Synthesis with 1,1-Diurethanes

Benzylurethanes from Aryl Ethers

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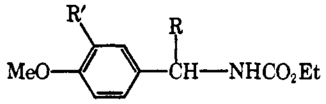
Benzylurethanes ware prepared from aryl ethers and 1,1-diurethanes. In a typical preparation an aryl ether (25 mmol), diurethane (25 mmol), BF_3-etherate (1 ml) were refluxed in toluene (30 ml) for 24 hr. After workup, the following derivatives of 1 were prepared (R, R′, mp and % yield given): H, H, 39–40°, 29%; Ph, H, 128–9°, 51%; H, OMe, 49–50°, 20%; Ph, OMe, 98.5–9.5°, 37%; $COCH_3$, OMe, 80–1°, 46%.



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The new preparation of benzylurethanes from aryl ethers and 1,1-diurethanes is described.

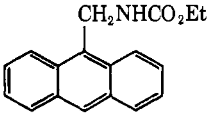
The chemistry of diurethanes, **1**, has been expanded to include diverse and unusual synthetic applications as a result of the discovery that reactive iminourethanes, or their protonated counterparts, **2**, are formed from **1** and a catalytic amount of BF_3 in refluxing benzene.

$$\underset{\mathbf{1}}{RCH(NHCO_2Et)_2} \rightarrow \underset{\mathbf{2}}{[RCH = NHCO_2Et]^+[NHCO_2Et]^-}$$

One property of **2**, dienophilicity, has been exploited in the synthesis of tetrahydropyridines from **1** and dienes (*2, 3, 7–10, 12*). A second property of **2**, behavior as a cation, has led to syntheses of 1,3-diaminopropanes from **1** and styrene (*9, 10*), of 4-substituted chromanes from salicylaldehyde diurethane and styrene (*10*), and of enol alkylation products of **1** and β-diketones (*1*).

In an unsuccessful attempt to extend the reaction scope of **2** to include aromatic substitution of aryl ethers, Wilkins (*13*) found anisole to be unreactive, although Merten et al. (*11*) had shown benzyl urethanes to be formed from certain phenols under the same reaction conditions above. We here report that if toluene is substituted for benzene as solvent, moderate yields of benzyl urethanes can in fact be obtained from anisole **3** and veratrole **4** and a variety of substituted diurethanes (Table I). With the higher boiling xylene as solvent, only polymeric material was obtained; this behavior is reminiscent of polymer formation from acid-catalyzed cleavage of pyrrole methylene urethane (*4*).

Efforts to effect reaction of diurethane **1**, R = H, with polycyclic aromatic compounds naphthalene, phenanthrene, and pyrene were unsuccessful, although we have confirmed the reaction of anthracene to form **10** (*13*). Phenylmethylene diurethane **1**, R = Ph, was unreactive; however, presumably because of transition-state interaction of the peri hydrogens of anthracene with the phenyl ring.



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EXPERIMENTAL SECTION

Melting points were measured on a Thomas-Hoover melting point apparatus and are uncorrected. Nmr spectra (60 Mc) were taken with a Varian A-60 instrument with $DCCl_3$ as solvent and TMS as internal standard. Microanalyses were performed by Micro-Analysis, Inc., Wilmington, Del. Infrared spectra were taken with a Perkin-Elmer 137 instrument with chloroform solvent.

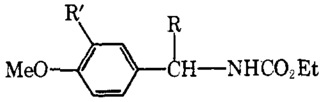
Preparation of 1,1-Diurethanes. Methylene diurethane was prepared according to the procedure of Cava and Wilkins (*2*). Phenylmethylene diurethane and acetylmethylene diurethane were prepared according to Harter and Liisberg (*7*).

Reaction of 1,1-Diurethanes. *General Procedure.* To an equimolar solution of 25 mmol of aryl ether and 25 mmol of diurethane in toluene (30 ml) was added BF_3-etherate (1 ml). After a 24-hr reflux, solvent was removed at aspirator vacuum and the residue was partitioned between water and ether. The ethereal layer was washed successively with water, saturated sodium bicarbonate, water, and dried ($MgSO_4$). Removal of solvent afforded benzylurethanes as described below.

p-Methoxybenzylurethane (**5**). Anisole (2.7 grams, 25 mmol) and methylene diurethane (4.7 grams, 25 mmol) were reacted as described above. Removal of solvent and distillation at 127–8°C (0.2 mm) yielded 1.7 grams (33%) of a colorless oil which solidified to a white solid. The distillate consisted of 17% *o*-methoxybenzylurethane and 83% *p*-methoxybenzylurethane (glpc 3% SE 30 100/120 Varaport 30 at 150°C). Recrystallization of the solid (ether–pet ether) afforded pure *p*-methoxybenzylurethane, mp 39–40°C [reported bp 117–19°, 0.2 mm, mp 40–1° (*6*)]; ir 3400 cm^{-1}, 1700 cm^{-1}; nmr δ 1.18 (*t*, 3, J = 7 Hz), 4.08 (*q*, 2, J = 7 Hz), 5.65 (NH), 4.21 (*d*, 2, J = 6 Hz), 3.72 (*s*), 7.02 (*dd*, 4, J = 9 Hz, J = 15 Hz).

α-Phenyl-p-methoxybenzylurethane (**6**). Anisole (2.7 grams, 25 mmol) and phenylmethylene diurethane (6.65 grams, 25 mmol) yielded 3.4 grams (51%) of a white solid, mp 128–9° (ether/ethanol), ir 3400 cm^{-1}, 1700 cm^{-1}; nmr δ 1.18 (*t*, 3, J = 7 Hz), 4.06 (*q*, 2, J = 7 Hz), 5.88 (*d*, 2, J = 8 Hz), 3.69 (*s*, 3), 5.35 (*d* broad, NH, J = 8 Hz), 6.9 (*dd*, 4, J = 12 Hz, J = 8 Hz), 7.2 (*s*, 5). *Anal.* Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.98. Found: C, 71.42; H, 6.59; N, 4.91.

TABLE I. Synthesis of Benzylurethanes from Aromatic Ethers



Substrate	RCH-$(NHCO_2Et)_2$	Benzylurethane	Yield, %
3	R = H	**5** R = H, R′ = H	27
3	R = Ph	**6** R = Ph, R′ = H	51
4	R = H	**7** R = H, R′ = OMe	20
4	R = Ph	**8** R = Ph, R′ = OMe	37
4	R = $COCH_3$	**9** R = $COCH_3$, R′ = OMe	46

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3,4-Dimethoxybenzylurethane (Veratrylamine Urethane) (**7**). Veratrole (3.46 grams, 25 mmol) and methylene diurethane (4.72 grams, 25 mmol) afforded 1.2 grams (20%) of a colorless oil, bp 163–7° (0.035 mm), which solidified to a white solid, mp 49–50°C (ether/pet ether), ir 3400 cm^{-1}, 1700 cm^{-1}; nmr δ 1.16 (t, 3, J = 7 Hz); 4.02 (q, 2, J = 7 Hz), 3.70 (s, 6), 4.15 (d, 2, J = 6 Hz), 5.45 (b, NH), 6.67 (bs, 3). *Anal.* Calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.86. Found: C, 59.74; H, 7.18; N, 5.98.

Urethane **7** was prepared independently from veratrylamine and ethylchlorocarbonate and was converted to N-methyl veratrylamine hydrochloride, mp 201–3°C [reported 202–4° (*5*)].

α-Phenyl-3,4-dimethylbenzylurethane (**8**). Veratrole (3 grams, 22 mmol) and phenyl methylene diurethane (5.85 grams, 22 mmol) afforded 2.35 grams (37%) of white solid, mp 98.5–99.5° (90% ethanol). Ir 3450 cm^{-1}, 1700 cm^{-1}; nmr δ 7.15 (s, 5); 6.67 (s, 3), 5.81 (d, one, J = 9 Hz), 5.22 (d broad, one, J = 9 Hz), 4.08 (q, 2, J = 7.5 Hz), 3.76 (s, 3), 3.73 (s, 3), 1.2 (t, 3, J = 7.5 Hz). *Anal.* Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.68; H, 6.52; N, 4.54.

α-Acetyl-3,4-dimethoxybenzylurethane (**9**). Veratrole (4.0 grams, 29 mmol) and α-acetyl-1,1-diurethane (6.75 grams, 29 mmol) afforded, after elution from florisil with 50/50 ether/pet ether, 3.71 grams (46%) of a white solid, mp 80–1°C (ether). Ir 3375 cm^{-1}, 1700 cm^{-1} broad; nmr δ 6.78 (s, 5), 6.26 (d, one, J = 6 Hz), 5.23 (d, one J = 6 Hz), 4.0 (q, 2, J = 7 Hz), 3.77 (s, 6), 2.08 (s, 3), 1.15 (t, 3, J = Hz). *Anal.* Calcd for $C_{14}H_{19}NO_5$: C, 59.78; H, 6.81; N, 4.98. Found: C, 59.82; H, 6.84; N, 5.06.

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Esterification and Addition Reactions of Perfluoroacryloyl Chloride

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Perfluoroacryloyl chloride was prepared from the acid using phosphorus pentachloride, and 3-chloro-2,3,3-trifluoropropionyl chloride was obtained as an unexpected by-product. 2,2-Difluoro-2-nitroethyl perfluoroacrylate was prepared using triethylamine and aluminum chloride. The physical properties and stereochemistry of the compounds are described.

Our interest in the synthesis of energetic monomers led to development of a synthesis for 2,2-difluoro-2-nitroethanol and its acrylate ester (*6*). This work was extended to include the preparation of 2,2-difluoro-2-nitroethyl perfluoroacrylate, IV. During the course of this work, some unusual addition reactions of hydrogen chloride and difluoronitroethanol to the perfluoroacryloyl group were observed. We now report the ester synthesis and a stereochemical analysis of the adducts.

The direct esterification of perfluoroacrylic acid, I, with difluoronitroethanol by conventional methods proved difficult; consequently, the esterification of perfluoroacryloyl chloride, II was investigated. To obtain the chloride, I was first prepared using a modification of Knunyants' procedure which involved the treatment of $CF_2 = CFMgI$ with carbon dioxide followed by acidification (*3*). The synthesis of II in 75% yield by the reaction of I with phosphorus pentachloride was reported by Gruz et al. (*3*), but the reaction conditions were not described. As a result several exploratory reactions were carried out to find optimum conditions for the preparation of II. When I was treated with an equimolar amount of phosphorus pentachloride at ambient temperature, II (10%) and 3-chloro-2,3,3-trifluoropropionyl chloride, III (40%), resulted, Reaction 1.

$$\underset{\text{I}}{CF_2 = CFCO_2H} + PCl_5 \rightarrow \underset{\text{II}}{CF_2 = CFCOCl} + \underset{\text{III}}{ClCF_2CHFCOCl} \quad (1)$$

The formation of III by the addition of hydrogen chloride to II was unusual when one considers the mild conditions used. Although several examples of nucleophilic and hydrogen halide addition to the double bond of the perfluoroacryloyl group have been reported (*1, 3, 7, 9, 10*), hydrogen halide additions usually require high temperatures and pressures. The structure of III was confirmed and differentiated from its other possible positional isomer, 2-chloro-2,3,3-trifluoropropionyl chloride, by proton and fluorine nmr spectral analyses. The best procedure developed for preparation of II was the dropwise addition of a benzoyl chloride solution of I to a slurry of phosphorus pentachloride in benzoyl chloride at 7 mm Hg. With use of this technique, II was removed from the reaction vessel as formed and was obtained in 60% yield with a 10% yield of III. Those reactions in which the pressure was allowed to rise to 15-20 mm showed a considerable increase in the yield of III.

The esterification of II with 2,2-difluoro-2-nitroethanol to obtain 2,2-difluoro-2-nitroethyl perfluoroacrylate, IV, was carried out by two different methods. First, II was treated with difluoronitroethanol at −35° to −40°C in the presence of triethylamine. IV was obtained in 8% yield, and a by-

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