

## Photocyclization of *NN*-Disubstituted Benzoylacetamides and Acetoacetamides

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*NN*-Dialkyl-benzoylacetamides (1a—e and j—n) and -acetoacetamides (1f—i), and *N*-methylbenzoylacetanilide (1o) undergo photocyclization involving  $\delta$ -hydrogen abstraction by the ketone carbonyl group to give *N*-substituted 4-hydroxypyrrolidin-2-ones (2a—o) in high yields.

ALTHOUGH the photochemistry of  $\beta$ -diketones<sup>1-5</sup> and  $\beta$ -oxo-esters<sup>5-7</sup> has been studied extensively, that of  $\beta$ -oxo-amides has been paid little attention.<sup>8-10</sup> Photocyclization involving intramolecular hydrogen abstraction by excited carbonyl oxygen is a well known reaction of carbonyl compounds;<sup>11</sup> however, much less is known about the cyclization of  $\beta$ -dicarbonyl compounds.<sup>12</sup> We report here the photocyclization of  $\beta$ -oxo-amides involving hydrogen abstraction by ketone carbonyl.

Irradiation of a solution of *NN*-dimethylbenzoylacetamide (1a) in a Pyrex vessel under nitrogen with a high-pressure mercury lamp gave 4-hydroxy-1-methyl-4-phenylpyrrolidin-2-one (2a) in 88% yield. Similarly,

irradiation of the  $\beta$ -oxo-amides (1b—k) gave the corresponding 4-hydroxypyrrolidin-2-ones (2b—k') in high yields. In the cases of the oxo-amides (1i, j, and k) stereoisomers (2i and i'; j and j'; k and k') were formed, whereas only one isomer was produced from the oxo-amides (1b—c, e, and g). The structures of the pyrrolidin-2-ones (2a—k') were elucidated by i.r., n.m.r., and mass spectra, and by elemental analyses. The i.r. spectra showed characteristic hydroxy (*ca.* 3 300 cm<sup>-1</sup>) and five-membered lactam carbonyl absorptions (*ca.* 1 660—1 680 cm<sup>-1</sup>).

The configurations of the substituents in the pyrrolidin-2-ones were elucidated on the basis of the n.m.r. spectra.† The n.m.r. spectrum of (2d) showed peaks at

† The absolute configuration of the substituents is not still elucidated.

<sup>1</sup> C. K. Johnson, B. Dominy, and W. Reusch, *J. Amer. Chem. Soc.*, 1963, **85**, 3894.

<sup>2</sup> P. De Mayo, H. Takeshita, and A. B. M. A. Sattar, *Proc. Chem. Soc.*, 1962, 119.

<sup>3</sup> G. Kornis and P. De Mayo, *Canad. J. Chem.*, 1964, **42**, 2822.

<sup>4</sup> R. B. LaCount and C. E. Griffin, *Tetrahedron Letters*, 1965, 1549.

<sup>5</sup> D. Veierov, T. Bercovici, E. Fisher, Y. Mazur, and A. Yogev, *J. Amer. Chem. Soc.*, 1973, **95**, 8173.

<sup>6</sup> P. Markov, L. Shiskova, and Z. Zdravkova, *Tetrahedron Letters*, 1972, 4017.

<sup>7</sup> S. P. Singh and J. Kagan, *Chem. Comm.*, 1969, 1121.

<sup>8</sup> J. Reisch and D. Niemeyer, *Tetrahedron Letters*, 1968, 3247.

<sup>9</sup> J. Reisch and D. H. Niemeyer, *Tetrahedron*, 1971, **27**, 4637.

<sup>10</sup> W. R. Oliver and L. R. Hamilton, *Tetrahedron Letters*, 1971, 1837.

<sup>11</sup> A. A. Lamola and N. J. Turro, 'Energy Transfer and Organic Photochemistry,' Interscience, New York, 1969.

<sup>12</sup> T. Hasegawa and H. Aoyama, *J.C.S. Chem. Comm.*, 1974, 743.



The  $\beta$ -oxo-amides and  $\beta$ -oxo-anilide were prepared according to previously described methods.<sup>14-19</sup>

**General Procedure for Photoreactions of  $\beta$ -Oxo-amides.**—A solution of the  $\beta$ -oxo-amide (1) in benzene was irradiated in a Pyrex vessel under nitrogen with a high-pressure mercury lamp for 1–50 (1a–e and j–o) or 160–200 h (1f–i). The solvent was removed and the residue chromatographed on silica gel. Elution with benzene–ethyl acetate afforded the pyrrolidin-2-one (2).

(i) 4-Hydroxy-4-phenylpyrrolidin-2-one (2a) had m.p. 139–140 °C;  $\nu_{\max}$ (KBr) 3 275 and 1 660  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  2.80 (2 H, ABq,  $J$  17.3 Hz, 3-H<sub>2</sub>), 2.87 (3 H, s, NCH<sub>3</sub>), 3.53 (2 H, ABq,  $J$  10.5 Hz, 5-H<sub>2</sub>), 3.77br (1 H, s, OH, D<sub>2</sub>O-exchangeable), and 7.2–7.5 (5 H, m, aromatic) (Found: C, 69.3; H, 6.8; N, 7.1. C<sub>11</sub>H<sub>13</sub>NO<sub>2</sub> requires C, 69.1; H, 6.85; N, 7.35%).

(ii) 1-Ethyl-4-hydroxy-5-methyl-4-phenylpyrrolidin-2-one (2b) had m.p. 148–149 °C;  $\nu_{\max}$ (KBr) 3 220 and 1 670  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  1.00 (3 H, t,  $J$  7.2 Hz, CH<sub>2</sub>·CH<sub>3</sub>), 1.11 (3 H, d,  $J$  5.8 Hz, 5-CH<sub>3</sub>), 2.74 (2 H, ABq,  $J$  18.0 Hz, 3-H<sub>2</sub>), 3.05 (1 H, q,  $J$  5.8 Hz, 5-H), 3.65 (2 H, q,  $J$  7.2 Hz, NCH<sub>2</sub>·CH<sub>3</sub>), 3.80 (1 H, s, OH), and 7.1–7.6 (5 H, m, aromatic) (Found: C, 71.15; H, 7.8; N, 6.2. C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub> requires C, 71.2; H, 7.8; N, 6.4%).

(iii) 5-Ethyl-4-hydroxy-4-phenyl-1-n-propylpyrrolidin-2-one (2c) had m.p. 91–91.5 °C;  $\nu_{\max}$ (KBr) 3 350 and 1 680  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  0.78 (3 H, t,  $J$  6.5 Hz, CH<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>), 0.89 (3 H, t,  $J$  6.5 Hz, CH<sub>2</sub>·CH<sub>3</sub>), 1.2–2.0 (4 H, m, CH<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub> and CH<sub>2</sub>·CH<sub>3</sub>), 2.80 (2 H, ABq,  $J$  17.1 Hz, 3-H<sub>2</sub>), 2.91 (1 H, t,  $J$  6.8 Hz, 5-H), 3.13br (1 H, s, OH), 3.72 (2 H, t,  $J$  6.9 Hz, NCH<sub>2</sub>), and 7.2–7.6 (5 H, m, aromatic) (Found: C, 72.8; H, 8.4; N, 5.5. C<sub>15</sub>H<sub>21</sub>NO<sub>2</sub> requires C, 72.85; H, 8.55; N, 5.65%).

(iv) 4-Hydroxy-1-isopropyl-5,5-dimethyl-4-phenylpyrrolidin-2-one (2d) had m.p. 193–194 °C;  $\nu_{\max}$ (KBr) 3 200 and 1 675  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  0.77 (3 H, s, 5-CH<sub>3</sub> *cis* to 4-Ph), 1.36 (3 H, s, 5-CH<sub>3</sub> *trans* to 4-Ph), 1.42 (6H, d,  $J$  7.5 Hz, CHMe<sub>2</sub>), 2.83 (2 H, ABq,  $J$  15.1 Hz, 3-H<sub>2</sub>), 3.05br (1 H, s, OH, D<sub>2</sub>O-exchangeable), 3.36 (1 H, septet,  $J$  7.5 Hz, CHMe<sub>2</sub>), and 7.2–7.6 (5 H, m, aromatic) (Found: C, 73.0; H, 8.75; N, 5.65. C<sub>15</sub>H<sub>21</sub>NO<sub>2</sub> requires C, 72.85; H, 8.55; N, 5.65%).

(v) 1-Benzyl-4-hydroxy-4,5-diphenylpyrrolidin-2-one (2e) had m.p. 137–138 °C;  $\nu_{\max}$ (KBr) 3 300 and 1 675  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  3.00 (2 H, ABq,  $J$  15.6 Hz, 3-H<sub>2</sub>), 3.08br (1 H, s, OH, D<sub>2</sub>O-exchangeable), 3.57 (1 H, d,  $J$  15.0 Hz, NCH<sub>2</sub>·Ph), 4.53 (1 H, s, 5-H), 5.24 (1 H, d,  $J$  15.0 Hz, NCH<sub>2</sub>·Ph), and 6.5–7.25 (15 H, m, aromatic);  $m/e$  343 ( $M^+$ ) (Found: C, 80.35; H, 6.15; N, 4.05. C<sub>23</sub>H<sub>21</sub>NO<sub>2</sub> requires C, 80.45 H, 6.15; N, 4.1%).

(vi) 4-Hydroxy-1,4-dimethylpyrrolidin-2-one (2f) had b.p. 125 °C at 2 mmHg;  $\nu_{\max}$ (film) 3 400 and 1 670  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  1.42 (3H, s, 4-CH<sub>3</sub>), 2.44 (2 H, s, 3-H<sub>2</sub>), 2.81 (3 H, s, NCH<sub>3</sub>), 3.33 (2 H, s, 5-H<sub>2</sub>), and 3.65 (1 H, s, OH, D<sub>2</sub>O-exchangeable);  $m/e$  129 ( $M^+$ ) (Found: C, 55.3; H, 8.5; N, 10.65. C<sub>6</sub>H<sub>11</sub>NO<sub>2</sub> requires C, 55.8; H, 8.6; N, 10.85%).†

(vii) 1-Ethyl-4-hydroxy-4,5-dimethylpyrrolidin-2-one (2g) had b.p. 155 °C at 4 mmHg;  $\nu_{\max}$ (film) 3 350 and 1 670

$\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  1.17 (3 H, t,  $J$  5.9 Hz, CH<sub>2</sub>·CH<sub>3</sub>), 1.27 (3 H, d,  $J$  7.5 Hz, 5-CH<sub>3</sub>), 1.39 (3 H, s, 4-CH<sub>3</sub>), 2.46 (2 H, s, 3-H<sub>2</sub>), 2.64 (1 H, s, OH, D<sub>2</sub>O-exchangeable), 2.96 (1 H, q,  $J$  7.5 Hz, 5-H), and 3.57 (2 H, q,  $J$  5.9 Hz, NCH<sub>2</sub>·CH<sub>3</sub>) (Found: C, 60.45; H, 9.4; N, 8.7. C<sub>8</sub>H<sub>15</sub>NO<sub>2</sub> requires C, 61.1; H, 9.6; N, 8.9%).†

(viii) 4-Hydroxy-1-isopropyl-4,5,5-trimethylpyrrolidin-2-one (2h) had m.p. 72.5–73 °C;  $\nu_{\max}$ (KBr) 3 300 and 1 665  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  1.17 (6 H, d,  $J$  6.4 Hz, CHMe<sub>2</sub>), 1.25 (3 H, s, 5-CH<sub>3</sub>), 1.33 (3 H, s, 4-CH<sub>3</sub>), 1.45 (3 H, s, 5-CH<sub>3</sub>), 2.37 (2 H, s, 3-H<sub>2</sub>), 3.45 (1 H, septet,  $J$  6.4 Hz, CHMe<sub>2</sub>), and 3.49 (1 H, s, OH, D<sub>2</sub>O-exchangeable) (Found: C, 65.1; H, 10.2; N, 7.45. C<sub>10</sub>H<sub>19</sub>NO<sub>2</sub> requires C, 64.85; H, 10.35; N, 7.6%).

(ix) The 1-benzyl-4-hydroxy-4-methyl-5-phenylpyrrolidin-2-ones (2i and i') could not be separated because of difficulties in crystallization and distillation. The 6:1 mixture had  $\nu_{\max}$ (film) 3 375 and 1 670  $\text{cm}^{-1}$ . The isomer (2i) showed  $\delta(\text{CDCl}_3)$  1.28 (3 H, s, 4-CH<sub>3</sub>), 2.1br (1 H, s, OH), 2.54 (2 H, ABq,  $J$  16.2 Hz, 3-H<sub>2</sub>), 3.50 (1 H, d,  $J$  15.0 Hz, NCH<sub>2</sub>·Ph), 4.14 (1 H, s, 5-H), 5.16 (1 H, d,  $J$  15.0 Hz, NCH<sub>2</sub>·Ph), and 6.9–7.5 (10 H, m, aromatic); the isomer (2i') showed  $\delta(\text{CDCl}_3)$  0.92 (3 H, s, 4-CH<sub>3</sub>), 2.1br (1 H, s, OH), 2.54 (2 H, ABq,  $J$  16.2 Hz, 3-H<sub>2</sub>), 3.50 (1 H, d,  $J$  15.0 Hz, NCH<sub>2</sub>·Ph), 4.31 (1 H, s, 5-H), 5.16 (1 H, d,  $J$  15.0 Hz, NCH<sub>2</sub>·Ph), and 6.9–7.5 (10 H, m, aromatic).

(x) The 1-benzyl-4-hydroxy-3-methyl-4,5-diphenylpyrrolidin-2-ones (2j and j') could not be separated. The 7:3 mixture had m.p. 135–151 °C;  $\nu_{\max}$ (KBr) 3 330 and 1 670  $\text{cm}^{-1}$ . The isomer (2j) showed  $\delta(\text{CDCl}_3)$  1.21 (3 H, d,  $J$  7.0 Hz, 3-CH<sub>3</sub>), 2.43 (1 H, s, OH, D<sub>2</sub>O-exchangeable), 3.35 (1 H, q,  $J$  7.0 Hz, 3-H), 3.62 (1 H, d,  $J$  14.0 Hz, NCH<sub>2</sub>·Ph), 4.45 (1 H, s, 5-H), 5.28 (1 H, d,  $J$  14.0 Hz, NCH<sub>2</sub>·Ph), and 6.6–7.4 (15 H, m, aromatic). The isomer (2j') showed  $\delta(\text{CDCl}_3)$  1.17 (3 H, d,  $J$  7.0 Hz, 3-CH<sub>3</sub>), 2.43 (1 H, s, OH, D<sub>2</sub>O-exchangeable), 3.35 (1 H, q,  $J$  7.0 Hz, 3-H), 3.65 (1 H, d,  $J$  14.0 Hz, NCH<sub>2</sub>·Ph), 4.65 (1 H, s, 5-H), 5.25 (1 H, d,  $J$  14.0 Hz, NCH<sub>2</sub>·Ph), and 6.6–7.4 (15 H, m, aromatic). [Found (for mixture): C, 80.25; H, 6.5; N, 3.75. Calc. for C<sub>24</sub>H<sub>23</sub>NO<sub>2</sub>: C, 80.65; H, 6.5; N, 3.9%].

(xi) The 1-benzyl-4-hydroxy-3,3-dimethyl-4,5-diphenylpyrrolidin-2-ones (2k and k') were obtained in 65% yield (ratio 2:1). The pyrrolidin-2-one (2k') was isolated by fractional recrystallization, but complete purification of (2k) was not achieved; the latter showed  $\delta(\text{CDCl}_3)$  0.73 (3H, s, 3-CH<sub>3</sub> *cis* to 4-Ph), 1.27 (3 H, s, 3-CH<sub>3</sub> *trans* to 4-Ph), 1.7br (1 H, s, OH), 3.62 (1 H, d,  $J$  14.1 Hz, NCH<sub>2</sub>·Ph), 5.10 (1 H, s, 5-H), 5.35 (1 H, d,  $J$  14.1 Hz, NCH<sub>2</sub>·Ph), and 6.8–7.5 (15 H, m, aromatic). The isomer (2k) had m.p. 176–177 °C;  $\nu_{\max}$ (KBr) 3 450 and 1 665  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  1.11 (3 H, s, 3-CH<sub>3</sub> *cis* to 4-Ph), 1.23 (3 H, s, 3-CH<sub>3</sub> *trans* to 4-Ph), 2.5br (1 H, s, OH), 3.67 (1 H, d,  $J$  14.1 Hz, NCH<sub>2</sub>·Ph), 4.50 (1 H, s, 5-H), 5.32 (1 H, d,  $J$  14.1 Hz, NCH<sub>2</sub>·Ph), and 6.6–7.3 (15 H, m, aromatic) (Found: C, 81.05; H, 6.85; N, 3.75. C<sub>25</sub>H<sub>25</sub>NO<sub>2</sub> requires C, 80.85; H, 6.8; N, 3.75%).

(xii) 7-Hydroxy-7-phenyl-4-oxa-1-azabicyclo[4.3.0]nonan-9-one (2l) had m.p. 165–166 °C;  $\nu_{\max}$ (KBr) 3 250 and 1 680  $\text{cm}^{-1}$ ;  $\delta(\text{CDCl}_3)$  2.80 (2 H, ABq,  $J$  17.3 Hz, CO·CH<sub>2</sub>), 3.4 (1 H, m, methine), 3.79 (5 H, m, CH<sub>2</sub>·CH<sub>2</sub> + NCH<sub>2</sub>), 4.0

† The analyses are poor because these pyrrolidin-2-ones are so hygroscopic and volatile.

<sup>14</sup> H. Aoyama, T. Hasegawa, T. Nishio, and Y. Omote, *Bull. Chem. Soc. Japan*, 1975, **48**, 1671.

<sup>15</sup> H. Bredereck, R. Gompfer, K. Klem, and B. Föhlisch, *Chem. Ber.*, 1961, **94**, 3119.

<sup>16</sup> G. E. Utzinger, *Helv. Chim. Acta*, 1952, **35**, 1359.

<sup>17</sup> J. R. Treffer, U.S.P. 3,105,079/1963 (*Chem. Abs.*, 1964, **60**, 2913d).

<sup>18</sup> C. F. Koelsch and J. W. Britain, *J. Org. Chem.*, 1959, **24**, 1551.

<sup>19</sup> A. L. Searles and D. Ressler, *J. Amer. Chem. Soc.*, 1958, **80**, 3656.

(2 H, m, NCH<sub>2</sub> + OH; one D<sub>2</sub>O-exchangeable), and 7.2—7.6 (5 H, m, aromatic) (Found: C, 66.4; H, 6.4; N, 5.7. C<sub>13</sub>H<sub>15</sub>NO<sub>3</sub> requires C, 66.95; H, 6.5; N, 6.0%).

(xiii) 4-Hydroxy-4-phenyl-1-azabicyclo[3.3.0]octan-2-one (2m) had m.p. 175—176 °C;  $\nu_{\max}$ (KBr) 3 300 and 1 670 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.0 (4 H, m, CH<sub>2</sub>·CH<sub>2</sub>), 2.8 (2 H, m, methine + OH; one D<sub>2</sub>O-exchangeable), 3.02 (2 H, ABq, *J* 16.2 Hz, CO·CH<sub>2</sub>), 3.6 (1 H, m, NCH<sub>2</sub>), 4.22 (1 H, m, NCH<sub>2</sub>), and 7.2—7.55 (5 H, m, aromatic) (Found: C, 71.75; H, 6.9; N, 6.15. C<sub>13</sub>H<sub>15</sub>NO<sub>2</sub> requires C, 71.85; H, 6.95; N, 6.45%).

(xiv) 4-Hydroxy-4-phenyl-1-azabicyclo[4.3.0]nonan-2-one (2n) had m.p. 157—158 °C;  $\nu_{\max}$ (KBr) 3 400 and 1 680 cm<sup>-1</sup>;

$\delta$ (CDCl<sub>3</sub>) 1.5 (6H, m, CH<sub>2</sub>·CH<sub>2</sub>·CH<sub>2</sub>), 2.7 (1 H, m, methine), 2.80 (2 H, ABq, *J* 16.2 Hz, CO·CH<sub>2</sub>), 3.4 (1 H, m, NCH<sub>2</sub>), 3.68 (1 H, s, OH, D<sub>2</sub>O-exchangeable), 4.1 (1 H, m, NCH<sub>2</sub>), and 7.1—7.5 (5 H, m, aromatic) (Found: C, 72.45; H, 7.35; N, 5.9. C<sub>14</sub>H<sub>17</sub>NO<sub>2</sub> requires C, 72.7; H, 7.4; N, 6.05%).

(xv) 4-Hydroxy-1,4-diphenylpyrrolidin-2-one (2o) had m.p. 178—179 °C;  $\nu_{\max}$ (KBr) 3 300 and 1 670 cm<sup>-1</sup>;  $\delta$ [(CD<sub>3</sub>)<sub>2</sub>SO] 2.96 (2 H, ABq, *J* 17 Hz, 5-H<sub>2</sub>), 4.08 (2 H, ABq, *J* 9.5 Hz, 3-H<sub>2</sub>), 5.93 (1 H, s, OH, D<sub>2</sub>O-exchangeable), and 7.1—7.9 (10 H, m, aromatic) (Found: C, 75.5; H, 5.95; N, 5.3. C<sub>16</sub>H<sub>15</sub>NO<sub>2</sub> requires C, 75.85; H, 5.95; N, 5.55%).

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