(room temperature, 13 h; 55 °C, 3.5 h), then poured into a saturated brine solution (20 mL), and extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and filtered and the volatiles removed under vacuum to yield the crude product (2.478 g). This was chromatographed (silica gel, 60 g; benzene, then benzene–ethyl acetate mixtures) to yield chromatographically pure samples of the starting ester (0.165 g, 11%), **6** (1.909 g, 82%), and pyrrolidine-2-thione (0.126 g, 16%). Attempted distillation of **6** under high vacuum (5×10^{-5} mmHg) resulted in extensive decomposition via the retro-Michael reaction, but it could be crystallized from petroleum ether/ethyl acetate: mp 58.5–60 °C; ^1H NMR δ 1.68–2.04 (2 H, m), 2.93 (2 H, t, J = 8 Hz), 3.10–3.34 (1 H, m), 3.50–4.58 (4 H, m), 3.65 (3 H, s), 3.73 (3 H, s), 6.83 (2 H, d, J = 8 Hz), 7.22 (2 H, d, J = 8 Hz); IR 1738, 1612, 1513 cm^{-1}; UV 229 (11 800), 270 (15 500) nm; mass spectrum, m/e 293 (34, M^+), 193 (16), 192 (100), 133 (36), 114 (17), 85 (16); molecular ion calcd for $C_{15}H_{19}NO_3S$ 293.1086, found 293.1057. Anal. Calcd for $C_{15}H_{19}NO_3S$: C, 61.41; H, 6.53; N, 4.77. Found: C, 61.20; H, 6.46; N, 4.89.

Methyl 2-(4-Methoxyphenyl)-3-[2-[(methoxycarbonyl)-methylene]pyrrolidin-1-yl]propionate (7). Methyl bromoacetate (5.15 g, 33.3 mmol) was added to a solution of **6** (7.25 g, 24.7 mmol) in dry THF (50 mL) and stirred at room temperature (16 h). The volatiles were removed under vacuum, the residue was dissolved in acetonitrile (100 mL), and triphenylphosphine (6.6 g, 25 mmol) and triethylamine (4 mL, 29 mmol) were added at room temperature. An exothermic reaction occurred immediately. The solution was stirred (30 min), the volatiles were removed under vacuum, and the residue was chromatographed (silica gel, 250 g, petroleum ether (60–80 °C)/ether 9:1). The product so obtained was contaminated with a small amount of triphenylphosphine sulfide and was purified by extraction into 2 M HCl, basification with concentrated NH_3 and extraction back into CH_2Cl_2. After the solution was dried (Na_2SO_4), the solvent was removed to yield a crystalline product (6.053 g, 74%), mp 85–88 °C. Recrystallization from petroleum ether (60–80 °C)/ethyl acetate gave an analytical sample: mp 86.5–88 °C; ^1H NMR δ 1.60–1.94 (2 H, m), 3.09 (2 H, t, J = 8 Hz), 2.76–4.10 (5 H, m), 3.62, 3.65, 3.78 (each 3 H, s), 4.57 (1 H, br s), 6.84 (2 H, d, J = 8 Hz), 7.18 (2 H, d, J = 8 Hz); IR 1732, 1688, 1580, 1508 cm^{-1}; UV 229 (12 200), 280 (29 300) nm and after addition of acid 228 (11 200), 277 (6500), 282 (6600) nm; mass spectrum, m/e 333 (16, M^+), 192 (46), 154 (100), 122 (13), 45 (35), 43 (17); molecular ion calcd for $C_{18}H_{23}NO_5$: 333.1576, found 333.1608. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.96; N, 4.21. Found: C, 64.62; H, 7.08; N, 4.30.

Sodium 2-(4-Methoxyphenyl)-3-[2-[(methoxycarbonyl)-methylene]pyrrolidin-1-yl]propionate (8). **7** (5.5 g, 16.5 mmol) was suspended in water (40 mL), and NaOH (0.680 g, 17 mmol) was added. The suspension was refluxed until the mixture became homogeneous (2.5 h). The water was removed under vacuum, the last traces were azeotroped off with benzene, and the resulting solid (5.66 g) was dried (room temperature, 0.1 mmHg). This salt was used without any further purification.

Methyl 1-Aza-3-(methoxyphenyl)-4-oxobicyclo[4.3.0]-5-nonene-5-carboxylate (9). **8** (0.844 g, 2.5 mmol) was suspended in dry THF (25 mL) under a N_2 atmosphere, and a catalytic amount (0.020 g) of tetrabutylammonium iodide was added. Methyl chloroformate (0.20 mL, 2.6 mmol) was added, and the solution was stirred at room temperature (8 h). The volatiles were removed and the dried residue was chromatographed (silica gel, 25 g; benzene–acetone 7:3, then increasing amounts of acetone up to pure acetone) to yield chromatographically pure samples of **7** (0.093 g, 11%) and **9** (0.572 g, 77%). An analytical sample was obtained by recrystallization from methanol–benzene (1:1): mp 126–127 °C; ^1H NMR δ 1.90–2.26 (2 H, m), 3.30 (2 H, t, J = 8 Hz), 3.40–3.85 (5 H, m), 3.70 (3 H, s), 3.74 (3 H, s), 6.80 (2 H, d, J = 8 Hz), 7.10 (2 H, d, J = 8 Hz); IR 3400, 1660, 1617, 1580, 1518 cm^{-1}; UV 226 (10 200), 246 (13 700), 285 sh (6800), 304 (11 700) nm and after addition of acid 226 (14 900), 244 sh (5700), 303 (8200) nm; mass spectrum, m/e 301 (40, M^+), 135 (24), 134 (100), 119 (18), 91 (14), 44 (20); molecular ion calcd for $C_{17}H_{19}NO_4$ 301.1314, found 301.1300. Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.75; H, 6.36; N, 4.65. Found: C, 67.76; H, 6.20; N, 4.93.

1-Aza-3-(4-methoxyphenyl)bicyclo[4.3.0]-5-nonen-4-one (11). An aqueous solution of KOH (1 M, 25 mL) was deaerated by bubbling N_2 through it overnight. **9** (0.471 g, 1.56 mmol) was then added and the solution was refluxed (1 h). It was then cooled, acidified (concentrated HCl), stirred at room temperature (30 min), basified (concentrated NH_3), and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and filtered, and the solvent was removed under vacuum to yield chromatographically pure **11** (0.352 g, 93%). The aqueous layer was reacidified (concentrated HCl) and extracted with CH_2Cl_2 (3 × 10 mL) to yield, after drying and removal of the solvent, **10** (0.032 g, 7%). On some occasions greater proportions of **10** were obtained; it could, however, be converted to **11** simply by warming with 2 M HCl. **10** was recrystallized from nitromethane; mp 186–188 °C; IR 3430, 2650, 1705, 1565, 1495 cm^{-1}; UV 232 (15 600), 241 (17 100), 285 sh (6900), 307 (12 200) nm, and essentially no change on addition of acid, but on addition of base 226 (16 000), 241 sh (8300), 284 sh (3600), 322 (13 100) nm; mass spectrum, m/e 287 (25, M^+), 135 (32), 134 (100), 119 (40), 91 (35), 69 (30), 65 (18); molecular ion calcd for $C_{16}H_{17}NO_4$ 287.1158, found 287.1179. Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88. Found: C, 66.71; H, 6.05; N, 5.42.

11: Recrystallization from a variety of solvents did not yield material having a sharp melting point. A sample recrystallized finally from benzene, mp 125–138 °C, gave acceptable analytical results and was used for spectral characterization: ^1H NMR δ 1.86–2.24 (2 H, m), 2.70 (2 H, t, J = 8 Hz), 3.26–3.70 (5 H, m), 3.74 (3 H, s), 5.08 (1 H, s), 6.80 (2 H, d, J = 8 Hz), 7.14 (2 H, d, J = 8 Hz); IR 1633, 1616, 1585, 1520 cm^{-1}; UV 224 (11 600), 278 sh (3300), 285 sh (4200), 318 (15 200) nm and after addition of acid 224 (11 400), 276 sh (5200), 284 sh (6800), 307 (10 000) nm; mass spectrum, m/e 243 (36, M^+), 135 (19), 134 (100), 119 (22), 91 (22). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.14; H, 7.04; N, 5.76. Found: C, 74,47; H, 7.06; N, 5.87.

1-Aza-3-(4-methoxyphenyl)bicyclo[4.3.0]nonan-4-one (12). Vinylogous amide **11** (0.173 g, 0.71 mmol) was dissolved in dry THF (10 mL), $LiAlH_4$ (0.007 g, 0.18 mmol) was added, and the solution was stirred at room temperature. After 20 min, TLC (benzene–acetone 1:1) showed that approximately equal amounts of starting material and product were present, so more $LiAlH_4$ (0.007 g) was added. Stirring was continued for 10 min, and then water (0.2 mL) and CH_2Cl_2 (10 mL) were added. The solution was dried (Na_2SO_4), and the volatiles were removed under vacuum to leave an oily residue (0.205 g) which was crystallized from an acetone–petroleum ether (40–60 °C) mixture (0.134 g, 77%, mp 105–108 °C). Further recrystallizations from acetone raised the melting point to 109–110 °C (lit. 105–106 °C,[5] 105.5–106 °C [6]): ^1H NMR δ 1.4–3.9 (series of m), 3.77 (3 H, s), 6.84 (2 H, d, J = 8 Hz), 7.04 (2 H, d, J = 8 Hz); IR (5% solution in CH_2Cl_2) 2950, 2800, 1715, 1618, 1518 cm^{-1}; mass spectrum, m/e 245 (28, M^+), 134 (100), 133 (26), 131 (17), 119 (22), 97 (16), 96 (16), 91 (15), 69 (73); molecular ion calcd for $C_{15}H_{19}NO_2$ 245.1416, found 245.1405.

Registry No. **5**, 50415-68-4; **6**, 73048-93-8; **7**, 73048-94-9; **8**, 73048-95-0; **9**, 73048-96-1; **10**, 73048-97-2; **11**, 73048-98-3; **12**, 73048-99-4; pyrrolidine-2-thione, 2295-35-4; dimethyl oxalate, 553-90-2; methyl (4-methoxyphenyl)acetate, 23786-14-3.

Migration of the Acyl Group in Substituted *o*-Aminophenols: Acetyl–Chloroacetyl Derivatives

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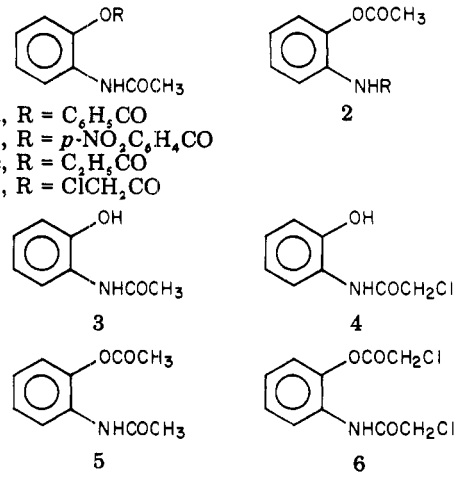
Received October 10, 1979

Smith and Elrod have recently reported that the diacyl-*o*-aminophenols **1a**, **1b**, and **1c** predominate over their isomers **2a**, **2b**, and **2c** in the equilibrium mixtures formed

0022-3263/80/1945-1715$01.00/0

Chart I. Acyl-o-aminophenols



1a, R = C_6H_5CO
b, R = p-$NO_2C_6H_4CO$
c, R = C_2H_5CO
d, R = $ClCH_2CO$

2

3

4

5

6

Table I. Isomerization Results

starting isomer	isomerzn method	time to equilib	solvolysis	% 2d in mixture
2d	abs EtOH	very fast	extensive[a]	86
1d	80% EtOH	60 min	none	87
2d	80% EtOH	5 min	none	86
1d	pyridine	4 h	extensive[b]	91
2d	pyridine	15 min	none	88
1d, 2d	reflux in *m*-xylene	12 h	none	94

[a] To 3 (72%) and 4 (4%). [b] To 3 (59%); 4 not detected.

by solvent-catalyzed isomerization of either isomer[2] (see Chart I). This finding is consistent with the hypothesis of LeRosen and Smith that the more stable isomer should be the one with the weaker electron-donor acyl group bonded to nitrogen.[3b] However, since the relative stabilities of two pairs of acyl(alkoxycarbonyl)-*o*-aminophenols do not conform to this hypothesis,[4] it was of interest to study an isomer pair of the type **1**, **2** in which the acetyl group is the stronger electron donor, so that the *O*-acetyl isomer should be the more stable. We selected the acetyl–chloroacetyl pair **1d**–**2d**. This pair was studied earlier by Nelson et al.,[5] who reported that saponification of either **1d** or **2d** gave only *o*-acetamidophenol **3**. They concluded that a molecular rearrangement had occurred during saponification and that the *N*-acetyl isomer **1d** was the more stable of the pair. However, it was later shown that saponification of diacyl-*o*-aminophenols does not identify reliably the more stable isomer of the pair.[3]

We have now found that solvent-catalyzed and thermal isomerizations of **1d** and **2d** give equilibrium mixtures containing 86–94% of the *N*-chloroacetyl compound **2d**, thus establishing it as the more stable isomer of the pair. Our results are summarized in Table I.

Saponification of either **1d** or **2d** gave a mixture of monoacyl compounds containing 90% **3** and 10% **4**. This result conforms to the prediction of LeRosen and Smith that a mixture of monoacyl compounds should always be formed by saponification of diacyl-*o*-aminophenols. Apparently Nelson et al. did not detect the minor component.

We have also compared the rates of solvolysis of the symmetrical compounds **5** and **6**. In absolute ethanol, **6** was completely solvolyzed to **4** in 15 min, whereas **5** was only 92% converted to **3** after 65 h.

The results of these isomerization and solvolysis experiments support the hypothesis that qualitative prediction of the more stable isomer of a pair of diacyl-*o*-aminophenols can be made by comparing the electron-donor properties of the two acyl groups. The acyl(alkoxycarbonyl) analogues appear not to conform to this hypothesis.

Experimental Section

Melting points were taken on a Fisher digital melting point analyzer and are not corrected. IR spectra were recorded from potassium bromide disks on a Perkin-Elmer Model 21 spectrophotometer. UV spectra were recorded with a Bausch and Lomb Model 600 UV–vis spectrophotometer. Stock solutions (0.2%) of the compounds in chloroform were diluted with cyclohexane so as to obtain absorbances in the range 0.3–0.9 at the wavelength absorption maximum.

Chromatographic analyses were made with a Waters ALC/GPC 202 liquid chromatograph equipped with a differential UV detector (254 nm) and a 30 cm × 4 mm (i.d.) μ-Porasil column. Chloroform (ethanol stabilized) containing 0.2% acetic acid was used as the developing solvent. No evidence for isomerization of the mixed diacyl compounds in chloroform solution was observed over several weeks at room temperature.

Isomerization and solvolysis experiments were carried out by evaporating 20-μL aliquots of 0.2% solutions of the compounds in an air stream. The residues were redissolved in 200 μL of chloroform and 5–10-μL aliquots analyzed by high-pressure LC.

Saponifications were carried out by stirring 0.1 g of the compound in 10 mL of 1% NaOH for 15 min at room temperature; 5% HCl was then added to make the solutions acidic to Congo Red. The acidic solutions were extracted with three 25-mL portions of chloroform, and extracts were combined, diluted to volume in 100-mL volumetric flasks, and analyzed by high-pressure LC.

A. Monoacyl Derivatives. Compound **3** was obtained from Aldrich Chemical Co., and **4** was prepared by the method of

Table II. Properties of Acyl-o-aminophenols

compd	mp, °C obsd	mp, °C lit.	IR abs, μm ester	IR abs, μm amide	UV abs λ, nm	UV abs 10^{-3} ε	LC response rt,[c] min	LC response mm/μg
1d	129-130[5]	128-130[5]	5.64	5.93	239, 280	21.3, 2.6	3.2	59
2d	111-112	113-114[5,6]	5.76	5.92	241	13.8	1.3	209
3	208-210	203-204[3a]		6.00	244[b]	10.5[b]	7.5	25
4	137-138	138-140[b]		6.07	285	3.0	2.2	91
5	129-130	124-125[3a]	5.74	5.91	240	13.5	4.1	38
6	133-134[a]		5.68	5.92	241	20.5	1.2	146

[a] New compound. Anal. Calcd for $C_{10}H_9O_3NCl$: C, 52.76; H, 4.43; Cl, 15.57. Found: C, 52.66; H, 4.45; Cl, 15.66. [b] Data from M.S. thesis of Lee Elrod, Jr., University of Arkansas, 1977. [c] Response time.

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Groenvik.[7] Both gave only a single peak when analyzed by high-pressure LC.

B. Preparation of Diacyl Derivatives. Compounds **1d**, **2d**, **5**, and **6** were prepared by the method described by Jacobs[6] and by Nelson.[5] A slurry of the acylamidophenol (0.007–0.03 mol) in a 5–15 molar excess of chloroacetyl chloride, acetyl chloride, or acetic anhydride was treated with a few drops of concentrated H_2SO_4, stirred for 15 min at 80 °C, and then poured into ice–water and stirred. The crude product was isolated by filtration, washed with water, dried, and recrystallized from benzene. All derivatives gave a single peak on high-pressure LC analysis.

Properties of the six compounds used in this study are listed in Table II. There is no correlation between UV absorbance and LC response because the latter depends on both retention time and UV absorbance. Thus, of two compounds with the same UV absorbance, the one with the shorter LC retention time will have the greater LC peak height per microgram.

Registry No. 1d, 73048-40-5; **2d**, 73037-92-0; **3**, 614-80-2; **4**, 10147-68-9; **5**, 5467-64-1; **6**, 37161-45-8.

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Synthesis of a Sulfone α-Tosylate. Benzyl (Tosyloxy)methyl Sulfone

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Received August 22, 1979

In our studies of leaving-group activities in base-induced 1,3-elimination reactions of α-X sulfones, it was necessary to prepare related sulfones bearing an α′ H in which X = halogen,[1] NO_2,[2] and OTs. For OTs, benzyl (tosyloxy)methyl sulfone (**6**) was prepared. Its base-induced reactivity proved to be quite unexpected.[3] No sulfone α-sulfonate like **6** has previously been reported.[4] Because this new class of compound appears to have unusual properties warranting further investigation, and because the usual methods for preparing sulfonates seem to be ineffective in these cases, we are describing the synthesis of **6** (Scheme I).

Failure of conventional approaches to provide tosylate **6** (vide infra) led us to consider the synthetic route of Engberts and Zwanenburg employing α-diazo sulfones.[4–6] As illustrated by reaction C in Scheme I, this approach was successful; **6** was formed in ca. 90% yield from the reaction of benzyl diazomethyl sulfone (**5**) with *p*-toluenesulfonic acid under very mild conditions. This reaction is interesting insofar as it involves a rare example of a rather facile intermolecular nucleophilic displacement of an α substituent of a sulfone, systems which usually resist such displacement reactions.[7] It was suggested that with α-diazo sulfones the reaction proceeds through the collapse of the intimately ion-paired diazonium salt intermediate; expulsion of stable N_2 from this highly energetic intermediate provides a very favorable transition energy.[4–6]

Scheme I

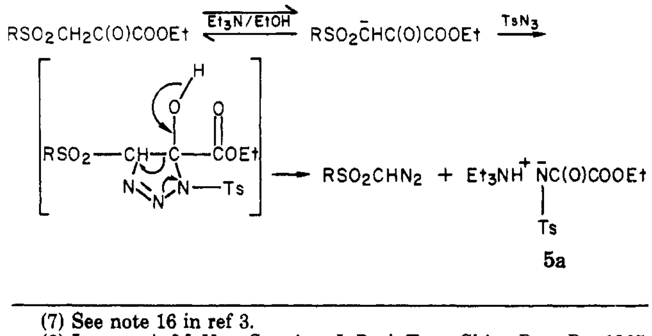
A. $PhCH_2SO_2Na$ (**1a**) + $BrCH_2C(O)COOEt$ (**2**) $\xrightarrow[10\ h\ (N_2)]{EtOH,\ reflux}$ $PhCH_2SO_2CH_2C(O)COOEt$ **3** (53%)

B. **3** + p-$CH_3C_6H_4SO_2N_3$ (**4**) $\xrightarrow[10-15\ °C,\ 1\ h\ (N_2)]{Et_3N,\ EtOH}$ $PhCH_2SO_2CHN_2$ **5** (64%)

C. **5** + p-$CH_3C_6H_4SO_3H$ $\xrightarrow[25\ °C,\ 2\ h\ (N_2)]{ClCH_2CH_2Cl}$ $PhCH_2SO_2CH_2OSO_2C_6H_4CH_3$-$p$ **6** (88%)

$$RSO_2\overset{+}{C}H\overset{}{N}_2 + TsOH \rightleftharpoons RSO_2CH_2\overset{+}{N}{\equiv}N\ \overset{-}{O}Ts \longrightarrow RSO_2CH_2OTs + N_2$$

In preparing **5** we had a choice of several methods which have been used to make α-diazo sulfones: (1) cleavage of *N*-nitroso-*N*-(sulfonylmethyl)urethanes with alkali or neutral alumina;[8] (2) cleavage of α-diazo-β-oxo sulfones by treatment with triethylamine;[9] (3) base-catalyzed reaction of α-sulfonyl aldehydes with tosyl azide;[10] and (4) base-catalyzed reaction of sulfonylpyruvic esters with tosyl azide.[11] The last method seemed to be the most advantageous because sulfonylpyruvic esters appeared to be more easily obtained or, in some cases, more stable than the substrates required by the other methods, and because of the simple product isolation it afforded. As indicated by reaction B in Scheme I, we obtained **5** by this route in 64% yield from the brief treatment of ethyl (benzylsulfonyl)pyruvate (**3**) with *p*-toluenesulfonyl azide (**4**) in cold $Et_3N/EtOH$ followed by the addition of water. Separation of **5** from the reaction mixture was also quite simple: it was readily extracted into ether, coformed triethylammonium imido salt **5a** remained in the aqueous solution,



5a

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