

CeCl₃·7H₂O catalyzed Clauson-Kaas reaction. Synthesis and derivatization of *N*-Arylpyrroles

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INTRODUCTION

Pyrroles are an important class of heterocycles which represents not only useful building blocks in natural product synthesis, but also basic structural units in compounds that exhibit remarkable pharmacological activities.¹ One of the most common methods to synthesize pyrroles is the reaction of 2,5-dimehoxytetrahydrofuran with primary amines under acid catalysis, known as Clauson-Kaas reaction.²

On the other hand, substituted compounds with a thiocyanate group are important intermediates in organic synthesis because they can easily be transformed into various functional groups of sulfur, as sulfide, thioesters, disulfides, thiols, thiocarbamates, etc.³ Thus, thiocyanation of pyrroles have great applicability in organic synthesis as a direct pathway to form carbon-sulfur bonds in the synthesis of new pyrroles derivatives, as disulfides and 1-aryl-2-(trichloromethylthio)-1*H*-pyrroles.

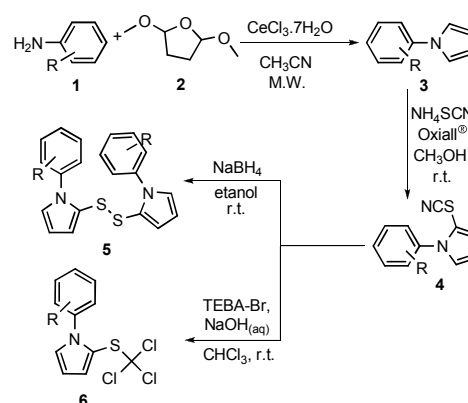
RESULTS AND DISCUSSION

In this work we describe a new methodology for the synthesis of 1- arylpyrroles **3** by a Clauson-Kaas reaction employing cerium (III) chloride heptahydrate (0.06 eq.) as a catalyst. The reaction was performed in acetonitrile at reflux temperature under microwave irradiation (Scheme 1).

In a second step, we synthesize 1-aryl-2-thiocyanate-1*H*-pyrroles **4** from 1-aryl pyrroles employing Oxiall[®] (600 mg/ mmol), an oxidant for the treatment of swimming pools based on monopersulfate potassium. The reaction was carried out at room temperature using methanol as solvent (Scheme 1).

Finally, we performed the synthesis of a new class of disulfides **5**, derived from aryl-2-thiocyanate-1*H*-pyrroles **4** by reduction of thiocyanate group with sodium borohydride (1 eq.) in ethanol at room temperature. The 1,2-bis(1-aryl-1*H*-pyrrole-2-yl) disulfides **5** were obtained in good yields. Also from **4**, 1-aryl-2-(trichloromethylthio)-1*H*-pyrroles **6** were prepared in good yields, by phase transfer condition, using chloroform, TEBA-Br (0.05 eq.) and aqueous solution of sodium hydroxide (Scheme 1).⁴

The results for these transformations can be seen in Table 1.



Scheme 1.

Table 1. Results for synthesis of products **3** to **6**.

#	R	3		4		5		6	
		Time ^a	% ^b	Time ^a	% ^b	Time ^a	% ^b	Time ^a	% ^b
1	H	12,5	90	120	89	30	90	120	72
2	<i>p</i> -Cl	2,5	89	90	92	30	90	90	73
3	<i>p</i> -OMe	20	84	30	92	30	94	120	75
4	<i>o</i> -Me	10	88	70	90	30	93	120	70

^a Time in minutes. ^b Isolated yields.

CONCLUSION

In conclusion, we developed a new protocol for the synthesis of pyrroles using microwave irradiation and cerium (III) chloride heptahydrate as catalyst. The products were obtained in high yields and short reaction times. We also developed an important method for thiocyanation of pyrroles using Oxiall[®], a cheap and accessible reagent. Finally, we performed the synthesis of two new classes of compounds from 1-aryl-2-thiocyanate-1*H*-pyrroles **4**, the 1,2-bis(1-aryl-1*H*-pyrrole-2-yl) disulfides **5** and the 1-aryl-2-(trichloromethylthio)-1*H*-pyrroles **6**.

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