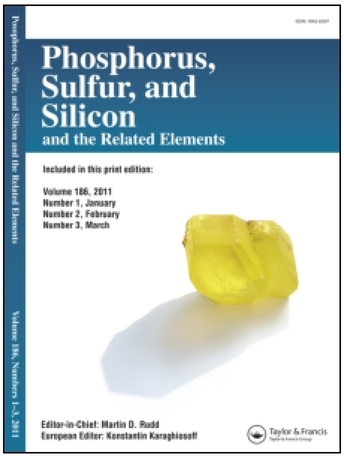


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Alkylation of Thiophenes and Preparation of Benzothiophenes Using Modified Montmorillonite Clay Catalysts

Peter D. Clark[a]; Andrew Kirk[a]; Shaun T. Mesher[a]; James G. K. Yee[a]
[a] Department of Chemistry, The University of Calgary, Calgary, Alberta, Canada

To cite this Article Clark, Peter D. , Kirk, Andrew , Mesher, Shaun T. and Yee, James G. K.(1994) 'Alkylation of Thiophenes and Preparation of Benzothiophenes Using Modified Montmorillonite Clay Catalysts', Phosphorus, Sulfur, and Silicon and the Related Elements, 95: 1, 441 — 443

To link to this Article: DOI: 10.1080/10426509408034269

URL: http://dx.doi.org/10.1080/10426509408034269

Phosphorus, Sulfur, and Silicon, 1994, Vol. 95–96, pp. 441–443
Reprints available directly from the publisher
Photocopying permitted by license only

ALKYLATION OF THIOPHENES AND PREPARATION OF BENZOTHIOPHENES USING MODIFIED MONTMORILLONITE CLAY CATALYSTS

PETER D. CLARK *, ANDREW KIRK, SHAUN T. MESHER AND JAMES G.K. YEE
Department of Chemistry, The University of Calgary, 2500 University Drive N.W., Calgary, Alberta, T2N 1N4, Canada.

Abstract Regioselective benzylation of thiophene and benzothiophene using benzyl chloride and a $ZnCl_2$-promoted montmorillonite catalyst is described. An improved process for the cyclization of (arylthio)acetaldehyde dialkyl acetals to benzothiophenes using the same catalyst is also documented.

INTRODUCTION

Preparation of alkylthiophenes by Friedel-Crafts alkylation of thiophene using standard procedures is not viable because of the sensitivity of thiophene to acidic conditions and its tendency to undergo polyalkylation and polymerization [1]. Similarly, poor yields of mixtures of alkylbenzothiophenes are obtained by direct alkylation using $AlCl_3$, $ZnCl_2$ and other conventional Friedel-Crafts catalysts [2]. Recently, Lewis acid-promoted montmorillonite clays have been shown to be efficient catalysts for the alkylation of simple benzenes [3]. In this work, we have attempted to extend this methodology to the preparation of alkylthiophenes and benzothiophenes with the expectation that the restricted pores within the clay catalyst would inhibit polyalkylation and polymerization reactions. In addition, clay-catalyzed intramolecular cyclization of (arylthio)acetaldehyde dialkyl acetals to benzothiophenes has been investigated to determine if this potentially useful method for benzothiophene synthesis [2] can be improved to give practical yields.

EXPERIMENTAL

Clay catalysts were prepared by stirring a methanolic solution of $ZnCl_2$ with K_{10}-montmorillonite clay (ex-Fluka) (2 mmol g^{-1} clay) for 30 min., removal of the methanol by rotary evaporation and activation of the catalysts at 300°C for 12 h. In a typical alkylation experiment, benzyl chloride (8 mmol) was added to a stirred solution of either thiophene or benzothiophene (40 mmol) and the clay catalyst (1 g for thiophene experiments and 10 g for benzothiophene alkylations) (see Table 1 for details of conditions). Products were isolated by standard techniques and were purified by column chromatography when necessary [4].

(Arylthio)acetaldehyde acetals [2] were cyclized by two methods: (a) in chlorobenzene at various temperatures using a 5:1 acetal/clay ratio or (b) by a vapour-phase technique in which the acetal was drawn through the catalyst (1 g) packed in a tube heated to 300°C, at a pressure of 0.025 mm Hg. Approximately 2 g h^{-1} of acetal were passed through the catalyst and products were collected in a trap cooled by liquid nitrogen. No purification of products was necessary for vapour phase experiments. Results and conditions for the cyclizations are shown in Table 2.

RESULTS AND DISCUSSION

Table 1. Benzylation of Thiophene (TP) and Benzo[b]thiophene (BT)

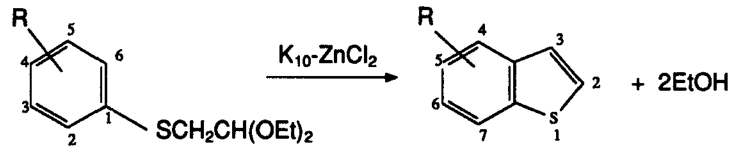
Substrate	Catalyst	Solvent	T°C	Time (h)	Products (% Yield) [a]		
					2-Benzyl	3-Benzyl	Dibenzyl
TP	$ZnCl_2$	PhCl	80	>30	60	20	10
TP	K_{10}	PhCl	80	>25	60	20	11
TP	K_{10}-$ZnCl_2$	PhCl	80	0.25	60	20	9
TP	K_{10}-$ZnCl_2$	CH_2Cl_2	40	1.5	61	29	9
TP	K_{10}-$ZnCl_2$	$PhNO_2$	80	<0.1	91	-	9
					2,-5-or6-Monobenzyl	3-Benzyl	Dibenzyl
BT	$ZnCl_2$	CH_3NO_2	20	2	15	28	43
BT	K_{10}	CH_3NO_2	20	24	20	22	23
BT	K_{10}-$ZnCl_2$	CH_3NO_2	20	0.5	29	37	10
BT	K_{10}-$ZnCl_2$	CH_3NO_2	-18	2	7	58 (74) [b]	13

[a] Remaining percentage was unreacted TP or BT.
[b] Yield assuming re-cycle of BT.

Data on the benzylation of TP (Table 1) show that K_{10} clay and free $ZnCl_2$ are relatively inactive materials when used alone, but produce a highly effective catalyst in combination. Solvation of the reaction intermediates at the K_{10}-$ZnCl_2$ catalyst seems to be important as a significant increase in reaction rate was observed when nitrobenzene was used as solvent. With this solvent, the reaction was complete in < 0.1 h yielding 2-benzylTP as the sole mono-benzylated product. To our knowledge, this is the first example of a completely regioselective alkylation of thiophene. Further studies have shown [4] that the 2-isomer is the kinetic product, which if left in contact with catalyst, undergoes rearrangement to a mixture of 3-benzylTP and 2,5- and 3,5-dibenzylTP and TP.

Alkylation of BT is, potentially, more difficult as 6 mono-substituted isomers may be observed (3-, 2- and 5-products are usually formed) along with di-substituted products and polymeric material. As was noted in the benzylation of TP, K_{10}-$ZnCl_2$ is much more active than the virgin clay or dissolved $ZnCl_2$, but gives only partial regioselectivity to the 3-isomer. Nevertheless, the 74% yield (assuming recovery of BT, which is, in fact, readily accomplished by flash chromatography) of the kinetically controlled 3-benzylBT obtained at -18°C is the most selective and highest yielding alkylation of BT recorded to date.

Table 2. Cyclization of (Arylthio)acetaldehyde Diethyl Acetals



Substrate	Method a	Product	Isolated Yield
R = H	**a**, PhCl, 80°C	BT	10-46%
R = H	**b**, 300°C	BT	84%
R = 2-Me	**b**, 300°C	7-MeBt	85%
R = 3-Me	**b**, 300°C	4-/6-MeBT	98%
R = 4-Me	**b**, 300°C	5-MeBT	81%
R = 4-Cl	**b**, 300°C	5-ClBT	82%
R = 4-Br	**b**, 300°C	5-BrBT	87%
R = 3-OMe	**b**, 300°C	4-/6-OMeBT	67%

See experimental section for description of methods **a** and **b**.

Cyclization of (arylthio)acetaldehyde acetals to BT derivatives has been known for some time [2] but yields are very variable because of the sensitivity of both reagents and products to the acidic conditions (PPA) necessary to promote the reaction. Disappointing yields of BT were obtained from our attempts to cyclize the acetals in chlorobenzene solution using the K_{10}-$ZnCl_2$ catalyst. Since the major by-product observed in solution, diphenyl disulfide, likely arises by intermolecular processes, vapour phase conditions were employed to promote the desired intramolecular reaction. This strategy resulted in very good isolated yields of BT and its derivatives with little or no by-product formation. Some by-products were observed if the rate of passage of the acetal through the catalyst was too high, but if rates were limited (see experimental, method b), BT products could be recovered from the cold trap in very high purity (> 99.5%).

REFERENCES

1. R. Taylor, Chapter 1, Electrophilic Substitution of Thiophene and Its Derivatives in Advances in Heterocyclic Compounds, "Thiophene and Its Derivatives", Part II, edited by S. Gronowitz (John Wiley and Sons, New York, 1986).
2. B. Iddon and R.M. Scrowston, Adv. Heterocycl. Chem., 11, 177 (1970).
3. P. Lazlo and A. Mathy, Helv. Chim. Acta., 70, 577 (1987).
4. P.D. Clark, A. Kirk and R.A. Kydd, Catalysis Letters, 25, 163 (1994).