lowed. The change in the absorbance A of β-DPNH at 340 mμ with respect to time (in minutes) is measured on a Colman Junior II spectrophotometer, which is equal to the rate of creatine phosphokinase reaction. The results are given in the Results and Discussion section.

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Registry No.—**2a,** 52555-34-7; **2a** HCl, 52555-35-8; **2b,** 52555-36-9; **2b** $(H_2SO_4)_{1/2}$, 52555-37-0; **5,** 2208-07-3; **6b,** 52555-38-1; **8,** 35404-50-3; **9,** 52555-39-2; glycine, 56-40-6; sarcosine HCl, 637-96-7; sodium chloroacetate, 3926-62-3; ethylenediamine, 107-15-3.

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Some New Arenesulfonate Leaving Groups Less Reactive Than the *p*-Toluenesulfonate Group

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The wide use and advantages of sulfonate, and particularly arenesulfonate, leaving groups in the study of reaction mechanisms are well known. Their reactivity spread, which is one of their advantages, has been successfully extended in the direction of groups more reactive than the usual *p*-toluenesulfonate,[2] but not so in the opposite direction.

Our attempts to moderate the solvolytic reactivity of some 3-aryl-2-butyl sulfonate derivatives had led us to a search for such "poor" sulfonate leaving groups. Of such groups synthesized and studied, the arenesulfonate derivatives of 3-*p*-tolyl-2-butanol (Table I) and their solvolytic reactivities, as measured by their polarimetric[3] rate of solvolysis in 65% aqueous ethanol (Table II), are reported in this communication.

Table I
Summary of Physical and Analytical Data of Some Arenesulfonyl Chlorides and (+)-*threo*-3-*p*-Tolyl-2-butyl Arenesulfonates

Compd[a]	Registry no.	Mp, °C	$[\alpha]^{25}D$[b]
2,4,6-$(MeO)_3$-I[c]	52499-93-1	134–136	
$(Me)_5$-I[c]	52499-94-2	80–81	
II[d]	52499-95-3	43–44	35.2
III[e]	52499-96-4	43–44	29.5
4-Me-III	52499-97-5	69–70	21.2
$(Me)_5$-III	52499-98-6	112–113	29.1
4-MeO-III	52499-99-7	46–47	22.5
2,4,6-$(MeO)_3$-III	52522-72-2	76–77	8.0

[a] Satisfactory combustion analytical data (±0.7% for C and H) have been provided for all of the compounds in this table. Ed. [b] In benzene solution (1.3%). [c] I = benzenesulfonyl chloride. [d] II = (+)-*threo*-3-*p*-tolyl-2-butyl methanesulfonate. [e] III = benzenesulfonate ester of (+)-*threo*-3-*p*-tolyl-2-butanol.

Table II
Relative Leaving Group Abilities Based on Polarimetric Rates in the Solvolysis of Some (+)-*threo*-3-*p*-Tolyl-2-butyl Arenesulfonates in 65% (Wt/Wt) Aqueous Ethanol[a]

			50 °C		
Compd	Temp,[b] °C	$k \times 10^2$, min^{-1}[c]	$k \times 10^2$, min^{-1}[d]	k_{OTs}/k	k_{III}/k
II[e]	63.43	7.243 ± 0.033	1.722	1.26	1.66
	58.80	4.593 ± 0.022			
	53.54	2.540 ± 0.021			
III[f]	53.54	4.211 ± 0.022	2.859	0.76	1.00
	46.45	1.923 ± 0.024			
4-Me-III	53.54	3.223 ± 0.051	2.168	1.00	1.32
	46.45	1.445 ± 0.023			
4-MeO-III	60.50	3.646 ± 0.017	1.135	1.91	2.52
	53.54	1.696 ± 0.017			
2,4,6-$(MeO)_3$-III	72.28	2.924 ± 0.009	0.273	7.94	10.47
	69.90	2.333 ± 0.031			
	66.48	1.626 ± 0.016			
$(Me)_5$-III	72.28	3.123 ± 0.013	0.255	8.50	11.21
	66.48	1.665 ± 0.018			

[a] Containing 35.0% (wt/wt) water (Karl Fischer determination), and being 0.03 M in NaOAc and 0.02 M in the ester. [b] The temperatures given are those inside the polarimeter cell. [c] Each rate constant represents the average of two to three rate constant determinations followed from 12 to 83% reaction. [d] Rate constants extrapolated to 50°. [e] (+)-*threo*-3-*p*-Tolyl-2-butyl methanesulfonate. [f] Benzenesulfonate ester of (+)-*threo*-3-*p*-tolyl-2-butanol.

The methanesulfonate derivative has also been studied. Methanesulfonates have been reported to be some three times less reactive than tosylates,[4] thus being the slowest reacting sulfonate derivatives known.[5] In our hands and in the solvolytic system used, the mesylate proved to be only 26% less reactive than the tosylate at 50° (Table II). Against this minimal deceleration achieved with the methanesulfonate group and the small retardation by the *p*-methoxybenzenesulfonate group (mosylate, –OMos), 1.9-fold at 50°, the decelarations realized with the now reported 2,4,6-trimethoxybenzenesulfonate group (trimosylate or trosylate, –OTmos or –OTms), 7.9-fold at 50°, and even more that with the pentamethylbenzenesulfonate group (pesylate, –OPmes or –OPms), 8.5-fold, become quite substantial. Of these two new arenesulfonate groups,

the latter has also superior handling features, such as crystallinity of the chloride and the ester derivative, higher yield in the synthesis of the chloride, and higher rotation of the ester derivative.

The present results render the pentamethylbenzenesulfonate group the least reactive sulfonate group known; they also extend the reactivity spread of sulfonate leaving groups from the known 8×10^4-fold range—from trifluoromethanesulfonates to *p*-toluenesulfonates[2]—up to a 7×10^5-fold range, from trifluoromethanesulfonates to pentamethylbenzenesulfonates.[3]

Several uses of "poor" sulfonate leaving groups can be envisaged. Among them, one can mention some of those for which this study was undertaken. Thus, *e.g.*, the use of the pentamethylbenzenesulfonate ester of (+)-*threo*-3-*p*-anisyl-2-butanol has rendered possible the measurement of the polarimetric rate of formolysis of this system, which was not possible for its *p*-toluenesulfonate ester since its formolysis was very rapid even near the freezing point of formic acid.[6] Similarly, the polarimetric rate of trifluoroacetolysis of the same ester of (+)-*threo*-3-phenyl-2-butanol could be measured more conveniently and accurately at temperatures above zero, *e.g.*, 8°,[6] as compared to the difficult and very inconvenient rate measurements conducted earlier with the *p*-toluenesulfonate derivative at −8°.[7]

It is of interest to assess the effect of successive substitution by methyl and methoxy groups on the reactivity of arenesulfonates. For this purpose, the unsubstituted benzenesulfonate ester itself was also studied. Comparison with this derivative (Table II) indicates that introduction of one methyl group in the para position slows down the solvolysis by a factor of only 1.31, whereas the fully methylated derivative solvolyzes 11.21 times slower. Introduction of a *p*-methoxy group decelerates the reaction by 2.52-fold, whereas the 2,4,6-trimethoxybenzenesulfonate derivative solvolyzes 10.47 times slower.

Other sulfonate leaving groups are under study and will be reported subsequently.

Experimental Section

The melting points reported are corrected. A Perkin-Elmer Model 141 photoelectric polarimeter was used for the measurement of polarimetric rates. The temperatures inside the polarimeter cell were measured with the use of thermistors and a thermistor actuated differential thermometric bridge allowing differential reading between these temperatures and the corresponding ones of the bath used to thermostat the polarimeter cell (jacket). The bath temperatures were corrected against factory calibrated (Thermoschneider, W. Germany) standard thermometers. The temperatures in the kinetic runs were maintained constant to within ±0.002°.

Arenesulfonyl Chlorides. *p*-Methoxybenzenesulfonyl chloride was prepared as previously reported.[8] The pentamethylbenzenesulfonyl chloride and the 2,4,6-trimethoxybenzenesulfonyl chloride were prepared from pentamethylbenzene and 2,4,6-trimethoxybenzene, respectively, by a known general procedure for the synthesis of arenesulfonyl chlorides.[9]

The following is a typical synthesis. A 0.09*M* solution of chlorosulfonic acid in dry chloroform was added dropwise over a period of about 30 min to a stirred 0.03 *M* solution of pentamethylbenzene in dry chloroform kept at about −5° during the addition. The reaction mixture was then allowed to reach room temperature and was poured into 5% aqueous sodium carbonate containing crushed ice. The chloroform layer was washed with cold 5% aqueous sodium bicarbonate followed by saturated aqueous sodium chloride and was dried over magnesium sulfate. The solvent was removed under reduced pressure. The solid residue, mp 79–81° (53%), was recrystallized twice from hexane giving the pure product, mp 80–81°. Analytical data are given in Table I.

Arenesulfonate Esters of (+)-*threo*-3-*p*-Tolyl-2-butanol. These were prepared by reaction of (+)-*threo*-3-*p*-tolyl-2-butanol[10] with the appropriate arenesulfonyl chloride (methanesulfonyl chloride in the synthesis of the methanesulfonate) by the usual procedure.[11] Room temperature and 2–3 days of reaction time were used for the preparation of the pentamethyl and the trimethoxy derivatives. The pure esters were obtained in about 75% yield. Physical and analytical data of these esters are given in Table I.

Kinetic Measurements. Polarimetric rates of solvolysis were measured by following the change in the optical rotation, at 436 mμ, of the appropriate solutions of the esters placed in a thermostated 1-dm cell of a photoelectric polarimeter. The solvolysis medium, 65% (wt/wt) aqueous ethanol, contained an excess of sodium acetate used to react with the arenesulfonic acid liberated during reaction. Neither the resulting acetic acid nor sodium acetate had any measurable effect on observed rates of such ethanolysis reactions at the molarities involved (0.03 *M*), as concluded from earlier studies in our laboratory.[6] The polarimetric rates were followed from 12 to about 83% completion and showed good first-order kinetics. The pseudo-first-order rate constants were obtained from a least-squares treatment of the data.

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Reaction Kinetics of Furansulfonyl Chlorides with Anilines in Methanol and Reactivities of Benzene-, Thiophene-, and Furansulfonyl Chlorides

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The side-chain reactivity of pentatomic heterocycles toward nucleophiles is affected by opposite effects. Thiophen and furan are, in fact, electron withdrawing by inductive effect[1] and electron donating by resonance effect.[2,3] In the latter case, moreover, the conjugation between the furan ring and the side chain can be greater or smaller than that of the thiophene ring, depending on the electron de-