

A novel acylative ring cleavage of benzothieno[3,2-*b*]pyran-4-ols: application to the synthesis of dibenzothiophenes and fused-ring derivatives

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Received (in Liverpool, UK) 26th January 1999, Accepted 11th February 1999

The benzothienopyranols **3**, readily available from the ketone **1**, are transformed to the carbamates **5** on treatment with *N,N*-dimethylcarbamoyl chloride, subsequent thermal electrocyclic ring closure provides access to dibenzothiophene derivatives **6** and **11–13**.

Dibenzothiophene and its congeners are not only of intrinsic interest but find applications as intermediates for the synthesis of dyes, pharmaceuticals, organic conductors and novel heterohelicenes^{1,2} and hydrocarbons.³ Dibenzothiophene and, especially, its benzologues are also of environmental concern because of their presence in fossil fuels and their combustion products.^{4a,b}

The most frequently employed ring syntheses of dibenzothiophenes employ Friedel–Crafts related chemistry.⁵ Routes involving the benzologation of benzo[*b*]thiophene by alternative means are less common. Thus, cycloadditions to benzo[*b*]thiophene-2,3-quinodimethanes⁶ and Diels–Alder reactions of benzothienopyran-2- and 3-ones⁷ have been investigated. The photodehydrocyclisation of 1-aryl-2-(thienyl)ethylenes has proved to be of value for construction of polycyclic condensed thiophenes.^{4a,5,8} In contrast, benzannulation of thiophenes, in particular, benzo[*b*]thiophene, by thermal electrocyclisations has been much less studied.⁵ 3-Substituted dibenzothiophene-1-carbonitriles are accessible from a tandem thermal cyclisation–elimination reaction of 2-(3-benzothieryl)-5-(dimethylamino)penta-2,4-dienonitriles.⁹ More recently, 1-acetoxydibenzothiophenes have been obtained by thermolysis of 4-(2-benzothieryl)-2,3-disubstituted cyclobut-2-enones.¹⁰

We now report a novel thermal electrocyclic ring closure–elimination protocol for the synthesis of dibenzothiophenes in which the key step involves formation of the carbamates **5** by an unprecedented acylative ring cleavage of benzothieno[3,2-*b*]pyran-4-ols **3** with Me₂NCOCl. The pyranols are readily prepared as shown in Scheme 1.[†]

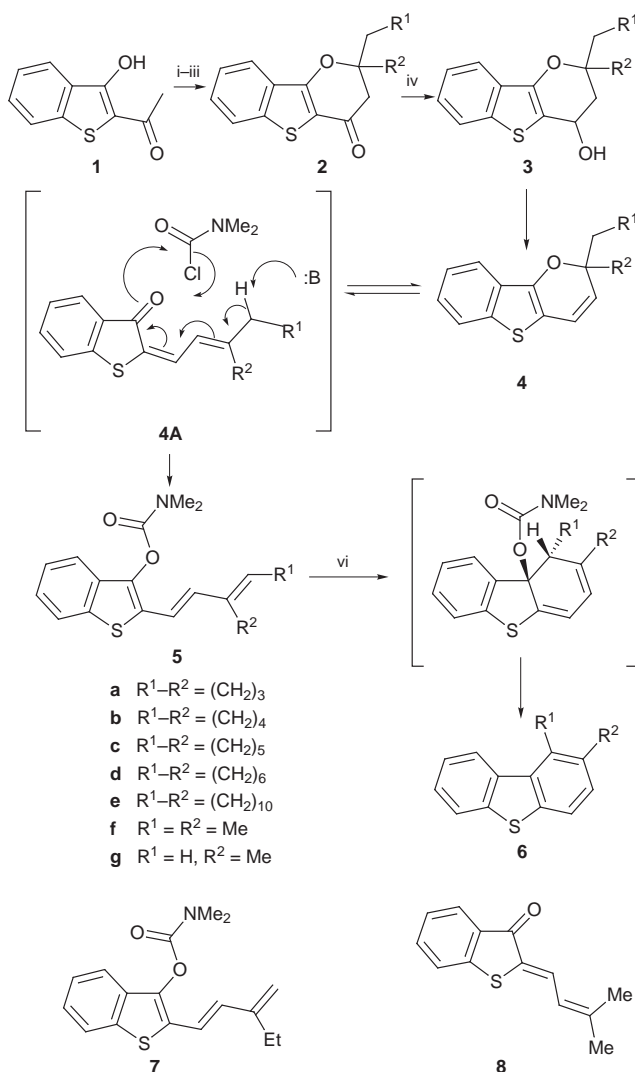
2-Acetyl-3-hydroxybenzo[*b*]thiophene **1**, accessible in a single step from thiosalicylic acid,¹¹ was treated with 2 equiv. of LDA in THF at –40 °C to give a deep red solution of the dianion. Addition of the appropriate ketone (1 equiv.) followed by aqueous work-up provided the corresponding β-hydroxy ketone that was cyclised with methanolic-HCl to the benzothienopyranones **2a–g** (62–70%). Subsequent reduction gave **3a–g** in high yield.

Attempts to dehydrate **3a** to **4a** which, we envisaged, would function as a Diels–Alder diene, with TsOH in toluene, or with TsCl or MsCl in pyridine, failed to give a tractable product. The Chugaev-type elimination *via in situ* formation of the thiocarbonate from PhOCSCl was also unsuccessful. A mechanistically related, though little used, route to alkenes from alcohols involves the formation of carbamates, (from R₂NCOCl–pyridine), the elimination step being accomplished separately by flow pyrolysis at *ca.* 300–500 °C.¹² When **3a** was heated with Me₂NCOCl in pyridine (*ca.* 5 h) the anticipated *O*-acyl derivative was not obtained, the only isolable product was, remarkably, **5a** (mp 134–135 °C). Yields were optimised (74%) when 2 equiv. of Me₂NCOCl were used. Under the same conditions **3b–f** gave **5b–f** in excellent yields (70–90%). The ¹H

NMR spectra of these compounds indicated *trans* stereochemistry of the alkene moiety.[‡]

We suggest that the benzothiophenes **5** are formed *via* initial *O*-acylation of **3** followed by elimination to give the pyran **4§** which undergoes electrocyclic ring opening to the dienone **4A**. Subsequent deprotonation followed by *O*-acylation generates **5**. In accord with this proposal, it has recently been demonstrated that in solution (CDCl₃) 5,5-dimethyl-5*H*-thieno[3,2-*b*]pyran is in equilibrium with its dienone valence tautomer.¹³

Interestingly this elimination–acylation reaction not only affords carbamates **5** stereospecifically, but regioselectively also. Thus **3f** gave **5f** (mp 116–118 °C, 85%) exclusively. None of the terminal alkene **7**, arising by deprotonation of the methyl



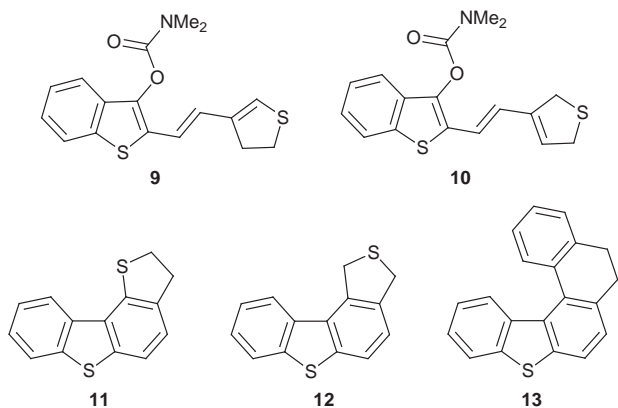
Scheme 1 Reagents and conditions: i, LDA, THF, –40 °C; ii, R¹CH₂COR², dil. HCl; iii, MeOH–HCl; iv, NaBH₄, EtOH; v, Me₂NCOCl (2 equiv.), pyridine, reflux; vi, triethylene glycol, reflux.

group in **4Af**, was observed.¶ The *E,E* stereochemistry of **5f** was established from its ¹H NMR spectrum and a NOESY experiment which confirmed the *cis* disposition of the methyl groups.

Support for the intermediacy of **4A** was provided by the behaviour of **3g**, which gave the yellow (*Z*)-dienone **8** (mp 118–120 °C, 50%),|| *via* isomerisation of **4Ag**, as the only identifiable product. Attempts to convert **8** into **5g** by further reaction with Me₂NCOCI–pyridine were unsuccessful. Formation of the least substituted alkene is, apparently, disfavoured.

The carbamates **5** possess a contiguous triene system and have the potential to cyclise with extrusion of Me₂NCO₂H to give dibenzothiophenes. After much experimentation, it was found that when **5a–f** were heated in triethylene glycol (bp 285 °C) for 6 h formation of a new, non-polar compound was complete (TLC). Aqueous work-up followed by flash chromatography gave the novel fused systems **6a–e** (30–42%). The preparation of **6f** (28%) represents an improved route to this compound.¹⁴ Thermal isomerisation of the *trans* alkene moiety in **5** precedes disrotatory ring closure and a concomitant *E_i* reaction generates **6**.

The dianion of **1** and 3-oxotetrahydrothiophene gave, ultimately, **9** and **10** (38 and 25% from the pyranol), which were



readily separated by flash chromatography. Thermal cyclisation provided the tetracycles **11** (mp 84–85.5 °C, 44%) and **12** (mp 79–80.5 °C, 35%) respectively. In like manner the pentacycle **13** (mp 108–109 °C, 28%) was obtained *via* 2-tetralone.

Although the yields are modest this method offers a facile entry to polycyclic thiophenes which is complementary to the current protocols. Existing procedures would not permit ready access to tetracycles **6a–e** nor to the isobenzothiophene **12**. Applications to the synthesis of more complex polycycles will be forthcoming.

We thank the EPSRC for provision of the mass spectrometry service at the University of Wales, Swansea, and James Robinson Ltd. for financial support to J.-L. T.

Notes and references

† All new compounds were characterised by ¹H and ¹³C NMR, HRMS and elemental analysis.

‡ The *vicinal* alkene protons appeared as doublets at *ca.* δ 6.5 and 6.7, *J* 16 Hz, (CDCl₃) for **5a,b,e** and **f**. However, in **5c,d** the signals were coincidental (δ 6.59, 2H, *s* for both) and *trans* stereochemistry was assumed for these compounds by analogy with the other examples.

§ We are unaware of any examples in which carbamoylation with Me₂NCOCI is accompanied by *in situ* elimination. The nature of the elimination step (**3** to **4**) is a matter of conjecture but a pericyclic (*syn*) process cannot be excluded. Examples of such non-pyrolytic carbamate eliminations are rare, but the thermolysis of 1,1,3,4-tetramethyl-3-(phenyl-carbamoyloxy)-2,3-dihydroisole (CCl₄, Δ, 10 h) to 1,1,3,4-tetramethylisole, is illustrative; A Laporterie, H. Iloughmane and J. Dubac, *Tetrahedron Lett.*, 1983, 3521.

¶ Existing models that account for the stereoselectivity of ketone and enone deprotonations are not easily extrapolated to explain the outcome from **4Af**. For a review see; J.O. Williams and M. J. Kelly, in *Comprehensive Organic Functional Group Transformations*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Pergamon, Oxford, 1995, vol. 1, p. 843.

|| Stereochemistry assigned by analogy with (*E*)- and (*Z*)-3-isobutenylidene-thiophen-2(3*H*)-ones (ref. 13). Compound **8**: δ (CDCl₃) 7.78 (1H, *d*, *J* 12.2, =CHCHMe₂).

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Communication 9/00730J