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Lac Sulfur on Alumina-Triethanolamine-An Effective Reagent for the Synthesis of Substituted Guanidines

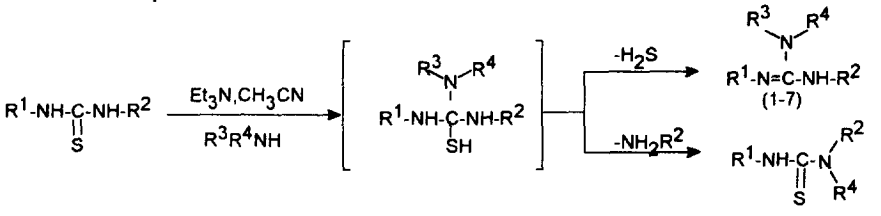
Krishnamurthy Ramadas

Centre for Agrochemical Research, SPIC Science Foundation,

110, Mount Road, Guindy, Madras 600 032, India.

Abstract: A direct synthesis of substituted guanidines is reported from their thiourea analogues. The strategy adopted is a concise approach to the synthesis of the title compounds.

Our recent report[1] on the facile conversion of symmetrical to unsymmetrical thioureas reflected the failure to transform 1,3-disubstituted thioureas to the corresponding guanidines which was then the object of our work. We had postulated the tetrahedral intermediate depicted below.



Use of triethanolamine instead of triethyl amine coupled with the use of lac sulfur dispersed on alumina[2] in the presence of amine nucleophile provided the desired guanidine through the expulsion of hydrogen sulfide.

Lac sulfur [3,4] facilitates the removal of hydrogen sulfide, which is effectively trapped by triethanolamine. This procedure is bound to trigger commercial interest since pollution due to hydrogen sulfide is avoided.

While the role of triethanolamine is being examined , use of triethylamine with lac sulfur or any other form of sulfur leads to poor formation of guanidines. Thus the combination of lac sulfur and triethanolamine provides a ready access to the guanidines from 1,3-disubstituted thioureas. The reagent works well for diaryl,arylalkyl and monoaryl substitued thioureas. The scope of the reagent is being extended to cover the dialkyl analogues as well. The table illustrates the specific examples studied. The guanidines were compared with those synthesised independently[5].

The process does not involve the use of toxic reagents like phosgene or unstable carbodiimides and fares well in comparison to other reported procedures for the guanidine synthesis which include our own published results[5] and references cited therein.

Dedicated to **Professor N.S.Narsimhan**, Director , CAR, SSF.

General Procedure:

A THF solution of thiourea (0.01mol,15mL), triethanolamine (0.01mol,2mL) and lac sulfur adsorbed on alumina (1:1,5g) was stirred before admitting morpholine*(0.01mol, 1mL). The reaction was stirred under gentle reflux and the guanidine formation was complete generally in about 2h. Work-up consisted of filtration and washing the residue with THF (2x5mL). The filtrate along with the washings was evaporated to give the product in respectable yields.

*.In practice, a two-fold excess of amine nucleophile assists in rapid product formation.

Table-Syntheses of guanidines using Lac sulfur-alumina

Ent. No	R^1	R^2	R^3	R^4	Reaction Time(h)	Yield(%)
1[a]	Phenyl	Phenyl	H	H	1.5	85
2	Phenyl	Phenyl	Et	Et	1.0	82
3[a]	o-Tolyl	o-Tolyl	H	H	1.0	68
4	Phenyl	phenyl	Morpholyl	H	1.5	85
5	o-Tolyl	o-Tolyl	Morpholyl	H	1.5	80
6	Phenyl	Cyclohexyl	Morpholyl	H	2.0	72
7	o-Tolyl	H	Morpholyl	H	2.0	80

a. 2 eqvt of sodamide was used as the amine.

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