O.

Preparative Photochemistry. All preparative experiments were carried out using a Hanovia 450-W medium-pressure mercury arc lamp in Pyrex equipment (λ >280 nm). Irradiations were carried out using toroidal Pyrex vessels in degassed methanol.

A. *o*-Acetylphenylacetonitrile (1a). A solution (50 mL) of **1a** (120 mg, 0.75 mmol) containing H_2O (20 mg, 1.1 mmol) was irradiated for 8 h. Solvent was removed in vacuo to give **3a** as a yellow oil. ^{1}H NMR showed that **1a** was converted into **3a** quantitatively. Purification by chromatography on silica gel gave **2a** as a white solid. For **3a**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56−7.52 (m, 1 H), 7.28−7.24 (m, 3 H), 6.24 (bs, 1 H), 5.82 (bs, 1 H), 3.77 (s, 2 H), 3.21 (s, 6 H), 1.53 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.8, 140.7, 133.3, 132.5, 128.2, 127.9, 127.2, 102.9, 48.7, 41.8, 25.2; IR ($CHCl_3$) 1679, 1590, cm^{-1}; MS m/z 246.1119 [(M + Na)$^+$, calcd for $C_{12}H_{17}NO_2Na$ 246.1106]. For **2a**: mp 206−209 °C dec; ^{1}H NMR (acetone-d_6, 300 MHz) δ 7.79 (dd, 1 H, J = 7.5, 1.2 Hz), 7.46−7.31 (m, 3 H), 6.81 (bs, 1 H), 5.15 (bs, 1 H), 3.76 (s, 2 H), 2.55 (s, 3 H); ^{13}C NMR (acetone-d_6, 75 MHz) δ 201.8, 171.8, 139.0, 135.1, 131.8, 130.9, 128.7, 126.6, 40.0, 28.5; IR (CH_3CN) 1690, 1630, 1600, cm^{-1}; MS m/z 177.0790 [M$^+$, calcd for $C_{10}H_{11}NO_2$-177.0790].

B. 2-(*o*-Acetylphenyl)propionitrile (1b). A solution of **1b** (70 mg, 0.40 mmol) and H_2O (10 mg, 0.56 mmol) in methanol (27 mL) was irradiated for 9 h. Solvent was removed in vacuo. The residue was purified by chromatography to give **3b** (43 mg, 45%), **4b** (5 mg, 7%), and **4c** (5 mg, 7%). For **3b**: mp 118−120 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51 (dd, 1 H, J = 7.8, 1.8 Hz), 7.44 (dd, 1 H, J = 7.8, 1.8 Hz), 7.32−7.20 (m, 2 H), 6.12 (bs, 1 H), 5.80 (bs, 1 H), 4.49 (q, 1 H, J = 7.2), 3.37 (s, 3 H), 3.24 (s, 3 H), 1.61 (s, 3 H), 1.42 (d, 3 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.2, 140.8, 139.2, 128.7, 128.5, 127.1, 126.5, 103.1, 49.5, 48.7, 40.6, 25.0, 18.5; IR ($CHCl_3$) 1683, 1592, cm^{-1}; MS m/z 260.1276 [(M + Na)$^+$, calcd for $C_{13}H_{19}NO_3Na$ 260.1263]. For **4b**: mp 204−205 °C dec; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.87 (d, 1 H, J = 8.4 Hz), 7.74 (d, 1 H, J = 9.0 Hz), 7.54−7.49 (m, 1 H), 7.21−7.16 (m, 1 H), 2.95 (s, 3 H), 2.51 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.4, 149.9, 140.0, 130.6, 126.3, 123.0, 122.0, 119.9, 109.8, 18.2, 10.4; IR ($CHCl_3$): 1633 cm^{-1}; MS m/z 173.0837 [M$^+$, calcd for $C_{11}H_{11}$-NO 173.0841]. For **4c** (5 mg, 7%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.03 (d, 1 H, J = 8.4 Hz), 7.88 (d, 1 H, J = 8.7 Hz), 7.60 (m, 1 H), 7.36 (m, 1 H), 4.08 (s, 3 H), 2.90 (s, 3 H), 2.48 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.9, 154.0, 138.2, 129.2, 126.0, 123.4, 123.0, 122.9, 107.4, 53.7, 21.8, 10.0; IR ($CHCl_3$) 1620, 1587, 1565, cm^{-1}; MS m/z 187.0999 [M$^+$, calcd for $C_{12}H_{13}NO$ 187.0997].

C. 2-(*o*-Acetylphenyl)-2-methylpropionitrile (1c). A solution of **1c** (129 mg, 0.69 mmol) and H_2O (20 mg, 1.1 mmol) in methanol (46 mL) was irradiated for 1 h. Solvent was removed in vacuo. The residue was purified by chromatography to give four products, the two diasteromeric hydroxy nitriles **12** (15 mg, 12%, ratio of two isomers is 83:17), **13** (44 mg, 34%), and **14** (25 mg, 19%). For major isomer of **12**: mp 71−73 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40−7.22 (m, 4 H), 3.38 (d, 1 H, J = 15.6), 3.07 (d, 1 H, J = 15.9), 1.98 (s, 1 H), 1.74 (s, 3 H), 1.49 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.0, 137.4, 129.1, 128.0, 125.2, 123.5, 123.0, 82.7, 47.6, 42.6, 25.3, 19.5; IR ($CHCl_3$) 3442, 2238, cm^{-1}; MS m/z 187.0994 [M$^+$, calcd for $C_{12}H_{13}NO$ 187.0997]. For **13**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83 (d, 1 H, J = 7.8 Hz), 7.51 (dt, 1 H, J = 7.5, 1.5 Hz), 7.40 (t, 2 H, J = 7.5 Hz), 3.24 (dd, 1 H, J = 12.3, 4.8 Hz), 3.11−3.04 (qm, 1 H, J_1 = 6.9 Hz), 2.93 (dd, 1 H, J = 12.3, 9.9 Hz), 2.62 (s, 3 H), 1.41 (d, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.2, 138.0, 136.6, 132.7, 132.3, 130.5, 127.5, 122.8, 38.9, 29.3, 27.6, 18.2; IR (neat) 2239, 1683, 1600, cm^{-1}; MS m/z 188.1072 [(M + H)$^+$, calcd for $C_{12}H_{14}NO$ 188.1075]. For **14**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58 (dd, 1 H, J = 7.8, 1.2 Hz), 7.43−7.26 (m, 2 H), 7.17 (d, 1 H, J = 7.2), 5.95 (s, 1 H), 5.63 (t, 1 H, J = 1.5 Hz), 5.09 (q, 1 H, J = 6.3), 3.69 (d, 2 H, J = 1.5 Hz), 1.91 (s, 1 H), 1.51 (d, 3 H, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.9, 131.9, 131.0, 130.4, 128.2, 127.9,

125.9, 122.6, 118.5, 66.6, 36.9, 24.5; IR ($CHCl_3$) 3457, 2227 cm^{-1}; MS *m/z* 187.1242 [$(M + NH_4 - H_2O)^+$, calcd for $C_{12}H_{15}N_2$ 187.1235].

D. [^{18}O]-*o*-Acetylphenylacetonitrile (1a-L). The procedure described for **1a** was employed. ^{13}C NMR (acetone-d_6, 75 MHz) of **2a-L** showed amide carbonyl signals at δ 171.809 and 171.781 and a single ketone carbonyl signal at δ 201.847. Mass spectral analyses of **2a-L** and **3a-L** showed each to contain 53−55% ^{18}O; the fragmentation patterns indicated that ^{18}O is located at the amide carbonyl.

Quantum Yield Measurements. All measurements were made at $\lambda \sim$313 nm in wet methanol in a merry-go-round with the concomitant formation of acetophenone from 4-chlorobutyrophenone[8] in benzene as the actinometer. Conversion was limited to <5%. Results were Φ (for disappearance) 0.1 (**1a**) and 0.03 (**1b**).

Acknowledgment. This research was supported by the National Science Foundation. NMR spectra were determined on instruments purchased with funds from the National Science Foundation, the National Institutes of Health, and the Keck Foundation.

Supporting Information Available: ^{1}H or ^{13}C NMR spectra for compounds **1b**,**c**, **2a**, **3a**,**b**, **4b**,**c**, **12** (one diastereomer), **13**, and **14** (10 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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