# Novel C-alkylation Reaction of Condensed Thiophenes with Enaminones, Enaminonitriles, Ethoxymethylene Malononitrile, Aryl Vinyl Ketones and $\omega$-Nitrostyrenes

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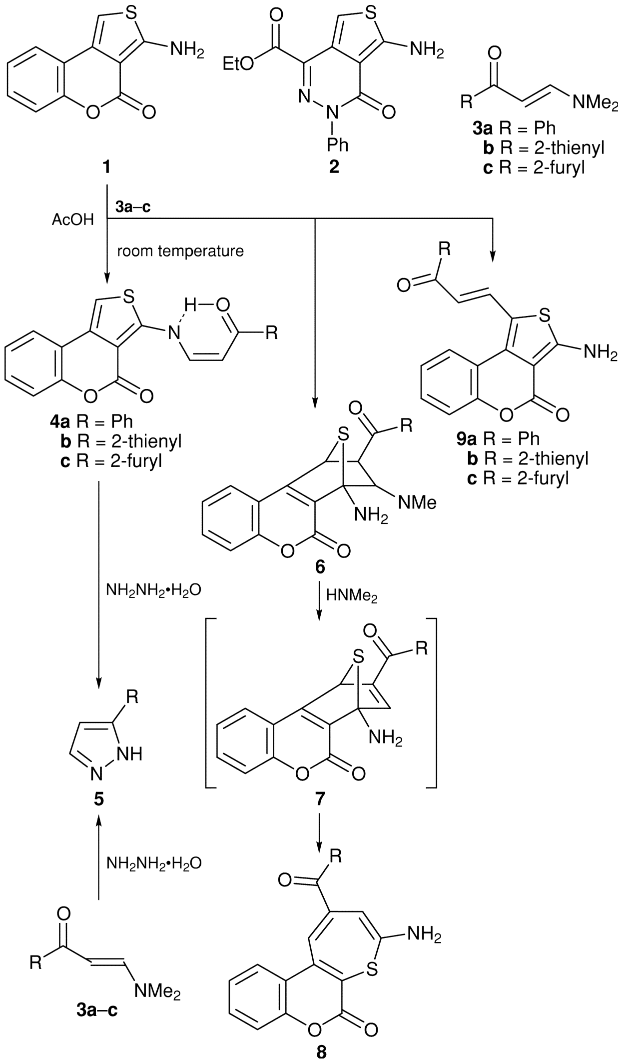
While the thienocoumarin **1** reacts with aryl vinyl ketones, $\omega$-nitrostyrene and ethoxymethylene malononitrile to yield only C-1 alkylation products, it reacts with enaminones (**3a**–**c**) to yield either N-alkylated derivatives (**4a**–**c**) or a mixture of **4a**–**c** and $\alpha,\beta$-unsaturated ketones (**9a**–**c**), the former rearranged into the latter on prolonged boiling under reflux in 1,4-dioxane solution in the presence of diethylamine.

In connection to our interest in reactivity of thienocoumarins and thienopyridazines in Diels–Alder reactions,[9] we investigated the behaviour of **1** and **2** towards several activated double bond systems. A new C-1 alkylation reaction occurred under conditions that led previously,[7–9] with electron-poor olefins and acetylenes, to a Diels–Alder type reaction. The formation of trace amounts of the C-alkylation product on the thiophene moiety upon reacting certain thienopyridines with electron-poor acetylenes has been observed earlier.[11] To our knowledge this is the first observed high yield reaction of this type with condensed thiophenes. It opens up a route for the synthesis of a variety of substituted thienocoumarins and thienoazines with substituents that are not readily obtainable, and seems to be of interest for utility in further chemical transformations. Thus, compound **1** reacted with **3a**–**c** in acetic acid at room temperature to yield (80–85%) products of addition and dimethylamine elimination. IR and $^1$H NMR spectra of these products indicated involvement of the amino function in this reaction. Therefore, structure **4a**–**c** was suggested for this product. The *cis* structure **4a**–**c** was preferred over the possible *trans* form based on $^1$H NMR, which showed the presence of an olefinic doublet at $\delta_H$ ~6.25 and 7.93 ppm with $J = 9$ Hz which is typical for *cis* protons. The predominance of the *cis* form for these reaction products is due to stabilization by hydrogen bonding as depicted in formula **4**. When treated with hydrazine hydrate in refluxing ethanol, compound **4a** was converted into a mixture of **1** and the pyrazole **5**. The latter was also synthesized from the reaction of **3a** and hydrazine hydrate, utilizing our reported procedure.[12] When the reaction of **1** with **3a**–**c** was conducted in refluxing acetic acid, solid products **4a**–**c** (33–43%) were isolated by filtering the hot solution. When the mother liquor was left to stand at room temperature, the C-alkylation products **9a**–**c** were isolated in 32–36% yields. These products were found to be isomeric with **4a**–**c**. Both IR and $^1$H NMR indicated that the amino function was not involved into the reaction. Initially, it was thought that this product was the thiepine **8**, which can be formed *via* intermediacy of **6** and **7** in a way similar to that recently suggested by us to account for thiepine formation on reacting **1** with electron-poor acetylenes.[9] However, the $^1$H NMR spectrum lacked the signals at $\delta$ 5.0–6.0 ppm that would be expected for C-3 and C-5 of the thiepine moiety **8**.[13,14] The $^1$H NMR spectrum indicated the presence of two *trans* olefinic protons at $\delta_H \approx 7.06$ and 8.40 ppm with $J = 14$ Hz. Thus, structures **9a**–**c** were established for the reaction products. When **4a**–**c** were refluxed in pyridine solution or in 1,4-dioxane–diethylamine solution they were largely converted (60–70%) into **9a**–**c**. Better conversion yields could not be achieved under a variety of conditions. It is thus believed that products **4** are kinetic products while **9** are the thermodynamic ones. Conversion of **4** into **9** in basic media is believed to proceed *via* base addition across the double bond and elimination of **1**, thus allowing more of the thermodynamic product to be formed.



Compound **1** was also reacted with ethoxymethylene malononitrile to yield the ylidenemalononitrile derivative **10**.

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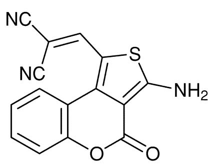
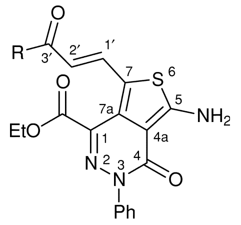
*To receive any correspondence.

Similar to the behaviour of **1** towards **3a**–**c**, compound **2** also reacted with **3a**,**b** to yield the thienopyridines **11a**,**b** in good yields.

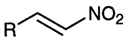


**10**

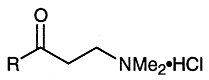


**11a** R = Ph
**b** R = 2-thienyl

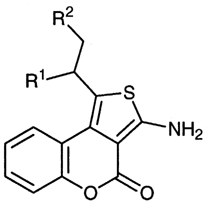
Compound **1** reacted with $\omega$-nitrostyrenes (**12a**–**c**) and with aryl vinyl ketones, generated *in situ* from corresponding dimethylaminopropanone hydrochlorides **13a**,**b**, to yield 1:1 adducts **14a**–**e**. These were stable under reflux in protic solvents, and thus the possible formation of cycloadducts similar to **6** was ruled out. Moreover, $^{13}C$ NMR of the reaction products indicated the presence of only two $sp^3$ carbons while in cycloadducts four such carbons should have been observed.



**12a** R = Ph
**b** R = 4-$CH_3OC_6H_4$
**c** R = 4-$ClC_6H_4$



**13a** R = Ph
**b** R = 2-thienyl



**14a** $R^1$ = Ph, $R^2$ = $NO_2$
**b** $R^1$ = 4-$CH_3OC_6H_4$, $R^2$ = $NO_2$
**c** $R^1$ = 4-$ClC_6H_4$, $R^2$ = $NO_2$
**d** $R^1$ = H, $R^2$ = PhCO
**e** $R^1$ = H, $R^2$ = 2-($C_4H_3S$)CO

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References: 15

Charts: 1

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