

SYNTHESIS OF 3-HALOBENZYL-4-HYDROXYCOUMARINS AND THEIR HYDROLYSIS

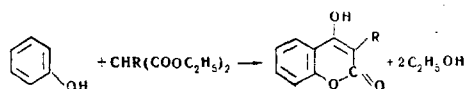
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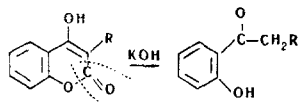
The thermal condensation of halobenzylmalonic esters with phenol has given a series of 3-halobenzyl derivatives of 4-hydroxycoumarin. Alkaline hydrolysis, with simultaneous decarboxylation, gives the corresponding *o*-hydroxy- β -halophenylpropiophenones.

We have previously used the thermal condensation of monosubstituted malonic esters with phenols [1] in the synthesis of various derivatives of 4-hydroxycoumarin [2]. The reaction mentioned may also be used in the synthesis of a series of 3-halobenzyl-substituted 4-hydroxycoumarins:



The reaction conditions and the constants of the products obtained are given in Table 1.

Compounds I-VI were subjected to alkaline hydrolysis and simultaneous decarboxylation:



The characteristics of the *o*-hydroxy- β -halophenylpropiophenones obtained are given in Table 2.

EXPERIMENTAL

The *o*-, *m*-, and *p*-bromobenzyl bromides were obtained by brominating the corresponding bromotoluenes, and the *o*-, *m*-, and *p*-chlorobenzyl chlorides by chlorinating the chlorotoluenes [3].

The halobenzylmalonic esters were obtained by the alkylation of sodiomalonic ester with alkyl halides [4] (Table 3).

The thermal condensation of the halobenzylmalonic esters with phenol was done in the apparatus described previously [5]. A 100-ml

flask was charged with 0.05 mole of the halobenzylmalonic ester and 0.1 mole of phenol. The mixture was heated in an oil bath from about 150° C to the condensation temperature over 2 hr. After completion of the decomposition reaction, the mixture was poured into a beaker containing toluene. The precipitated coumarin crystals (I-VI) were filtered off using suction, washed with toluene, and recrystallized from ethanol.

The *o*-hydroxy- β -halophenylpropiophenones (VII-XII) were each obtained by boiling 20-22 g of the appropriate coumarin with 600 ml of a 12% KOH solution over a period of 18-24 hr. To terminate the reaction, the solution was cooled and saturated with CO₂. The precipitated hydroxy ketone (VII-XII) was extracted with toluene, the extract was dried over MgSO₄, the toluene was evaporated, and the residue was distilled under a vacuum. The hydroxy ketones were recrystallized from petroleum ether.

REFERENCES

1. C. Mentzer and P. Verrier, *Mon.*, 88, 264, 1957.
2. L. P. Zalukaev and M. P. Alekseyuk *KhGS [Chemistry of Heterocyclic Compounds]*, 1, 139, 1965; M. P. Alekseyuk, A. I. Shcherban, and L. P. Zalukaev, *KhGS [Chemistry of Heterocyclic Compounds]*, 2, 176, 1966.
3. General Practical Handbook of Organic Chemistry [Russian translation], Mir, p. 142, 1965.
4. Organic Synthesis [Russian translation], II, Moscow, 3, 435, 1952.
5. L. P. Zalukaev and M. P. Alekseyuk, *Biologically Active Compounds [in Russian]*, Nauka, Moscow-Leningrad, p. 139, 1965.

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Table 1

3-Halobenzyl-4-hydroxycoumarins

| Compound | R | Mp, °C | Condensation temperature, °C | Condensation time, hr | Found, %* | | | Yield, % |
|----------|---|--------|------------------------------|-----------------------|-----------|------|-------|----------|
| | | | | | C | H | Hal | |
| I | <i>o</i> -BrC ₆ H ₄ CH ₂ | 244 | 296-299 | 7 | 58.01 | 3.44 | 24.30 | 73.5 |
| II | <i>m</i> -BrC ₆ H ₄ CH ₂ | 217.5 | 289-291 | 6 | 58.18 | 3.26 | 24.18 | 80.3 |
| III | <i>p</i> -BrC ₆ H ₄ CH ₂ | 252 | 288-291 | 7 | 58.08 | 3.37 | 24.15 | 71.0 |
| IV | <i>o</i> -ClC ₆ H ₄ CH ₂ | 239.5 | 289-293 | 8 | 67.14 | 3.85 | 12.32 | 80.3 |
| V | <i>m</i> -ClC ₆ H ₄ CH ₂ | 212 | 279-283 | 8 | 67.09 | 3.92 | 12.26 | 62.7 |
| VI | <i>p</i> -ClC ₆ H ₄ CH ₂ | 239.5 | 280-283 | 9 | 67.16 | 3.81 | 12.12 | 82.0 |

*For compounds I-III, calculated for C₁₆H₁₁BrO₃, %: C 58.02; H 3.35; Br 24.13; for compounds IV-VI, calculated for C₁₆H₁₁ClO₃, %: C 67.02; H 3.88; Cl 12.36.

Table 2

o-Hydroxy- β -halophenylpropiophenones

| Compound | R | Mp, °C | Bp, °C (mm) | Found, %* | | | Yield, % |
|----------|---|--------|----------------|-----------|------|-------|----------|
| | | | | C | H | Hal | |
| VII | <i>o</i> -BrC ₆ H ₄ CH ₂ | 53 | 163—165 (1.4) | 59.47 | 4.19 | 26.21 | 94.5 |
| VIII | <i>m</i> -BrC ₆ H ₄ CH ₂ | 40.5 | 163—164 (1.4) | 59.09 | 4.26 | 26.18 | 91.2 |
| IX | <i>p</i> -BrC ₆ H ₄ CH ₂ | 79.5 | 166—167 (~0.5) | 59.18 | 4.22 | 26.24 | 90 |
| X | <i>o</i> -ClC ₆ H ₄ CH ₂ | 59.5 | 144—145 (~1) | 69.03 | 5.06 | 13.50 | 86.8 |
| XI | <i>m</i> -ClC ₆ H ₄ CH ₂ | 35 | 176—177 (2.5) | 69.17 | 5.18 | 13.46 | 85.3 |
| XII | <i>p</i> -ClC ₆ H ₄ CH ₂ | 63.5 | 158—159 (~1) | 69.19 | 5.11 | 13.53 | 86.6 |

*For compounds VII-IX, calculated for C₁₅H₁₃BrO₂, %: C 59.03; H 4.30; Br 26.18; for X-XII, calculated for C₁₅H₁₃ClO₂, %: C 69.09; H 5.04; Cl 13.60.

Table 3

Halobenzylmalonic Esters

| Compound | Bp, °C (mm) | Yield, % |
|--|------------------|----------|
| <i>o</i> -BrC ₆ H ₄ CH ₂ CH(COOC ₂ H ₅) ₂ | 179—179.5 (8) | 71.4 |
| <i>m</i> -BrC ₆ H ₄ CH ₂ CH(COOC ₂ H ₅) ₂ | 135—137 (1.5) | 65.5 |
| <i>p</i> -BrC ₆ H ₄ CH ₂ CH(COOC ₂ H ₅) ₂ | 164—165 (2.6) | 60.0 |
| <i>o</i> -ClC ₆ H ₄ CH ₂ CH(COOC ₂ H ₅) ₂ | 105—106.5 (~0.5) | 68.0 |
| <i>m</i> -ClC ₆ H ₄ CH ₂ CH(COOC ₂ H ₅) ₂ | 163—166 (6.5) | 83.7 |
| <i>p</i> -ClC ₆ H ₄ CH ₂ CH(COOC ₂ H ₅) ₂ | 147—149 (2.3) | 62.0 |