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A NOVEL SYNTHESIS OF THIOPHENES[1]

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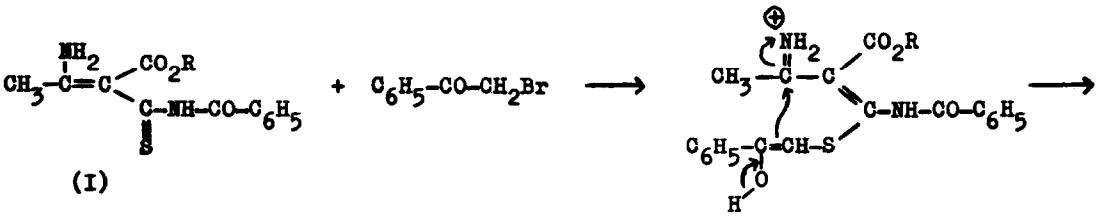
We have discovered that the 1:1 adducts of β-imino carbonyl derivatives and alkyl, aryl or acyl isothiocyanates[2] react with phenacyl bromide to produce tetra-substituted thiophenes. The yields range from 30 to 90%.

The reaction is carried out in refluxing isopropanol with equimolar quantities of the reactants, without any added base, and is complete within 30 minutes to an hour. The adduct (I) for instance, reacts with phenacyl bromide to give the thiophene (II) in over 50% yield. The proof of structure of this compound rests on analytical values, spectral properties (IR, UV, NMR), and further chemical transformations. We suggest that the active methylene in the intermediate adds to the protonated imine system, followed by elimination of ammonia (as ammonium bromide).

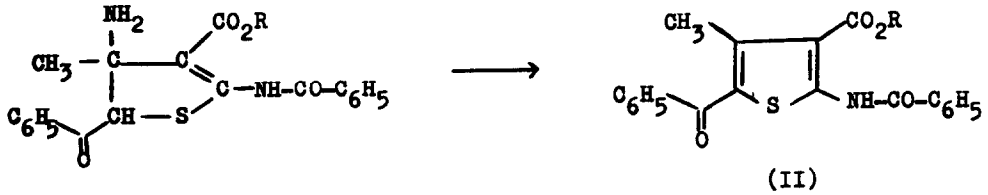
In the outcome, this reaction bears a formal resemblance to the thiophene synthesis recently reported by Smutny[3].

Extension of this synthesis to simpler enamines has provided interesting results. The morpholinocyclopentene-phenyl isothiocyanate adduct (III) reacts with phenacyl bromide to produce the thiophene (IV). However, the corresponding cyclohexene derivative (V) took a different course to give the known thiazole (VI) as the only isolable product.

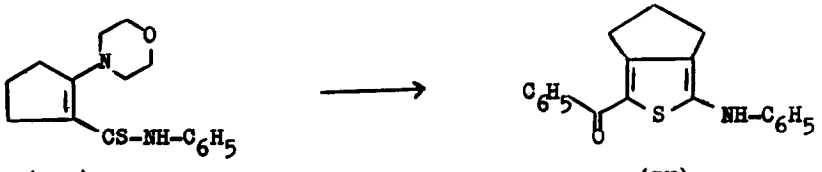
Further work is in progress to explore the full scope of this reaction.



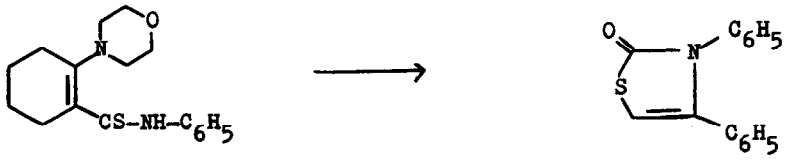
(I)



(II)



(III) (IV)



(V) (VI)

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2. For a brief review, see H. Ulrich in Cycloaddition Reactions of Heterocumulenes, Academic Press, New York, 1967, pp. 221-231.
3. E.J. Smutny, J. Am. Chem. Soc., 91, 208 (1969).