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ACTIVATION OF MIXED CARBOXYLIC α-BROMOTOLUOYL ANHYDRIDES BY SILVER TETRAFLUOROBORATE. SYNTHESIS OF ESTERS AND THIOL ESTERS

Satoshi Fukuoka,† Seiji Takimoto, Tsutomu Katsuki,* and Masaru Yamaguchi
Department of Chemistry, Faculty of Science, Kyushu University 33, Higashi-ku,
Fukuoka 812, Japan

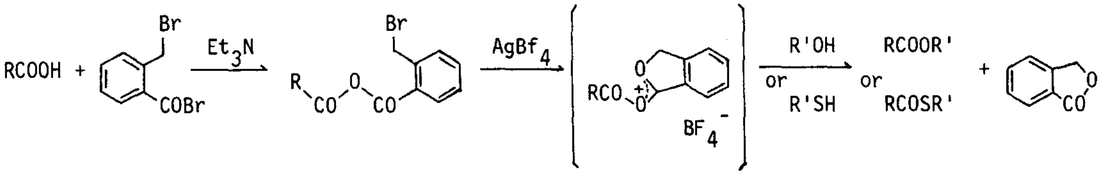
Summary: Mixed carboxylic α-bromotoluoyl anhydrides were activated by silver tetrafluoroborate through intramolecular cyclization and reacted with alcohols or thiols giving the corresponding esters or thiol esters in good yileds with the elimination of phthalide.

We previously reported a new type of mixed anhydrides (2) prepared from carboxylic acids and α-bromotoluoyl bromide (1),[1] which on heating at 80～145 °C in benzene or *N*,*N*,*N*',*N*'-tetramethylurea with alcohols gave carboxylic esters in good yields with the elimination of phthalide.[2] In this communication are described a new, non-thermal activation of this unique mixed anhydrides and its application to the synthesis of esters[3] and thiol esters.[4]

In a search for effective additives which make the anhydrides usable under mild conditions as a general and strong acylating agents, a stoichiometric amount of silver tetrafluoroborate has been found to be the most satisfactory one. Activation of **2** occurred very rapidly in dichloromethane or acetonitrile at room temperature, and the subsequent addition of alcohols or thiols led to the formation of the corresponding esters or thiol esters in good yields. The results obtained are shown in Table 1. For the acylation of benzenethiol, however, the use of dimethoxyethane (DME) throughout the activation and esterification processes gave the best result. It is noteworthy that no epimerization was detected in the esterification of methyl hydrogen *meso*-2,4-dimethylglutarate. Cyclized cationic species (**3**) are postulated as the active intermediates for the reaction and the facile elimination of phthalide (**4**) from them is considered to promote their acyl-transfer property.

The experimental procedure is exemplified by the preparation of *S*-isopropyl 2-methylpentanethioate. The acylation of alcohols was carried out in the same manner.

α-Bromo-o-toluoyl bromide (1, 75 μl, 0.5 mmol) was added to a stirred mixture of 2-methylpentanoic acid (63 μl, 0.5 mmol), triethylamine (70 μl, 0.5 mmol), and ether (0.8 ml). After 1 h, the mixture was filtered through Celite, concentrated, and diluted with acetonitrile (0.8 ml). To this solution were added silver tetrafluoroborate (92 mg, 0.5 mmol) and, after



(1) (2) (3) (4)

Table 1. Reaction of Mixed Anhydrides (**2**) Activated by Silver Tetrafluoroborate with Alcohols and Thiols

R in RCOOH	R'OH or R'SH'	Solvent	Time(min)[a]	Yield[b] of Ester or Thiol Ester
$CH_3CH_2CH_2$	$(CH_3)_2CHOH$	CH_2Cl_2	8	84(67)
$CH_3CH_2CH_2(CH_3)CH$	CH_3CH_2OH	CH_2Cl_2	10	81(72)
$CH_3CH_2CH_2(CH_3)CH$	$(CH_3)_2CHOH$	CH_2Cl_2	30	85(75)
$(CH_3)_3C$	<u>cyclo</u>-$C_6H_{11}OH$	CH_2Cl_2	15	94
$(CH_3)_3C$	C_6H_5OH	CH_2Cl_2	1	77(69)
C_6H_5	$(CH_3)_2CHOH$	CH_2Cl_2	3	(62)
<u>meso</u>-$CH_3OCOCH(CH_3)CH_2(CH_3)CH$	$(CH_3)_2CHOH$	CH_2Cl_2	40	84[c]
$CH_3CH_2CH_2$	$(CH_3)_3CSH$	CH_2Cl_2	4	94(74)
$CH_3CH_2CH_2(CH_3)CH$	CH_3CH_2SH	CH_3CN	5	(83)
$CH_3CH_2CH_2(CH_3)CH$	$(CH_3)_2CHSH$	CH_3CN	10	83(80)
$(CH_3)_3C$	$(CH_3)_3CSH$	CH_3CN	15	(81)
$(CH_3)_3C$	C_6H_5SH	DME	15	82[d]
<u>meso</u>-$CH_3OCOCH(CH_3)CH_2(CH_3)CH$	$(CH_3)_3CSH$	CH_2Cl_2	5	72[c]

a) Reaction time required for alcoholysis or thiolysis of 2. b) Yields were determined by GLPC by comparing with appropriate internal standards. Isolated yields were given in parentheses. All the products were identified by ^{1}H-NMR by comparing with authentic specimens. c) No epimerization was detected by GLPC analysis. d) The reaction were carried out at -10 °C.

3 min, 2-propanethiol (46 μl, 0.5 mmol). The mixture was stirred for 10 min at room temperature, diluted with pentane (2 ml), and filtered. The filtrate was washed with saturated aqueous sodium hydrogencarbonate and water successively, dried over anhydrous sodium sulfate, and concentrated to a residue which was distilled to afford <u>S</u>-isopropyl 2-methylpentanethioate in 80% yield.

Further studies on the application of this type of anhydrides are in progress.

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† Present address; Goverment Industrial Research Institute, Shikoku, Hananomiya 2-3-3, Takamatsu 761

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