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The Utility of Phosphonium Ylides in Heterocyclic Synthesis: Synthesis of Pyridazinone and Tetrahydrocinnolinone Derivatives

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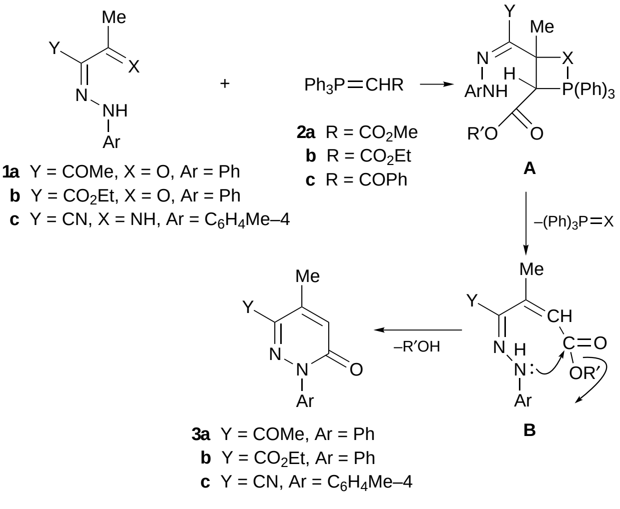
The synthesis of pyridazinone and tetrahydrocinnolinone derivatives *via* the reaction of phosphonium ylides with different hydrazines is accomplished; reaction of a pyridazinone derivative with Wittig reagents is also achieved.

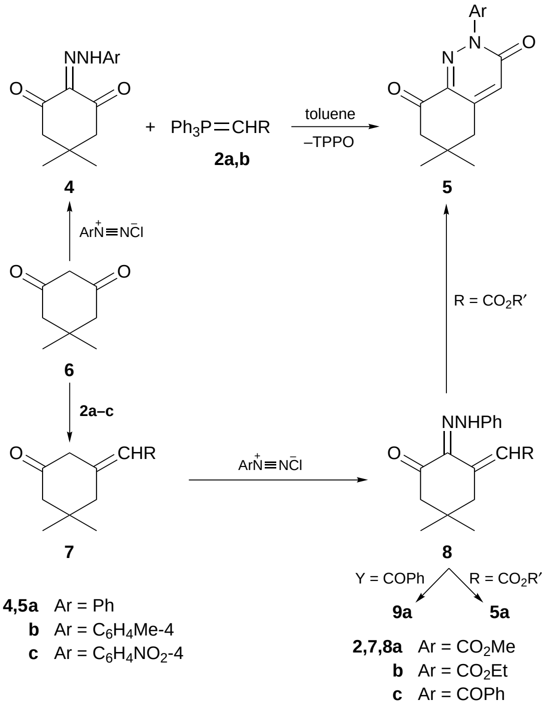
Arylhydrazones have been widely reported in the literature as reagents for the synthesis of heterocyclic compounds.[1–6] Indeed they are fundamental to the syntheses of a range of pharmaceutical fungicides and solvatochromic dyes. In this paper the preparation of pyridazinones and their fused systems *via* reaction of phosphonium ylides with different hydrazones is reported.

The starting arylhydrazones **1a–c** were readily obtained by coupling the appropriate methylene reagents with different arenediazonium salts as previously reported.[13,14] Compounds **1a–c** reacted smoothly with each of the Wittig reagents **2a,b** to give directly the corresponding pyridazinone derivatives **3a–c**. The structures of **3a–c** were confirmed by a thorough study of their MS and NMR data. The NMR spectrum of **3a** in different solvents as well as its ^{13}C NMR were in accordance with the structure of the product which had been previously prepared by another methodology.[6] The formation of compounds **3a–c** is assumed to proceed *via* nucleophilic addition of the phosphorus ylide **2** to the carbonyl group in **2a**,**b** or to the imine group in **1c** to give the betaine intermediate **A**. The latter undergoes irreversible decomposition to give **B** that cyclizes to give the final isolable pyridazine derivatives **3a–c** *via* alcohol elimination (Scheme 1).



Scheme 1

Similar to **1**, this synthesis was extended to the 2-arylhydrazonocyclohexane-1,3-dione derivatives **4a–c** which were readily obtained by coupling 3,3-dimethylcyclohexane-1,5-dione (**6**) with the appropriate arenediazonium chlorides as reported earlier.[15] The reaction of **4a–c** with either **2a** or **2b** afforded extensively the tetrahydrocinnolinone derivatives **5a–c**, respectively (Scheme 2). The cinnolinone **5a** was also prepared *via* an independent route involving the reaction of **2a**,**b** with 3,3-dimethylcyclohexane-1,5-dione **6** in boiling dry toluene to give the olefin intermediate **7a**,**b**. The latter afford **8a**,**b** on coupling with benzenediazonium chloride. Compounds **8a**,**b** cyclized on boiling in a solution of ethanol and piperidine to give the final product **5a** (Scheme 2).



Scheme 2

Compounds **4a–c** also reacted with **2c** in boiling toluene to afford the hydroxy derivatives **9a–c** (Scheme 3). Similarly the structure of **9a** was further established by the reaction of dimedone **6** with **2c** resulting in **7c** which reacted with benzenediazonium chloride to give **8c**. Upon boiling **8c** in an ethanol–piperidine solution, **9a** was obtained (Scheme 3).

The preparation of new tetrahydrocinnolinones from cyclic *β*-diketo derivatives was generalized. Thus, treatment of compounds **10–12** with benzenediazonium chloride gave the corresponding hydrazones **13–15** respectively.[13] The reaction of the phosphonium ylide **2a** with compounds **13–15** proceeded in boiling dry toluene to give the corresponding new condensed tetrahydrocinnolinones **16–18**, respectively, together with triphenylphosphine oxide which was isolated from the reaction medium. Analogues of these compounds have already been prepared.[16–18] The formation of **16–18** is assumed to proceed *via* the corresponding intermediate olefin, *e.g.* **19** (Scheme 4).

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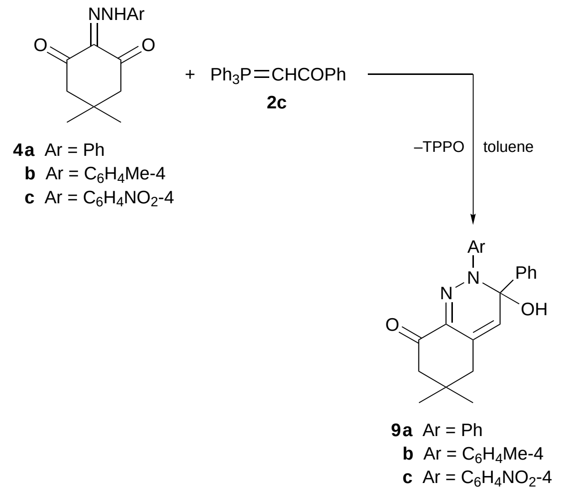
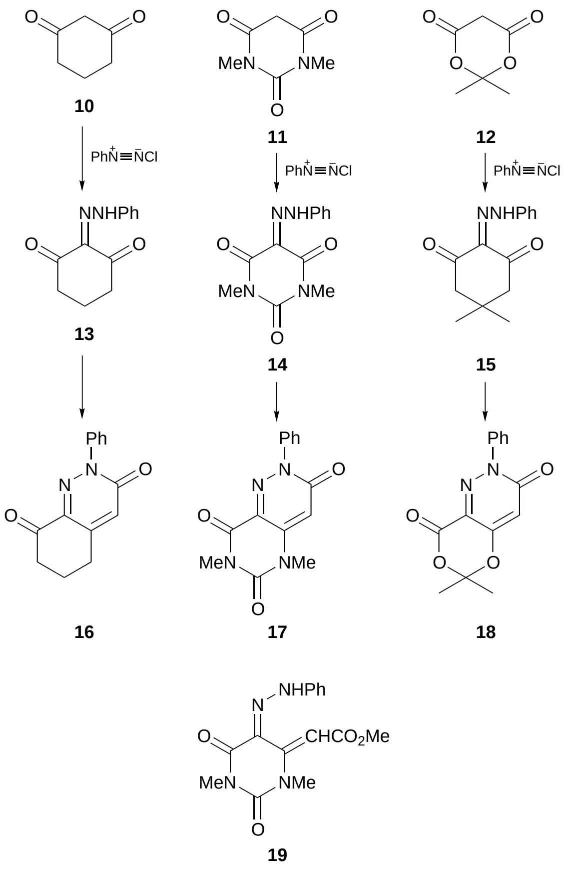
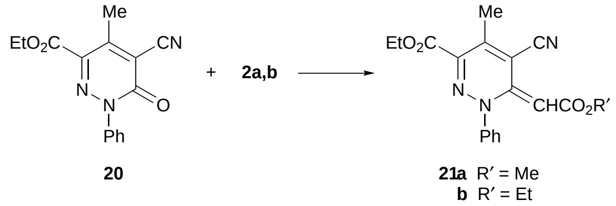


Scheme 3



Scheme 4



Scheme 5

We also investigated the reaction of Wittig reagents **2a**,**b** with a pyridazinone derivative. Thus, reaction of **2a,b** with ethyl 1-aryl-5-cyano-4-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylate **29**[19] in dry toluene afforded the corresponding olefins **21a**,**b** respectively (Scheme 5).

Techniques used: ^{1}H and ^{13}C NMR, MS, IR, elemental analysis

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