

## A New Synthetic Route to 5-Aminomethylene Derivatives of Barbituric Acids

Dmitrii V. Pestov

Institute of Macromolecular Compounds, Russian Academy of Sciences, 199004 St. Petersburg, Russian Federation.

Fax: +7 812 218 6869

Interaction of barbituric acid and dimethylformamide in the presence of amine salt leads to 5-aminomethylenebarbituric acids in good yield.

The reaction of barbituric acids<sup>1</sup> with *N,N*-substituted amides yields heterocyclic derivatives 3, Scheme 1. Also, as suggested earlier,<sup>1</sup> 5-dimethylaminomethylenebarbituric acids 2 are the intermediate compounds in the reaction with DMF.

TLC confirmed that compound 2b does occur in the early part of the reaction of 1,3-dimethylbarbituric acid 1b with DMF. It has also been found that, free of intramolecular hydrogen bonds, 5-aminomethylenebarbituric acids (e.g. compound 2b) are easily transaminated by primary amines. In this case, the aminomethylene derivatives formed are stabilized due to a strong intramolecular hydrogen bond.<sup>2</sup> For example, transamination of compound 2b in boiling DMF occurs rapidly under the action of aniline or even aniline chlorohydrate. We presume that 5-aminomethylenebarbituric acids will therefore appear instead of compounds 3. However, yields of 5-aminomethylenebarbituric acids in the barbituric acid reaction with DMF and primary amines are not good (5–45%). It unexpectedly appears that yields of 5-aminomethylenebarbituric acids when reacting not with amines themselves, but with their salts, are significantly better (60–95%)<sup>†</sup> The observed reaction is probably useful for the synthesis of aminomethylene derivatives of other  $\beta$ -diketones. Thus, 2-anilinomethylene-4,4-dimethylcyclohexane-1,3-dione was formed in the reaction of 4,4-dimethylcyclohexane-1,3-dione with aniline chlorohydrate and DMF in 31% yield. 2-Thiobarbituric acid under these conditions gave 5-aminomethylene-2-thiobarbituric acid (52%).

<sup>†</sup> Spectroscopic data for 4a–h:

4a: m.p. > 350 °C (DMF); <sup>1</sup>H NMR (CF<sub>3</sub>COOH)  $\delta$  3.47 (d, 3H, *J* 5 Hz, Me), 8.53 (d, 1H, *J* 16 Hz, CH).

4b: m.p. > 350 °C (DMF); <sup>1</sup>H NMR [(CD<sub>3</sub>)<sub>2</sub>SO]  $\delta$  1.13 (t, 3H, *J* 7 Hz, Me), 3.40 (m, 2H, CH<sub>2</sub>), 8.00 (d, 1H, *J* 15 Hz, CH), 10.26, 10.48 (2s, 2H, 2NH cycl.), 10.55 (wide NH).

4c: m.p. 400 °C decomp. (DMF); <sup>1</sup>H NMR [(CD<sub>3</sub>)<sub>2</sub>SO]  $\delta$  1.06 (t, 3H, *J* 6.6 Hz, 2Me), 3.22 (q, 4H, *J* 6.6 Hz, 2CH<sub>2</sub>) 6.99 (m, 4H, arom.), 7.88 (d, 1H, *J* 14 Hz, CH), 10.62, 10.76 (2s, 2H, 2NH cycl.), 11.79 (d, 1H, *J* 14 Hz, NH).

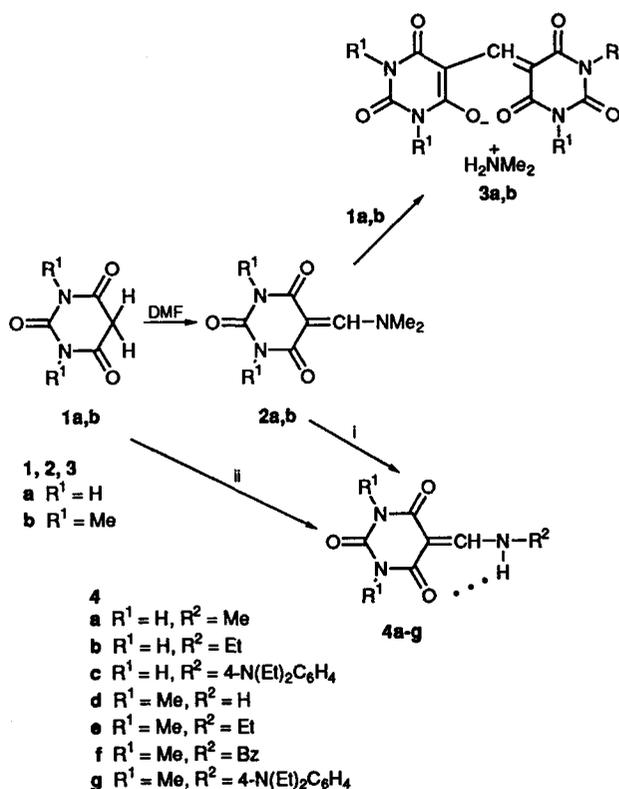
4d: m.p. 230–231 °C (DMF); <sup>1</sup>H NMR [(CD<sub>3</sub>)<sub>2</sub>SO]  $\delta$  3.40 (s, 6H, 2Me), 8.06 (d, 1H, *J* 17 Hz, CH), 10.00 (wide NH).

4e: m.p. 152–153 °C (propan-2-ol) <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.29 (t, 3H, *J* 7 Hz, Me), 3.25 (s, 6H, 2Me cycl.), 3.47 (m, 2H, CH<sub>2</sub>), 8.16 (d, 1H, *J* 14 Hz, CH), 10.28 (wide NH).

4f: m.p. 154–155 °C (Ph–Me) <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.19 (s, 6H, 2Me cycl.), 4.54 (d, 2H, *J* 7 Hz, CH<sub>2</sub>), 7.29 (m, 5H, arom.), 8.22 (d, 1H, *J* 15 Hz, CH), 10.48 (d, 1H, *J* 15 Hz, NH).

4g: m.p. 204 °C (propan-2-ol) <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.12 (t, 3H, *J* 6.6 Hz, 2Me), 3.35 (q, 4H, *J* 6.6 Hz, 2CH<sub>2</sub>), 6.85 (m, 4H, arom.), 8.52 (d, 1H, *J* 14 Hz, CH), 12.04 (d, 1H, *J* 14 Hz, NH).

<sup>‡</sup> It is interesting to note that the crystals of compounds 4c and 4g have high, non-linear properties.<sup>3</sup>



Scheme 1 Reagents and conditions: i, R<sup>2</sup>NH<sub>2</sub> or R<sup>2</sup>NH<sub>2</sub>·HX; ii, R<sup>2</sup>NH<sub>2</sub>·HX (1.2–1.3 mol), DMF (12.5 mol), 7 h; 4a 83%, 4b 79%, 4c 63%, 4d 58%, 4e 72%, 4f 93%, 4g 89%.

### References

- 1 H. Bredereck, R. Compner, F. Effenberger, K. H. Popp and G. Simchen, *Chem. Ber.*, 1961, **94**, 1241.
- 2 D. V. Pestov, V. I. Slesarev, A. I. Ginak and V. I. Slesareva, *Khim. Geterotsikl. Soedin.*, 1988, 952 [*Chem. Heterocycl. Compd. (Engl. Transl.)*, 1988, 782].
- 3 D. V. Pestov, E. V. Bursian and V. G. Zalesskii, *Izv. Akad. Nauk. Ser. Fiz.*, 1993, **57**, 197 [*Bull. Acad. Sci. Div. Phys. Sci. (Engl. Transl.)*, in press].

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