

REACTION OF ETHYL 4-BROMOCROTONATE WITH ACETOACETAMIDES

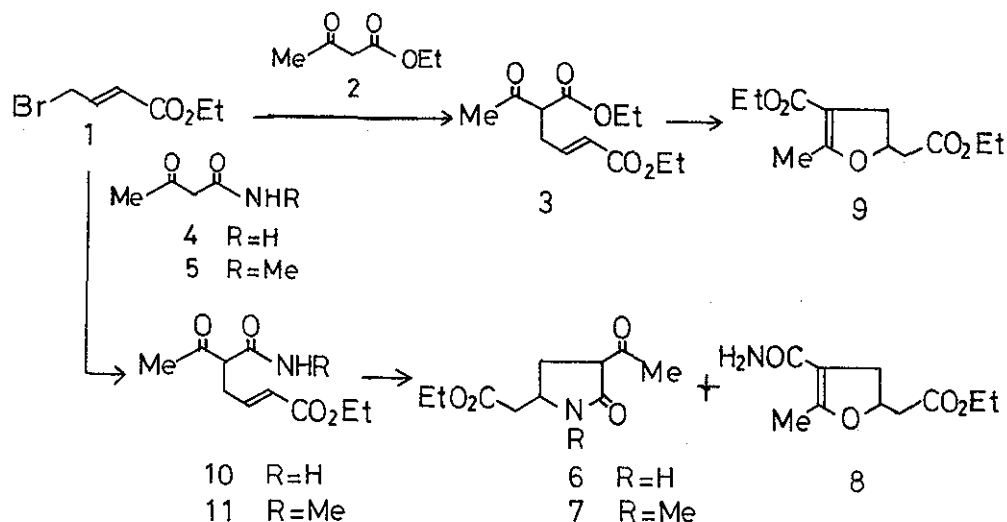
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Ethyl 4-bromocrotonate (1) reacted with acetoacetamide (4) at room temperature to give ethyl 5-carbamoyl-6-oxo-2-heptenoate (10), which was transformed into ethyl 3-acetyl-2-oxopyrrolidine-5-acetate (6) and ethyl 4-carbamoyl-2,3-dihydro-5-methylfuran-2-acetate (8).

Similar reaction of compound 1 with N-methylacetoacetamide (5) afforded ethyl 3-acetylecgoninate (7). Reaction of compound 1 with ethyl acetoacetate (2) gave rise to ethyl 2,3-dihydro-4-ethoxycarbonyl-5-methylfuran-2-acetate (9).

It is reported that ethyl 4-bromocrotonate (1) reacted with ethyl acetoacetate (2) to give ethyl 5-ethoxycarbonyl-6-oxo-2-heptenoate (3).<sup>1</sup> In the present communication we wish to report the reaction of compound 1 with acetoacetamide (4) and N-methylacetoacetamide (5) to give the pyrrolidone derivatives (6 and 7) and the furan derivative (8). In addition, during the course of this investigation, we reinvestigated the reaction of 1 with 2 and found that ethyl 2,3-dihydro-4-ethoxycarbonyl-5-methylfuran-

2-acetate (9) was obtainable besides compound 3, whose fact is also described in this paper.



When a solution of acetoacetamide (4) (0.03 mol) and ethyl 4-bromocrotonate (1) (0.025 mol) in absolute ethanol in the presence of sodium ethoxide (0.03 mol) was stirred at room temperature, ethyl 5-carbamoyl-6-oxo-2-heptenoate (10), mp 94.5-96°, was obtained in 52% yield. Found: C, 56.2; H, 7.2; N, 6.5.

$C_{10}H_{15}O_4N$  (10) requires C, 56.3; H, 7.1; N, 6.6%,  $\nu_{\max}$  3450, 3400, 1720 and 1700  $cm^{-1}$ ,  $\delta$  1.26 (3H, t, J 7 Hz,  $OCH_2CH_3$ ), 2.26 (3H, s,  $COCH_3$ ), 2.72 (2H, t, J 7 Hz,  $CH_2$ ), 3.50 (1H, t, J 7 Hz, 5-H), 4.15 (2H, q, J 7 Hz,  $OCH_2CH_3$ ), 5.84 (1H, d, J 17 Hz, 2-H), 5.90-6.50 (2H, br,  $NH_2$ ), 6.81 (1H, q, J 17 Hz, J 7 Hz, 3-H)<sup>2</sup>.

When this reaction was carried out under reflux, ethyl 3-acetyl-2-oxopyrrolidine-5-acetate (6), mp 67.5-68.5°, and ethyl 4-carbamoyl-2,3-dihydro-5-methylfuran-2-acetate (8), mp 99.5-101°, were obtained.

were obtained in 18% and 6% yields, respectively. Found C, 56.45; H, 7.05; N, 6.55.  $C_{10}H_{15}O_4N$  (6) requires C, 56.3; H, 7.1; N, 6.6%,  $\nu_{\max}$  3500, 1725 and  $1700\text{ cm}^{-1}$ ,  $\delta$  1.26 (3H, t, J 7 Hz,  $OCH_2CH_3$ ), 1.50-1.98 (1H, octet, J 13 Hz, J 9.5 Hz, J 6 Hz, 4-H), 2.40 (3H, s,  $COCH_3$ ), 2.54 (2H, d, J 5 Hz,  $CH_2$ ), 2.62-3.05 (1H, octet, J 13 Hz, J 6 Hz, J 5 Hz, 4-H), 3.58 (1H, q, J 6 Hz, J 9.5 Hz, 3-H), 3.80-4.20 (1H, m, 5-H), 4.18 (2H, q, J 7 Hz,  $OCH_2CH_3$ ), 6.40-6.70 (1H, br, NH). Found: C, 56.1; H, 7.0; N, 6.6.  $C_{10}H_{15}O_4N$  (8) requires C, 56.3; H, 7.1; N, 6.6%,  $\nu_{\max}$  3450, 1725 and  $1670\text{ cm}^{-1}$ ,  $\delta$  1.27 (3H, t, J 7 Hz,  $OCH_2CH_3$ ), 2.19 (3H, t, J 1.5 Hz,  $CH_3$ ), 2.69 (2H, q, J 7 Hz, J 3 Hz,  $CH_2$ ), 3.06 (2H, octet, J 10 Hz, J 13 Hz, J 1.5 Hz,  $CH_2$ ), 4.16 (2H, q, J 7 Hz,  $OCH_2CH_3$ ), 4.99 (1H, q, J 10 Hz, J 7 Hz, 2-H), 5.30-5.80 (2H, br,  $NH_2$ )<sup>2</sup>.

Refluxing a solution of compound 10 in absolute ethanol in the presence of sodium ethoxide afforded compounds 6 and 8 in 46% and 16% yields, respectively.

Similarly, refluxing a solution of compound 1 and N-methyl-acetoacetamide (5) in absolute ethanol in the presence of sodium ethoxide afforded ethyl 3-acetylcgoninate (7), bp  $95-98^\circ$  (0.03 mmHg), in 17% yield. If the reaction was carried out at room temperature, ethyl 5-(N-methylcarbamoyl)-6-oxo-2-heptenoate (11) was obtained besides compound 7. In this reaction the furan derivative corresponding to compound 8 was not detected. Found: C, 58.4; H, 7.55; N, 6.25.  $C_{11}H_{17}O_4N$  (11) requires C, 58.1; H, 7.55; N, 6.15%.  $\nu_{\max}$  3480, 1710 and  $1680\text{ cm}^{-1}$ ,  $\delta$  1.26 (3H, t, J 7 Hz,  $OCH_2CH_3$ ), 2.22 (3H, s,  $COCH_3$ ), 2.75 (3H, d, J 7 Hz,  $NHCH_3$ ), 3.45 (1H, t, J 7 Hz, 5-H), 4.22 (2H, q, J 7 Hz,  $OCH_2CH_3$ ), 5.72 (1H, d, J 17 Hz, 2-H), 6.1-6.4 (1H, br,  $NHCH_3$ ), 6.81 (1H, q, J 17 Hz,

J 7 Hz, 3-H). Found: C, 58.3; H, 7.6; N, 6.4.  $C_{11}H_{17}O_4N$  (7), requires C, 58.1; H, 7.55; N, 6.25%,  $\nu_{\max}$  1725, 1695 and 1685  $cm^{-1}$ ,  $\delta$  1.25 (3H, t, J 7 Hz,  $OCH_2CH_3$ ), 1.8-2.3 (2H, m,  $CH_2$ ), 2.40 (3H, s,  $COCH_3$ ), 2.6 (2H, dd, J 5 Hz, J 2 Hz,  $CH_2$ ), 2.78 (3H, s,  $NCH_3$ ), 3.2-3.5 (1H, m, 3-H), 3.6-3.9 (1H, m, 5-H), 4.15 (2H, q, J 7 Hz,  $OCH_2CH_3$ ).<sup>2</sup>

According to the procedure reported by Colonge<sup>1</sup>, reaction of 1 with 2 was carried out. Thus, refluxing a solution of compounds 1 and 2 in ethanol afforded ethyl 2,3-dihydro-4-ethoxycarbonyl-5-methylfuran-2-acetate (9), bp 124-127° (2 mmHg), and ethyl 5-ethoxycarbonyl-6-oxo-2-heptenoate (3), bp 126-127.5° (1 mmHg) (lit.<sup>1</sup>, bp 118° (0.7 mmHg)) in 33% and 10% yields, respectively. Found: C, 59.3; H, 7.5.  $C_{12}H_{18}O_5$  (3) requires C, 59.5; H, 7.5%,  $\nu_{\max}$  1725 and 1680  $cm^{-1}$ ,  $\delta$  1.26 (6H, t, J 7 Hz,  $OCH_2CH_3$ ), 2.15 (3H, t, J 1.5 Hz,  $CH_3$ ), 2.64 (2H, q, J 7 Hz, J 3 Hz,  $CH_2$ ), 3.08 (2H, octet, J 13 Hz, J 16 Hz, J 1.5 Hz,  $CH_2$ ), 4.15 (4H, q, J 7 Hz,  $OCH_2CH_3$ ), 4.98 (1H, q, J 13 Hz, J 7 Hz, 2-H).<sup>2</sup>

Since acetoacetamides (4,5) are easily available, this method will provide more accessible routes to these pyrrolidone and furan derivatives.

#### REFERENCES

- 1 J. Colonge, J. P. Cayrel, Bull. Soc. Chim. France, **12**, 3596 (1965).
- 2 I.r. spectra were taken for solutions in chloroform with a JASCO IR-S spectrophotometer. N.m.r. spectra were measured with a Hitachi R-20 instrument (tetramethylsilane as internal standard); [<sup>2</sup>H] chloroform was used as solvent.

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