Convenient heterocyclization reactions with 2-functionalized 3-amino-4-aryl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolines: synthesis of new thienoquinolines, pyridothienoquinolines, pyranothienoquinolines and pyrimidothienoquinolines

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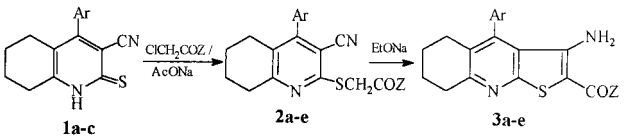
2-Functionalized-3-amino-4-aryl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolines (**3a-e**) underwent a sequence of heterocyclization reactions to afford the title compounds.

As a continuation of our previous work on the synthesis of new thieno[2,3-*b*]quinolines[15-17], we report herein the use of 2-functionalized-3-amino-4-aryl-5,6,7,8-tetrahydrothieno [2,3-*b*]quinolines (**3a–e**) for the synthesis of novel tetrahydrothieno[2,3-*b*]quinolines as well as their condensed heterocyclic derivatives which might show interesting biological activities.

The starting compounds **3a–e** were prepared by the reaction of 4-aryl-3-cyano-5,6,7,8-tetrahydroquinoline-2(1*H*)-thiones (**1a-c**)[22] with chloroacetone, ethyl chloroacetate or chloroacetamide followed by cyclization of the resulting *S*-alkylated derivatives **2a–e** in ethanol containing sodium ethoxide (Scheme 1).



1	Ar
a	C_6H_5
b	*p*-OCH_3-C_6H_4
c	*p*-Cl-C_6H_4

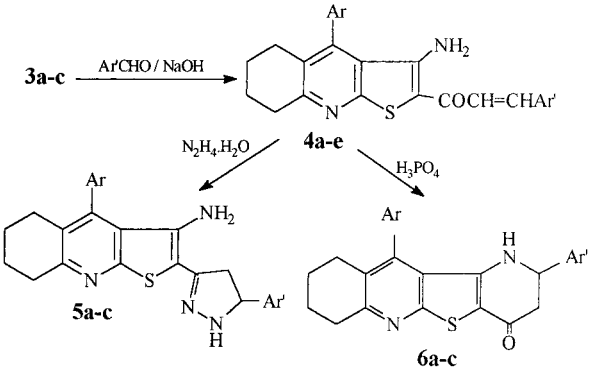
2, 3	Ar	Z
a	C_6H_5	Me
b	*p*-OCH_3-C_6H_4	Me
c	*p*-Cl-C_6H_4	Me
d	*p*-OCH_3-C_6H_4	OEt
e	*p*-OCH_3-C_6H_4	NH_2

Scheme 1

When *o*-aminoketones **3a–c** were allowed to condense with aromatic aldehydes, the 1-(3-amino-4-aryl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolin-2-yl)-3-aryl-2-propen-1-ones (**4a–e**) were produced. Refluxing of **4a–c** with hydrazine hydrate in ethanol afforded the pyrazoline derivatives **5a–c**. The intramolecular cyclization of **4a–c,** *via* Michael addition of the amino group to the α,β-unsaturated centre was achieved upon refluxing with orthophosphoric acid, when the hexahydropyrido[2′,3′:4,5]thieno[2,3-*b*]quinolin-4-ones (**6a–c**) were obtained (Scheme 2).

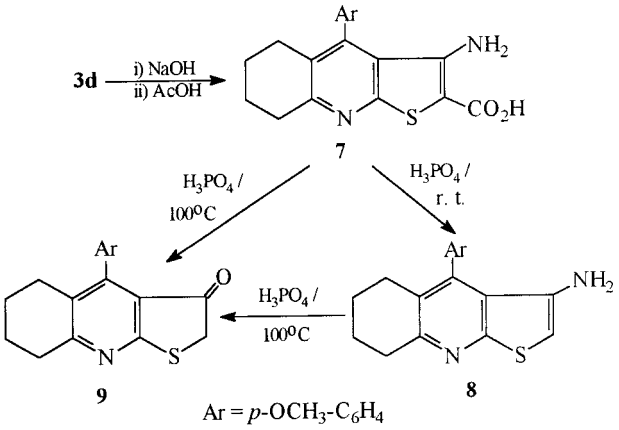
Saponification of the *o*-aminoester **3d** resulted in the formation of the corresponding carboxylic acid **7,** which upon treatment with orthophosphoric acid at room temperature underwent decarboxylation to give amino compound **8**.[19] When the latter reaction was performed at 100°C, the product was identified as thienoquinolinone **9** which was also prepared *via* treatment of **8** with orthophosphoric acid at 100°C (Scheme 3).

The reaction of **8** with ethyl α-cyano-β-ethoxyacrylate afforded the thienoquinoline **10** instead of its isomer **11.** When **10** was heated in acetic acid, the corresponding pyridothienoquinoline **12** was obtained (Scheme 4).

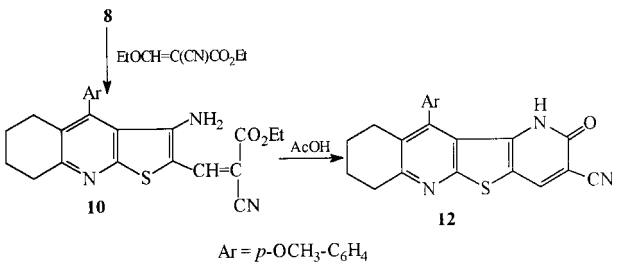


4-6	Ar	Ar'
a	C_6H_5	C_6H_5
b	*p*-OCH_3-C_6H_4	C_6H_5
c	*p*-OCH_3-C_6H_4	*p*-OCH_3-C_6H_4
d	*p*-OCH_3-C_6H_4	3,4-methylenedioxyphenyl
e	*p*-Cl-C_6H_4	C_6H_5

Scheme 2



Scheme 3



Scheme 4

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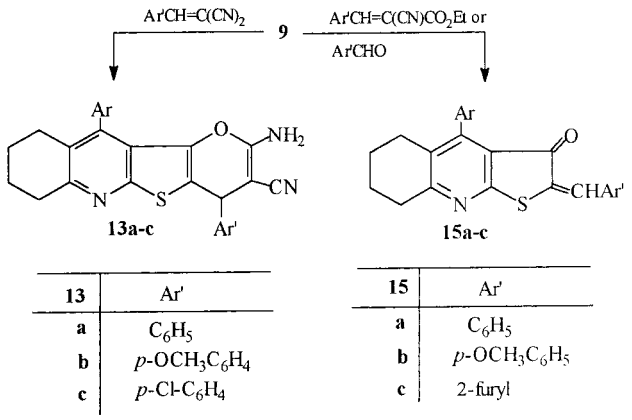
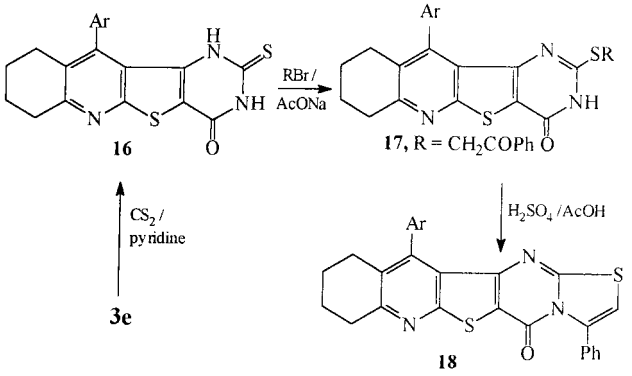
The reaction of **9** with arylmethylene malononitriles gave the target pyranothienoquinolines **13a-c**. In contrast, the interaction of **9** with ethyl β-aryl or (2-furyl)-α-cyanoacrylates did not afford the expected pyranothienoquinolines **14a-c** and instead of the chalcones **15a-c** were produced. The structures of **15a-c** were further confirmed by another route of preparation *via* direct condensation of **9** with the respective aldehydes (Scheme 5).



13	Ar'
a	C_6H_5
b	*p*-$OCH_3C_6H_4$
c	*p*-Cl-C_6H_4

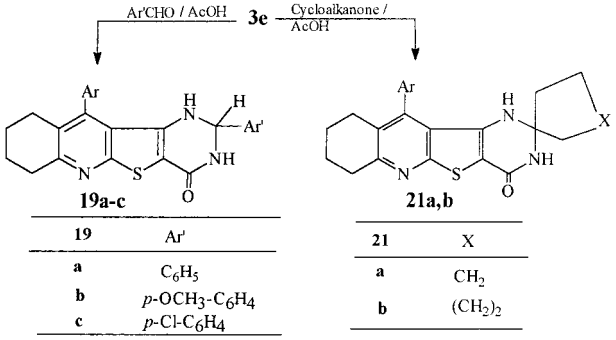
15	Ar'
a	C_6H_5
b	*p*-$OCH_3C_6H_5$
c	2-furyl

Scheme 5



Scheme 6

The interaction of *o*-aminocarboxamide **3e** with carbon disulfide led to the formation of oxopyrimidinethione derivative **16** which with phenacyl bromide afforded the ketone **17**. Compound **17** underwent cyclodehydration upon treatment with concentrated sulfuric acid to furnish thiazolopyrimidothienoquinoline derivative **18** (Scheme 6). The condensation of **3e** with aromatic aldehydes in refluxing acetic acid afforded the hexahydropyrimidothienoquinolinones **19a-c.** When **3e** was allowed to react with cyclopentanone or cyclohexanone, the products were identified as spiro compounds **21a,b**[21] rather than Schiff's bases **20a,b** (Scheme 7).



19	Ar'
a	C_6H_5
b	*p*-OCH_3-C_6H_4
c	*p*-Cl-C_6H_4

21	X
a	CH_2
b	$(CH_2)_2$

Scheme 7

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