



## Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

### AN EXPEDITIOUS ONE POT SYNTHESIS OF DIBENZO[a,g]FLUORENE

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Published online: 09 Nov 2006.

To cite this article: Bimal K. Banik, Chhanda Mukhopadhyay & Frederick F. Becker (2001) AN EXPEDITIOUS ONE POT SYNTHESIS OF DIBENZO[a,g]FLUORENE, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:16, 2399-2403, DOI: [10.1081/SCC-100105115](https://doi.org/10.1081/SCC-100105115)

To link to this article: <http://dx.doi.org/10.1081/SCC-100105115>

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SYNTHETIC COMMUNICATIONS, 31(16), 2399–2403 (2001)

## AN EXPEDITIOUS ONE POT SYNTHESIS OF DIBENZO[a,g]FLUORENE

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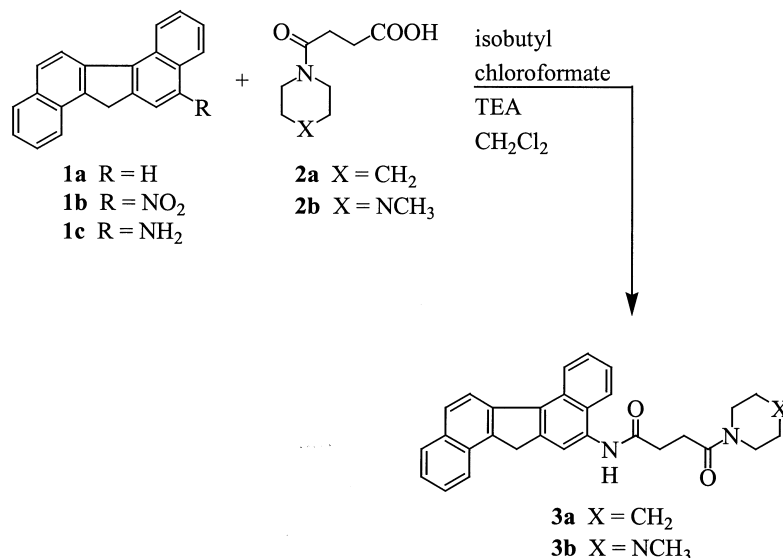
### ABSTRACT

A convenient one-pot synthesis of dibenzo[a,g]fluorene via enolate alkylation and cyclodehydration-aromatisation route has been developed.

Synthesis of polycyclic aromatic ring systems by various methodology has been the subject of extensive investigation for many years.<sup>1</sup> The carcinogenic properties of such compounds have been explained by advancing different mechanisms.<sup>2</sup> We observed from a prior study that suitably substituted chrysene derivatives act on the cancer cell as membrane stabilizing agents.<sup>3</sup> Recently, we also demonstrated the anti-tumor effects of structurally complex, angular dibenzofluorene [a,g] polycyclic systems (for example, **3**) with a very reactive *bridged* methylene group.<sup>4</sup> Diamide **3** was prepared through a series of reactions starting from the hydrocarbon **1a**. Hydrocarbon **1a** on nitration gave **1b** which on reduction produced the amino compound **1c**. Coupling reaction of **1c** with the acid **2** in the presence of isobutyl chloroformate afforded the diamide **3** (Scheme 1).

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*Scheme 1.*

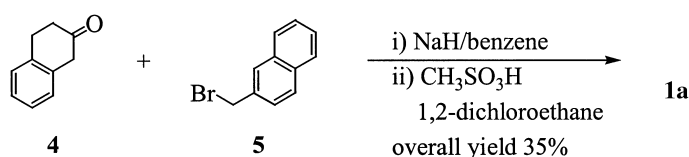
Synthesis of the hydrocarbon **1a** required for this study in pure and adequate quantities by following the method of Harvey *et al.*<sup>5</sup> proved difficult to us. Harvey *et al.* synthesized the hydrocarbon **1a** from  $\beta$ -tetralone **4** through a series of steps. For this reason, we became interested in developing a new synthetic method for the preparation of hydrofluorene derivatives. This paper describes a simple and convenient one pot method<sup>6</sup> for the synthesis of dibenzo[a,g]fluorene.

Environmentally benign chemistry is one of the attractive areas of chemical research. Disposal of solvents and chemical waste are matters of concern to the pharmaceutical manufacturer. Generally, chemical synthesis of any target molecule requires multi-step operation. Thus, to execute the synthesis of even a simple organic compound, extraction and purification either by chromatography or by crystallization are essential. For this reason, atom economy by Trost<sup>7</sup> can play a significant role. Combination of multi-step sequence into a fewer number of step or in an one pot can nicely fit into Trost's atom economy.

The enolate alkylation<sup>8</sup> and cyclization method has been used for the construction of multi-cyclic ring systems. But, surprisingly, the use of this method in the annulation of polycyclic non-alternate hydrocarbon has never been explored. We envisioned that enolate alkylation of the ketone and cyclization-aromatisation route in a one pot operation could be a viable



alternative of the existing method.<sup>5</sup> Towards this goal we treated  $\beta$ -tetralone (**4**) with sodium hydride using benzene as solvent at  $-10$  to  $-20^{\circ}\text{C}$ , reacted the enolate with 2-bromomethylnaphthalene (**5**) at the same temperature, neutralized and then benzene was evaporated under reduced pressure. The residue was refluxed with 10% methane sulfonic acid-dichloroethane for 12 h and obtained the hydrocarbon in 35% yield after purification<sup>9</sup> (Scheme 2). The entire procedure required only one extraction and a simple filtration through a column for the isolation of the final product. Using the method (enamine formation, alkylation of the enamine, cyclization and aromatisation) by Harvey *et al.*,<sup>5</sup> we required three weeks to produce the same amount of compound as this process required isolations at each stage either through distillation or extraction-chromatography.



Scheme 2.

In conclusion, we have demonstrated here a simple one-pot synthesis of dibenzofluorene, some of the derivatives of which have potent anticancer activities.<sup>4</sup>

## EXPERIMENTAL

A typical experimental procedure is as follows: To NaH (50% dispersion in oil, 0.068 mol) in benzene (10 mL) at  $-10^{\circ}\text{C}$  to  $-20^{\circ}\text{C}$  were added dropwise a solution of ketone **4** (0.034 mol) in benzene (10 mL). The immediate appearance of the deep blue color indicated the formation of the sodium enolate. The mixture was kept at the same temperature for 30 min and then bromomethylnaphthalene **5** (0.034 mol) in benzene (10 mL) was added to it. The temperature was slowly allowed to rise to room temperature and stirring was continued for 2 h. The reaction mixture was cooled in ice and excess NaH was decomposed by careful addition of methane sulfonic acid. Benzene was removed under reduced pressure, methane sulfonic acid-1,2-dichloroethane (100 mL, 10%, v/v) was added to the residue and the mixture was refluxed for 12 h. The reaction mixture was then poured into crushed ice, the dichloroethane layer was collected,



washed with sodium bicarbonate (5%), brine, dried ( $\text{Na}_2\text{SO}_4$ ) and solvent was evaporated. The crude product was purified by filtration through a short column of silica gel using hexanes as eluant. The isolated yield of the product was 35%; mp  $175^\circ\text{C}$  (lit.<sup>5</sup> mp  $174\text{--}175^\circ\text{C}$ ).

### ACKNOWLEDGMENTS

We are grateful for the funds from the Hubert L. and Olive Stringer Chair for the partial support of this research.

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**DIBENZO[a,g]FLUORENE**

**2403**

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Received in the USA November 6, 2000



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