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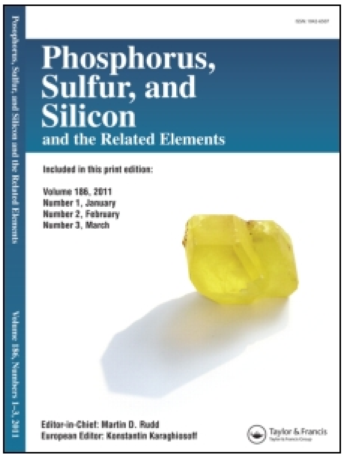

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A Remarkably Simple Conversion of Nitriles to Thioamides

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A REMARKABLY SIMPLE CONVERSION OF NITRILES TO THIOAMIDES

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Abstract Thiolacetic acid and light smoothly convert nitriles to thioamides.

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The acid catalyzed addition of thiolacetic acid to aromatic nitriles has already been reported to yield thioamides but the scope and limitations of the reaction were not explored and the potential advantages surprisingly unexploited.[1] Using a model reaction we discovered that when stoichiometric amounts of 4-butyronitrile, thiolacetic acid and $BF_3{\bullet}OEt_2$ were reacted at room temperature in dichloroethane, thiobutanamide **1** (48%) along with the acylthioimidates **2** and **3** were obtained, as predicted by analogy with the Pinner synthesis of imidates.[2] However when excess thiolacetic acid (2 equivalents) was used followed by a basic work-up (aqueous NH_4OH) a complete conversion of the intermediates occured and the product was obtained in 72% yield demonstrating the obvious potential of thiolacetic acid as a useful reagent for the thiolysis of nitriles. $BF_3{\bullet}OEt_2$ (2 equivalents) was found to be the Lewis acid of choice for the tranformation of structurally diverse aliphatic or aromatic nitriles with only few exceptions. Aromatic nitriles congugated with electron-donating substituents such as an alkoxy, exemplified by entry **#6**, are considerably less electrophilic at the carbon center and the addition of thiolacetic acid being the rate-determining step, the conversion is considerably slow. Fortunately, the use of aluminium chloride, a powerful oxygenophile, as the acid catalyst smoothly produces the corresponding thioamide in 93% yield. With the o- and m- cyanopyridines, similar arguments and the formation of insoluble complexes also dictate a particular attention and hydrogen chloride was found to be the catalyst of choice as can be seen with the results of entries **#8** and **#9**. Even though we were satisfied with this new procedure as such, much to our delight we discovered an even simpler procedure for the thiolysis of nitriles.

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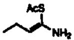
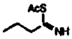
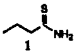
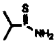
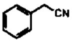
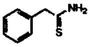
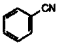
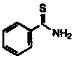
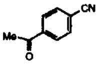
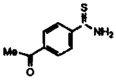
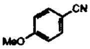
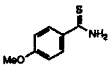
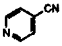
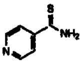
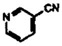
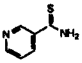
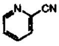
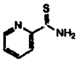
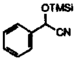
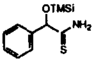
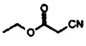
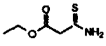
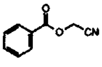
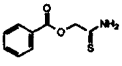
Considering the well known potential of thiol acids to give highly reactive radical species, we have obtained excellent results in the conversion of all classes of nitriles to their corresponding thioamides by simply illuminating a 0.2M CCl_4 solution of the nitrile and thiolacetic acid (2 equivalents) with a 150 watt floodlamp and allowing the mixture to react under nitrogen overnight. Typically the reaction mixture was concentrated to dryness and purified on a short column of silica gel. However in many cases the crystallized product in the reaction mixture was filtered and obtained in a pure enough state for most synthetic purposes. Thiolacetic acid is safe and easy to handle, commercially available and cheap, and its use in the acid catalyzed or light induced reactions described herein unambiguously provided the most simple, mild and apparently universal conversion of a wide range of structurally diverse nitriles to thioamides. Therefore, in all repects, it should be considered as the replacement of choice to other sources of sulphur for the thiolysis of nitriles in a procedure suitable for scale-up.[3]

ENTRY		PRODUCT	YIELD	
			LEWIS ACID	LIGHT
1		 2  3  1	$BF_3 \cdot OEt_2$ 72	
2			89	
3			75	
4			75	
5			91	86
6			$AlCl_3$ (2.4) 93	86
7			$BF_3 \cdot OEt_2$ 94	79
8			HCl (g,xs) 92	81
9			91	78
10				86
11			$BF_3 \cdot OEt_2$ 79	78
12			83	83

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2. J. Poupart, A. Bruylants, P. Crooy, Synthesis, 622 (1972).
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