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REACTIONS OF BISAMIDES. III. SYNTHESIS OF α -CARBETHOXY- β -ACETYLAMINO- β -ARYLETHYL METHYL KETONES

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In continuation of our studies (1, 2) on the reactivity of bisamides towards compounds possessing active hydrogen atoms, we have investigated the reaction of acetoacetic ester with bisamides. In this case one amide group of the bisamide is readily replaced by the acetoacetic ester group, as illustrated by the equation:



By heating various bisamides with acetoacetic ester in the presence of acetic anhydride, we obtained in good yields (up to 74%) α -carbethoxy- β -acetylamino- β -arylethyl methyl ketones (II), namely, α -carbethoxy- β -acetylamino- β -phenylethyl methyl ketone (R = C₆H₅), α -carbethoxy- β -acetylamino- β -(3, 4-dimethoxyphenyl)ethyl methyl ketone [R = C₆H₈(OCH₃)₂], and α -carbethoxy- β -acetylamino- β -(3, 4-methylenedioxyphenyl)ethyl methyl ketone (R = C₆H₃O₂CH₂).

These compounds are colorless substances which crystallize well; they are readily soluble in alcohol and warm water, not so easily in ether; they exist in two tautomeric forms like acetoacetic ester itself:



On standing, their alcoholic solutions give brown-red colorations with ferric chloride and decolorize bromine water, in agreement with their structure.

EXPERIMENTAL

1. α -Carbethoxy- β -acetylaminophenylethyl methyl ketone (II, $\mathbf{R} = \mathbf{C}_6\mathbf{H}_5$). A mixture of 20.6 g. (1/10 mole) of benzylidenebisacetamide, 13 g. (1/10 mole) of acetoacetic ester, and 10.2 g. (1/10 mole) of acetic anhydride is heated in a 100-cc. flask under a reflux condenser for 5 hours at 120°. Acetic anhydride is removed *in vacuo* at the lowest possible temperature. The cooled oil is poured into about 100 cc. of cold water. After several hours, the solidified

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mass is filtered and washed with a little cold ether, yielding 20 g. (72.2%) of crude product melting at 92°. After several crystallizations from 30% ethyl alcohol, it melts at 95-96°.

Anal. Calc'd for C15H19NO4: C, 64.94; H, 6.90; N, 5.05.

Found: C, 65.16; H, 7.13; N, 5.37.

2. α -Carbethoxy- β -acetylamino- β -(3,4-dimethoxyphenyl)ethyl methyl ketone [II, R = C₆H₃(OCH₃)₂]. Veratrylidenebisacetamide (5.3 g., (1/50 mole), 2.6 g. (1/50 mole) of aceto-acetic ester, and 10.2 g. (1/10 mole) of acetic anhydride are heated for 5 hours at 120°. After removing the acetic anhydride, cold water is added. The solidified mass is filtered and washed with a little cold ether, yielding 5 g. (74.6%) of crude product melting at 131–133°. After recrystallization from 50% ethyl alcohol, the product melts at 135–136°.

Anal. Cale'd for C₁₇H₂₃NO₆: C, 60.53; H, 6.67; N, 4.15.

Found: C, 60.58; H, 7.08; N, 4.48.

3. α -Carbethoxy- β -acetylamino- β -(3,4-methylenedioxyphenyl)ethyl methyl ketone (II, R = C₆H₃O₂CH₂). Piperonylidenebisacetamide (5 g., 1/50 mole), 2.6 g. (1/50 mole) of acetoacetic ester, and 2.1 g. (1/50 mole) of acetic anhydride are heated for 5 hours at 120°. Acetic anhydride is removed *in vacuo*, and cold water is added to the cooled mixture. After allowing the mixture to stand for 12 hours, the solidified mass is filtered and washed with a little cold ether, yielding 3.2 g. (50%) of crude product melting at 95–97°. After recrystallization from 30% ethyl alcohol, it melts at 100–101°.

Anal. Calc'd for C₁₆H₁₉NO₆: C, 59.78; H, 5.91; N, 4.36.

Found: C, 59.61; H, 6.20; N, 4.53.

SUMMARY

Bisamides react with acetoacetic esters in the presence of acetic anhydride by substitution of one amide group by the acetoacetic ester radical, resulting in the formation of α -carbethoxy- β -acetylamino- β -arylethyl methyl ketones.

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