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PREPARATION OF PREVIOUSLY UNAVAILABLE 6,6-DIALKYLHEXAHYDRO-1,3,5-TRIAZINE-2,4-DIONES

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A high-yield, two-step procedure for the preparation of 6,6-dialkylhexahydro-1,3,5-triazine-2,4-diones starting from ketones and dithiobiuret is reported.

1,3,5-Triazines and their derivatives have found numerous commercial applications (particularly as herbicides),¹ and thus new synthetic routes to these compounds are of some significance. As part of an ongoing program directed toward the preparation of heterocyclic N-halamines and their evaluation as biocidal agents,² the synthesis of a variety of hexahydro-1,3,5-triazine-2,4-diones (1) (hereafter referred to simply as "triazinediones") was required. Such compounds are typically prepared by any of several methods, including: 1) condensation of aldehydes with biuret³ or urea,⁴ 2) reaction of ketones with substituted biurets,⁵ and 3) reaction of imines with isocyanates⁶ or urea.⁷ While these procedures afford triazinediones with a variety of substitution patterns, none of

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these methods have been successfully applied to the synthesis of simple 6,6-dialkyl substituted triazinediones (1a). As compounds of this type were necessary to serve as precursors for N-halo compounds, a new synthetic method was required.



b) $R^{1}, R^{2}, R^{3}, R^{4}, = H, R^{5} = alkyl$

While condensation of biuret with aldehydes will produce 6-alkyl (and aryl) triazinediones (1b), attempts to extend this reaction to include ketones as substrates (to yield 1a) are reported to have failed.⁸ Indeed, numerous unsuccessful attempts were made in this laboratory to produce (1a) by the reaction of ketones with biuret under a variety of conditions.

A few examples of condensation of ketones with dithiobiuret to give 6,6-dialkyl-hexahydro-1,3,5-triazine-2,4dithiones (2), however, have been reported.⁹ By using a similar synthetic technique, additional examples of these dithiones have been prepared in this laboratory. Treatment of ethanolic solutions of ketones with dithiobiuret and HCl produced excellent yields of triazinedithiones (2) (see table). Triazinedithiones (2) were readily converted to the corresponding triazinediones (3) with basic hydrogen peroxide solution, also in excellent yield. Products were easily purified

Table

| | (2) | | | (3) | |
|-------------------------------|--|--|--|--|---|
| <u>R</u> | <u>R'</u> | <u>%Yield</u> a | <u>m.p.^b (Lit.)</u> | <u>%Yield</u> a | <u>m.p.</u> b |
| CH ₃ | CH3 | 88 | 283-4(282-3) ⁹ a | 85 | 298d |
| CH ₃ | C ₂ H ₅ | ; 90 | 215d | 86 | 268-70 |
| C_2H_5 | C ₂ H ₅ | ; 83 | 232d | 96 | 276-77d |
| (CH | 2)4 | 94 | 273d | 91 | 300-1 |
| (CH | 2)5 | 97 | 271d | 87 | 298-300 |
| C ₆ H ₅ | CH3 | 76 | 281-2d(281-2d) ⁹ a | 73 | 298-300 |
| | <u>R</u> CH ₃ CH ₃ C ₂ H ₅ (CH (CH C ₆ H ₅ | R R' CH3 CH3 CH3 C2H3 C2H5 C2H3 (CH2)4 (CH2)5 C6H5 CH3 | R $\frac{R}{2}$ $\frac{\%}{2}$ Yielda CH3 CH3 8 8 CH3 C2H5 90 C2H5 C2H5 83 (CH2)4 94 (CH2)5 97 C6H5 CH3 76 | RR' $\%$ Yieldam.p.b (Lit.)CH3CH388 $283-4(282-3)^{9a}$ CH3C2H590 $215d$ C2H5C2H583 $232d$ (CH2)494 $273d$ (CH2)597 $271d$ C6H5CH376 $281-2d(281-2d)^{9a}$ | RR' $\%$ Yieldam.p.b(Lit.) $\%$ YieldaCH3CH388 $283-4(282-3)^{9}$ a85CH3C2H590 215 d86C2H5C2H583 232 d96(CH2)494 273 d91(CH2)597 271 d87C ₆ H5CH376 $281-2d(281-2d)^{9}$ a73 |

a) Yields are isolated yields of crude products.

b) Melting points are those for products obtained by recrystallization of small samples of the crude products.¹⁰

by recrystallization (from water for diones (3) and from alcohols for dithiones (2)).

In summary, we have developed a short, efficient synthesis of 6,6-dialkylhexahydro-1,3,5-triazine-2,4-diones which are unobtainable by traditional synthetic methods. Halogenation and evaluation of the corresponding N-halo compounds as biocides will be reported elsewhere.



Typical Experimental Procedures 6.6-Dimethyl-1.3.5-triazine-2.4-(1H.3H)-dithione (2a)

1.35 g (0.010 mol) dithiobiuret was suspended in a solution of 0.65 g (0.011 mol) acetone in 8 mL ethanol. Dry HCl was bubbled through the solution for 30 min., followed by an additional 30 min. stirring at room temperature. The mixture was then treated with excess 1M NaOH and heated to 50 °C. Neutralization with HOAc at room temperature caused precipitation of the product, which was isolated by filtration and dried to yield 1.6 g (88%) of crude product melting at 280-2 °C. Recrystallization from MeOH gave colorless crystals of m.p. 283-284 (Lit.^{9a} 282-3). ¹H NMR (DMSO-d6) δ 1.75 (s, 6H), 5.8 (s, 2H), 8.5 (s, 1H). FTIR (KBr): 3176, 3078, 2970, 2944, 1580, 1415, 1388, 1245, 1136 cm⁻¹.

6.6-Dimethyl-1.3.5-triazine-2.4-(1H,3H)-dione (3a)

17.5 g (0.10 mol) 6,6-Dimethyl-1,3,5-triazine-2,4-(1H,3H)-dithione (2a) was dissolved in 176 mL of 2.5M NaOH and heated to 40-45 °C. 91 g of 30% H₂O₂ (0.82 mol) were added dropwise, maintaining the reaction temperature at 40-45 °C by means of an ice bath. After addition of the H₂O₂, the solution was heated briefly to 80 °C, then cooled to room temperature and neutralized with 2N H₂SO₄, causing precipitation of the product. The product was isolated by filtration and dried to yield 12.1 g (85%) of crude product. Recrystallization from water gave 11.5 g (81 %) of colorless crystals melting at 298 °C with decomposition. ¹H NMR (DMSO-d6) δ 1.31 (s, 6H), 8.0 (s, 2H), 9.55 (s, 1H). FTIR (KBr); 3200, 3078, 2969, 2935, 1720, 1351, 1194, 1085 cm⁻¹; Analysis calculated for $C_5H_9N_3O_2$: C, 41.95; H, 6.34; N, 29.35; O, 22.35. Found: C, 41.69; H, 6.39; N, 29.22.

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 Typically recrystallization raised the melting points of the crude products by two or three degrees, and reduced the yield by <u>ca</u>. 5%.
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