gave 3-carbamoyl-4,6-diphenyl-3,4-dihydro-2*H*-thiopyran (**13a**) (0.236 g) as colorless crystals: mp 223–224 °C; MS (70 eV) *m/e* 295 (M^+, 22), 224 (59), 223 (100); IR (KBr) 1660 cm^{-1} (C=O); NMR (Me_2SO) δ 4.16 (dd, 1 H, *J* = 7 and 4 Hz), 6.2 (d, 1 H, *J* = 7 Hz), 6.9 (br band, 2 H), and 7.0–7.6 (m, 10 H). Anal. Calcd for $C_{18}H_{17}NOS$: C, 73.19; H, 5.80; S, 10.85. Found: C, 73.21; H, 5.86; S, 10.88.

3-Carbamoyl-6-(*p*-methoxyphenyl)-4-phenyl-3,4-dihydro- (14a): mp 174–176 °C (recrystallized from benzene); MS (70 eV) *m/e* 321 (M^+, 52), 250 (44), 249 (100); IR (KBr) 1660 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.7–2.26 (m, 2 H), 2.56–3.2 (m, 5 H), 3.9 (d, 1 H, *J* = 6 Hz), 5.6 (br band, 2 H), and 6.9–7.6 (m, 9 H). Anal. Calcd for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; S, 9.97. Found: C, 74.98; H, 6.04; S, 9.95.

3-Carbamoyl-4-(*p*-methoxyphenyl)-5,6-dihydrobenzo[*h*]-thiochroman (14b): mp 175–176 °C (recrystallized from benzene); MS (70 eV) *m/e* 351 (M^+, 79), 280 (42), 279 (64); IR (KBr) 1660 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.9–3.1 (m, 7 H), 3.7 (s, 3 H), 3.9 (d, 1 H, *J* = 6 Hz), 5.5 (br band, 2 H), and 6.7–7.5 (m, 8 H). Anal. Calcd for $C_{21}H_{21}NO_2S$: C, 71.79; H, 5.98; S, 9.12. Found: C, 71.74; H, 5.96; S, 9.00.

3-Carbamoyl-4-(*p*-chlorophenyl)-5,6-dihydrobenzo[*h*]thiochroman (14c): mp 138–140 °C (recrystallized from benzene); MS (70 eV) *m/e* 355 (M^+, 28), 284 (17), 283 (29), 249 (36); IR (KBr) 1660 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.9–3.1 (m, 7 H), 3.9 (d, 1 H, *J* = 3 Hz), 5.8 (br band, 2 H), and 7.0–7.5 (m, 8 H). Anal. Calcd for $C_{20}H_{18}ClNOS$: C, 67.51; H, 5.06; S, 9.01. Found: C, 67.52; H, 5.11; S, 8.97.

Registry No.—**10b** isomer 1, 67254-69-7; **10b** isomer 2, 67254-70-0; acrylonitrile, 107-13-1; acrylamide, 79-06-1; acetophenone 98-86-2; tetraphosphorus decasulfide, 12066-62-5; chalcone, 94-41-7; 4′-methoxychalcone, 959-33-1; 2-benzylidene-1-tetralone, 6261-32-1; 2-(*p*-methoxybenzylidene)-1-tetralone, 49629-37-0; 2-(*p*-chlorobenzylidene)-1-tetralone, 49545-70-2.

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(7) We can account for the regioselectivity in these cycloadditions by frontier molecular orbital theory. A simple qualitative frontier orbital treatment of the reaction between methyl vinyl thione,[4] selected as a model for α,β-unsaturated thiones, and olefins,[7a] (C=CZ, Z = CN, CHO) is represented in Figure 1, and application of the "hard and soft" concept allows us to predict that the first bond would link the softest centers,[7b] i.e., atom 4 with 1′ to give **15**. (a) K. N. Houk, *J. Am. Chem. Soc.*, **95**, 4092 (1973). (b) G. Desimoni and G. Tacconi, *Chem. Rev.*, **75**, 651 (1975).
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Synthesis and Reactions of Some *N*-Acylated and *N*-Sulfonylated *N,N′*-Dialkylureas

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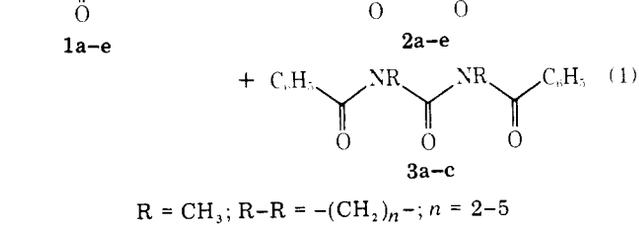
N,N′-Dialkylureas (**1**) are *N*-mono or *N,N′*-diacylated on treatment with various acyl chlorides: benzoyl chloride/base leads to *N*-benzoyl- and/or *N,N′*-dibenzoylureas (**2** and **3**). Similarly, cyclic *N*-mono- and *N,N′*-bisarenesulfonyl) ureas (**4** and **5**) are formed on reacting arenesulfonyl chlorides with imidazolidin-2-one and perhydropyrimidin-2-one. *N*-Benzoyl-*N′*-oxamoylureas (**12**) are obtained on successive treatment of **2** with oxalyl chloride and arylamine. Several *N*-benzoyl-*N′*-oxamoylureas undergo facile skeletal rearrangement on heating in methanol, yielding 1-aryl-3-(ω-benzamidoalkyl)imidazolidine-2,4,5-triones (**13**).

N,N′-Disubstituted ureas react with acylating agents on either the nitrogen or the carbonyl oxygen with formation of *N*- or *O*-acylated products. Evidence has been presented that many *N*-acylations of amides involve an initial attack on the more nucleophilic carbonyl oxygen; the thereby formed *O*-acylated intermediates rapidly rearrange to the thermodynamically more stable *N*-acylated products.[1] Detailed reports describing the synthetically important reactions of substituted ureas with phosgene and thionyl and phosphoryl chloride have been published.[2] Recently, we reported the *N*-benzoylation of cyclic *N,N′*-dialkylureas which lead to products of potential interest as masked isocyanates.[3] In conjunction with this work we investigated the feasibility of acylating and sulfonylating certain linear and cyclic *N,N′*-dialkylureas on both nitrogen atoms[4] and studied subsequent reactions of some of the obtained products. Treatment of *N,N′*-dimethylurea (**1a**) with molar amounts of benzoyl chloride in methylene chloride solution, using triethyl amine as an HCl scavenger, produces *N,N′*-dimethyl-*N*-benzoylurea (**2a**) in 81% yield and small amounts of *N,N′*-dimethyl-*N,N′*-dibenzoylurea (**3a**) (excess benzoyl chloride produces **3a** exclusively). Cyclic five- and six-membered ring ureas, such as imidazolidin-2-one (**1b**) and hexahydropyrimidin-2-one (**1c**), give mixtures of *N*-mono and



(1)

R = CH_3; R–R = $-(CH_2)_n-$; *n* = 2–5

N,N′-dibenzoylated products **2b,c** and **3b,c** under identical conditions while seven- and eight-membered ring ureas, i.e., perhydro-1,3-diazepin-2-one (**1d**) and perhydro-1,3-diazocin-2-one (**1e**), again produce *N*-monobenzoylated products exclusively.[3] Yields and melting points of all new compounds are presented in Table I.

The reaction of *N,N′*-dialkylureas with arenesulfonyl chlorides proceeds by O attack and subsequent elimination of sulfonic acid to give carbodiimides.[5,6] Treatment of the acyclic urea **1a** with benzenesulfonyl chloride and triethylamine in chloroform solution does indeed give *N,N′*-di-

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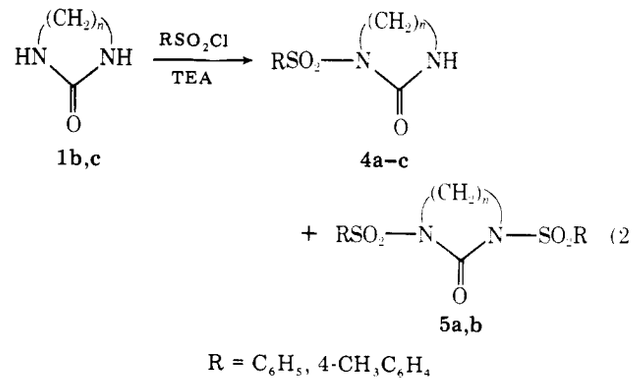
Table I. *N*-Acylated and -Sulfonylated Ureas and Their Rearrangement Products [a]

compd no.	registry no.	R	R'	*n*	mp, °C	yield, %
2a	67488-19-1	CH_3			97–98	88
2b	27034-77-1	$-(CH_2)_2-$			171–172	53[b]
2c	54236-66-7	$-(CH_2)_3-$			144–145	30[c]
3a	67488-20-4	CH_3			162–163	66
3b	5391-42-4	$-(CH_2)_2-$			240	27
3c	54236-74-7	$-(CH_2)_3-$			230[e]	50
4a	57451-91-9	C_6H_5		2	153–154	18[d]
4b	67488-21-5	p-$CH_3C_6H_4$		2	165–167	15
4c	67488-22-6	C_6H_5		3	208	18[f]
5a	67488-23-7	C_6H_5		2	193–194	60
5b	67488-24-8	p-$CH_3C_6H_4$		2	218	36
11b	67488-25-9			2	210	82
12a	67488-26-0	C_6H_5	H	2	205–207	84
12b	67488-27-1	C_6H_5	H	3	257	86
12c	67488-28-2	C_6H_5	H	4	166–168	quant
12d	67488-29-3	C_6H_5	H	5	160–161	81
12e	67488-30-6	C_6H_5	CH_3	2	182	95
12f	67488-31-7	C_6H_5	CH_3	5	108–110	50
13a	67488-32-8			2	174–176	74[g]
13b	67488-33-9			3	123	86
13c	67488-34-0			4	128	91
13d	67488-35-1			5	132–133	93[h]

[a] Satisfactory analytical values (±0.3% for C,H,N) were reported for all compounds. [b] 27% of **3b** is obtained as byproduct. [c] 50% of **3c** is obtained as byproduct. [d] 20% of **5a** is obtained as byproduct. [e] Soft at 218 °C. [f] A 37% yield is obtained with 2 equiv of benzenesulfonyl chloride. [g] From *N*-phenyl-*N'*-(β-benzamidoethyl)urea and oxalyl chloride. [h] A 45% yield is obtained from *N*-phenyl-*N'*-(5-benzamidopentyl)urea and oxalyl chloride.

methylcarbodiimide as evidenced by infrared spectroscopy. Since it is unlikely that carbodiimides are produced from the cyclic ureas **1b–e** on treatment with arenesulfonyl chloride it was of interest to investigate if rearrangement to *N*-sulfonylated products would occur.[7]

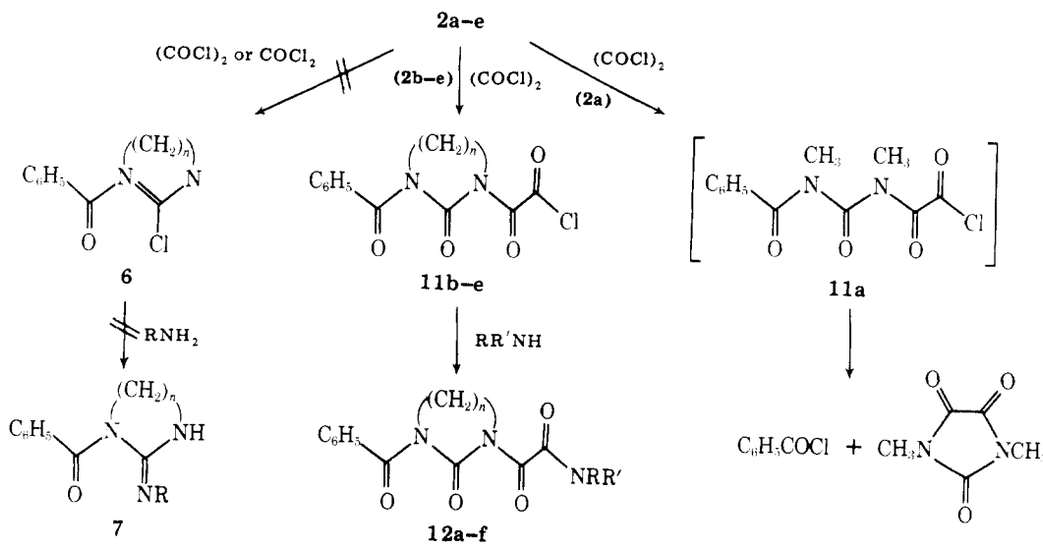
Treatment of **1b** and **1c** with benzene or *p*-toluenesulfonyl chloride in hot dimethoxyethane solution in the presence of triethylamine indeed gives mixtures of *N*-mono and/or *N,N'*-disulfonylated products **4a,b** and **5a,b** depending upon reaction conditions. Heating of molar amounts of **1b** and benzenesulfonyl chloride produces a mixture of **4a** (20%) and **5a** (18%) while reaction of **1b** with *p*-toluenesulfonyl chloride under similar conditions affords only the monosulfonylated urea **4b**. Heating of **1b** with 2 equiv of benzene or *p*-toluenesulfonyl chloride leads to formation of only the disulfonylated products **5a** and **5b**. The propyleneurea **1c** gives solely the monosulfonylurea **4c** on heating with benzenesulfonyl chloride in the presence of base regardless of reaction conditions. No



(2)

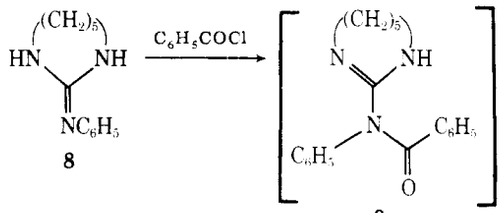
sulfonylated products could be obtained with the larger ring ureas **1d** and **1e** under a variety of conditions. The yields of all sulfonylated ureas (**4** and **5**) are low when compared with the *N*-benzoylated products (see Table I). This could in part

Scheme I

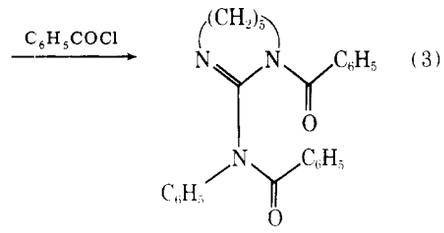


be due to a failure of *O*-sulfonylated intermediates to rearrange to *N*-sulfonylated products.[8] Compounds **4a–c** and **5a,b** are, to our knowledge, the only ureas of this kind obtained by sulfonylation with sulfonyl chlorides, a reaction which previously has not been observed.[11]

It was anticipated that the cyclic benzoylated ureas of type **2** would react with phosgene or oxalyl chloride via *O*-acylated intermediates to form *N*-benzoylated chloroformamidines **6** (Scheme I) which, on treatment with amine, would afford alicyclic guanidines **7** bearing a benzoyl group on one of the ring nitrogens. An attempt to prepare these compounds by benzoylation of the parent guanidines failed: octahydro-1,3-diaza-2-(*N*-phenylimino)cyclooctane (**8**) (prepared from **2e**, phosphoryl chloride, and aniline by analogy to a known procedure[12]) does not yield the 2-(*N*-phenylbenzamido) derivative **9**. Instead, the *N,N'*-dibenzoylated guanidine **10** is formed, regardless of the molar ratio of benzoyl chloride used (eq 3). H-NMR analysis of **10** excluded the presence of the equally possible dibenzoylated guanidine with both aroyl groups on the ring nitrogens.



8 **9**

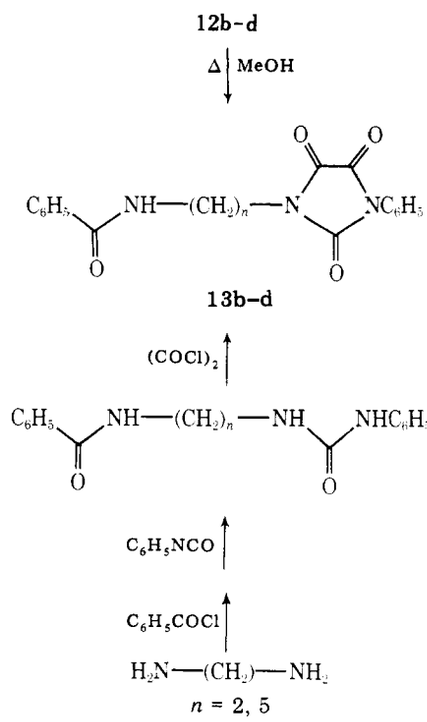


10 (3)

In pursuing the approach outlined above, we found that phosgene does not react with **2e** at room or slightly elevated temperature. Oxalyl chloride, however, reacts readily with **2e** as well as all the other cyclic benzoylated ureas affording *N*-benzoyl-*N'*-chlorooxoacetylureas **11b–11e** in virtually quantitative yield. The reactions, which are followed by IR, are generally completed within a few hours. Only in the case of **11b** was the chloride isolated in pure form; the compound proved to be surprisingly stable at ordinary conditions and could be recrystallized from acetone/hexane without noticeable decomposition. In all other cases, however, the crude reaction solutions of **11b–e** when treated with aromatic amines afford the corresponding *N*-benzoyl-*N'*-(*N*-aryloxamoyl)-ureas **12b–e** in high yields. The highly crystalline oxamides show a characteristic carbonyl band in the IR spectra (in $CHCl_3$) at 1680 cm^{-1} and a weaker band for the urea carbonyl group between 1715 and 1770 cm^{-1}, depending upon ring size. All H-NMR spectra are in agreement with the proposed structural formulas. A similar reaction between the acyclic urea **2a** and oxalyl chloride requires about 40 h for completion and produces a mixture of 1,3-dimethylimidazolidinetrione (*N,N'*-dimethylparabanic acid) and benzoyl chloride in high yield. Both compounds are probably formed via internal quaternization of the initially formed chloride **11a** (see Scheme I).

Several of the diacylureas of type **12** prepared from aniline and **11** proved to be rather labile compounds and were readily rearranged to 1-aryl-3-(ω-benzamidoalkyl)imidazolidine-2,4,5-triones **13** (parabanic acid derivatives) on brief heating in methanol. The rearrangement of this type was so facile in

Scheme II



the case of **12d** that methanol workup of crude products from the reaction of **11d** with aniline (Scheme I) lead to complete conversion to **13d.** The imidazolidintriones **13** show in the IR spectra (in $CHCl_3$) carbonyl bands characteristically different from the isomeric ureas **12:** a very sharp and intense band is found around 1740 cm^{-1} for all compounds; the H-NMR spectra are also in agreement with the proposed structure. Additional proof for the proposed structural formulas was obtained through independent synthesis of **13d** from 1,5-diaminopentane in several steps (see Scheme II). Since **13b** is formed readily on opening the relatively stable pyrimidine ring in **12b,** it was surprising to find that the ethyleneurea derivative **12a** could not be rearranged to the corresponding parabanate **13a** even on heating in methanol for 18 h (which led only to partial degradation of the molecule). To assure that **12a** had indeed the proposed structure, the isomeric **13a** was synthesized via the sequence outlined for **13d** in Scheme II.

The fact that the rearrangements proceed in a protic solvent like methanol seems to suggest an addition–elimination step involving ROH. It is remarkable that these reactions are relatively clean and produce high yields of **13** especially since bond cleavage prior to ring closure could occur at several places and not exclusively between the urea 1,2-(N–C) linkage. In an attempt to catalyze the rearrangememt of **12b** by adding small amounts of aniline to the methanolic reaction medium *N,N'*-diphenyl oxanilide was formed as byproduct resulting from cleavage of the exocyclic N–C bond at position 3 of the urea.

Since only oxamoyl derivatives with NH protons are capable of recyclization to parabanates, it was not expected that the fully substituted **12e** and **12f** would undergo a similar rearrangement in methanol. However, it was hoped that opening of the urea ring would occur, giving some insight into the reaction mechanism which operates in the above described ring rearrangements. It was, therefore, surprising to find that **12f** does not undergo ring opening in refluxing methanol.

Experimental Section[13]

A. Benzoylation of Ureas. *N,N'*-Dimethyl-*N*-benzoylurea (2a) was prepared by adding a solution of 5.0 g (0.05 mol) of triethylamine in 30 mL of dichloromethane dropwise over a period of 50 min to 4.40

g (0.05 mol) of N,N'-dimethylurea (**1a**) and 7.0 g (0.05 mol) of benzoyl chloride, dissolved in 30 mL of dichloromethane. Toward the end of the addition triethylamine hydrochloride precipitated. After 2.5 h of reaction time, the solvent was removed in vacuo and the solid residue was suspended in water. Solid **2a** (8.48 g) was collected and dried. Recrystallation from methanol containing small amounts of water gave colorless crystals; yield and mp are given in Table I.

Occassionally, samples of **2a** were contaminated by trace amounts of **3a**, which were difficult to remove by recrystallization, but both compounds could be separated by column chromatography on silica gel (Biorad Bio-Sil A) with toluene–acetone (9:1) as eluent.

N,N'-Dimethyl-N,N'-dibenzoylurea (3a) was obtained in a procedure similar to the one given above: 0.02 mol of N,N'-dimethylurea (**1a**) was reacted with 0.04 mol of benzoyl chloride and triethylamine each and gave on trituration with water 3.90 g (66%) of **3a**, which was recrystallized from methanol (large prisms); for yield and mp see Table I.

1-Benzoylimidazolidin-2-one (2b) and 1,3-Dibenzoylimidazolidin-2-one (3b). To a suspension of 10.0 g (0.116 mol) of imidazolidin-2-one (**1b**) in 70 mL of chloroform, containing 10.0 g (0.1 mol) of triethylamine, was added dropwise 14.0 g (0.1 mol) of benzoyl chloride in 40 mL of chloroform over a period of 100 min. A clear solution was obtained from which triethylamine hydrochloride separated on standing for several hours. Removal of solids left a filtrate which was evaporated to dryness in vacuo. The obtained solid residue was treated with ca. 100 mL of water, stirred for 30 min, and filtered and gave 14.30 g of a mixture of **2b** and **3b** as evidenced by IR. Repeated treatment of the crude product with methanol (3 × 75 mL) left 4.0 g of **3b**, which was recrystallized from acetone/hexane (colorless needles). The monobenzoyl derivative was obtained on evaporating the methanolic filtrates, which left 10.1 g of crude **2b**, which was recrystallized from acetone/hexane (colorless plates); yields and mp are given in Table I.

1-Benzoylhexahydropyrimidin-1-one (2c) and 1,3-Dibenzoylhexahydropyrimidin-2-one (3c). A solution of benzoyl chloride (70 g, 0.05 mol) in 40 mL of acetonitrile was added dropwise over a period of 30 min to a stirred suspension of 5.0 g (0.05 mol) of hexahydropyrimidin-2-one (**1c**) in 75 mL of acetonitrile at 80 °C. On additional stirring for 60 min a clear solution was obtained to which 5.0 g (0.05 mol) of triethylamine in 20 mL of acetonitrile was added dropwise, causing the separation of a colorless precipitate which dissolved on heating the mixture for another 2 h at 90 °C. Triethylamine hydrochloride precipitated on cooling in an ice bath.

Filtration and concentrating the filtrate in vacuo left a semisolid mass which was diluted with water and filtered. The residue, 3.95 g, contained exclusively the dibenzoylated urea **3c** which was recrystallized for analysis from DMF/MeOH/H_2O (colorless needles). The acetonitrile/water filtrate was further diluted with water leading to separation of 3.10 g of **2c**. Recrystallization from acetone/hexane gave colorless prisms of **2c**; yield and mp's are given in Table I.

The monobenzoylated ureas **2d** and **2c** were prepared as described earlier.[3]

B. Sulfonylation of Ureas. 1-Benzenesulfonylimidazolidin-2-one (4a) and 1,3-Bis(benzenesulfonyl)imidazolidin-2-one (5a). A suspension of 4.3 g (0.05 mol) of **1b** in 40 mL of 1,2-dimethoxyethane (DME) containing also 5.0 g (0.05 mol) of triethylamine and 8.8 g (0.05 mol) of benzenesulfonyl chloride was kept for 4.5 h in an oil bath at 65–70 °C during which time the urea slowly dissolved. Cooling the reaction solution to room temperature led to precipitation of triethylamine hydrochloride which was removed by filtration. A crystalline mixture of **4a** and **5a** (5.36 g) was obtained on evaporating the filtrate in vacuo to dryness and treating the oily residue with a small amount of water. Fractional crystallization of the crude mixture from acetone and gradual addition of water led to separation of **5a** (1.81 g, colorless needles) as first fraction followed by **4a** (2.01 g, colorless plates from methanol/water) as second fraction. Purity of both fractions was checked by IR and TLC; yields and mp's are given in Table I.

1,3-Bis(benzenesulfonyl)imidazolidin-2-one (5a) was formed exclusively on reacting **1b** with 2 equiv of benzenesulfonyl chloride and triethylamine under conditions as given in the procedure above (7 h reaction duration). Workup of the triethylamine hydrochloride free DME filtrate yielded 60% of **5a** in the form of colorless needles (acetone), identical by IR comparison with material obtained according to the procedure above.

1-(p-Toluenesulfonyl)imidazolidin-2-one (4b). A suspension of **1b** (4.3 g, 0.05 mol) in 40 mL of DME containing equimolar quantities of triethylamine and p-toluenesulfonyl chloride was kept at 90–95 °C for 7 h. Triethylamine hydrochloride precipitated during the reaction while **1b** slowly dissolved. After cooling the mixture to room temperature, the salt was filtered off and the yellow filtrate was concentrated in vacuo to yield an oil which was treated with water/methanol. Colorless crystals precipitated while unreacted p-toluenesulfonyl chloride was kept in solution. Filtration gave 1.86 g of **4b** which was recrystallized for analysis from chloroform/hexane yielding colorless prisms; yield and mp are given in Table I.

1,3-Bis(p-toluenesulfonyl)imidazolidin-2-one (5b) was prepared following a procedure similar to the one given above for **4b** using 2 equiv of p-toluenesulfonyl chloride and triethylamine per equiv of urea. The reaction filtrate, obtained after salt removal, concentrated in vacuo gave a semisolid mass which was taken up in a small amount of methanol. The product **5b**, which remained undissolved, was isolated by filtration and purified for analysis by recrystallization from acetone/water (colorless needles); for mp and yield see Table I.

1-Benzenesulfonylhexahydropyrimidin-2-one (4c) was obtained on heating a DME solution of 5.0 g (0.05 mol) of **1c** with 0.1 mol each of benzenesulfonyl chloride and triethylamine for 7 h at 90 °C. The product **4c** was isolated from the reaction mixture following procedures given for the preparation of **4a** and **4b**; the crude product was recrystallized from acetone/water (colorless prisms). Using an excess of sulfonyl chloride/base in this reaction produced a higher yield (37%) while equivalent amounts of all reagents gave only an 18% yield of **4c**.

Octahydro-1,3-diaza-2-(N-phenylimino)cyclooctane (8). Dropwise addition of a benzene solution (10 mL) of 1.35 g (0.01 mol) of phosphoryl chloride to 1.28 g (0.0 mol) of urea **1d** in 10 mL of benzene was leading to separation of a colorless oil which solidified after several hours. After 8 h of standing at room temperature aniline (1.86 g, 0.02 mol), dissolved in 10 mL of benzene, was added dropwise to the stirred suspension thereby transforming the phosphoryl chloride adduct into an amber oil. The mixture was refluxed for 5–6 h after which the benzene was decanted from the honeylike residue. Treatment of the residue with aqueous sodium hydroxide led to separation of solid **8** mixed with aniline; filtration after cooling in ice left 2.0 g (quantitative) of **8** which was recrystallized from methanol/water giving colorless crystals: mp 127–129 °C; IR ($CHCl_3$) 1620 cm^{-1} (C=N). Anal. Calcd for $C_{12}H_{17}N_3$: C, 70.90; H, 8.43; N, 20.67. Found: C, 70.54; H, 8.77; N, 20.57.

Hexahydro-1,3-diaza-1-benzoyl-2-(N-phenylbenzamido)cyclooctene-2 (10). A solution of guanidine **8** (0.41 g, 0.002 mol) in 10 mL of chloroform was treated with 0.56 g (0.004 mol) of benzoyl chloride dissolved in 10 mL of chloroform followed by addition of excess triethylamine (1.0 g, 0.01 mol) to neutralize the formed hydrogen chloride. After brief heating to 50–60 °C the reaction mixture was kept at room temperature for 1 h. Solvent evaporation in vacuo left a semisolid residue which crystallized on scratching and treatment with water. Filtration afforded 0.32 g (100%) of **10**: mp 172 °C (methanol); IR ($CHCl_3$) 1630 cm^{-1} (C=N) with shoulders at 1650 cm^{-1} (C=O). Anal. Calcd for $C_{26}H_{25}N_3O_2$: C, 75.89; H, 6.12; N, 10.21. Found: C, 75.78; H, 6.25; N, 10.77.

C. N-Benzoyl-N'-oxamidoureas and Precursors. Reaction of N,N'-Dimethyl-N-benzoylurea (2a) with Oxalyl Chloride. A solution of 3.82 g (0.02 mol) of **2a** and 2.52 g (0.02 mol) of oxalyl chloride in 30 mL of dichloromethane was kept at room temperature for 68 h. The progress of the reaction was observed by IR. Removal of the solvent in vacuo left a semisolid which, after trituration with hexane, was collected by filtration. Thus, 2.12 g (75%) of **1,3-dimethylimidazolidine-2,4,5-trione** was obtained. Evaporation of the filtrate gave 2.00 g (71% yield) of **benzoyl chloride.** Both products were identical in IR comparison and melting point with authentic samples.

1-Benzoyl-3-chlorooxoacetylimidazolidin-2-one (11b). Colorless crystals separated from a solution of 1.9 g (0.01 mol) of benzoylurea **1b** and 1.26 g (0.01 mol) of oxalyl chloride in 20 mL of chloroform on standing for 18 h. Filtration and washing with chloroform left 2.30 g of **11b** which was recrystallized for analysis from acetone/hexane (colorless needles); yield and mp are given in Table I.

1-Benzoyl-3-oxamoylimidazolidon-2-ones 12a and 12e were prepared by reacting the oxamoyl chloride **11b** with 3 equiv of aniline or N-methylaniline in chloroform at room temperature. The clear reaction solutions were concentrated after standing for 1 h and the solid residues were treated with water or water–methanol and **12a** and **12e** were collected by filtration. The crude products were recrystallized from acetone/water or acetone/hexane; yields and mp's are given in Table I.

1-Benzoyl-3-(N-phenyloxamoyl)hexahydropyrimidin-2-one (12b). Solutions of N-benzoylurea **1c** (2.04 g, 0.01 mol) in 50 mL of dichloromethane and oxalyl chloride (1.27 g, 0.01 mol) in 20 mL of the same solvent were mixed and kept at room temperature for 2 h after which 2.80 g (0.03 mol) of aniline, dissolved in 15 mL of CH_2Cl_2, was added slowly with stirring causing precipitation of aniline hydro-

chloride. The resulting suspension was kept at room temperature for 12 h. Filtration and concentration left a syrup which crystallized on scratching. The solid was suspended in water, filtered, and recrystallized from acetone/hexane giving colorless crystals.

The ***N*-benzoyl-*N'*-oxamoylureas 12c, 12d and 12f** were prepared following procedures similar to the one presented above employing dichloromethane or chloroform as solvents. Melting points and yields are given in Table I.

D. 1-Aryl-3-(ω-benzamidoalkyl)imidazolidine-2,4,5-triones (13b–d) from 12b–d (General Procedure). Suspensions of 1-benzoyl-3-oxamoylureas **12b–d** in methanol (ca. 1.0 g per 20–50 mL of solvent) were heated to reflux. The starting materials dissolved slowly and progress of the rearrangement was followed by TLC or IR. As soon as the reactions were complete (10 min to 2.5 h), part of the solvent was removed and water was added to precipitate the products, which were collected and purified for analysis by recrystallization from methanol/water. Extended heating of the methanolic solutions after completed rearrangement can cause further degradation of the parabanates and thus result in lower yields.

No rearrangement to **13a** was observed on prolonged heating of **12a** in methanol (18 h; the odor of methyl benzoate indicated partial cleavage in a different manner) or briefly in DMF or DMF/water.

1-Phenyl-3-(2-benzamidoethyl)imidazolidine-2,4,5-trione (13a) via Cyclization. *N*-Phenyl-*N'*-(2-benzamidoethyl)urea[14] (2.83 g, 0.01 mol) and oxalyl chloride (1.26 g, 0.01 mol) were heated to reflux for 1 h in 50 mL of dichloromethane. The resulting reaction solution was evaporated leaving an oily residue which was dissolved in acetone. Gradual addition of water to beginning turbidity and scratching caused separation of 2.48 g of **13a;** the crude material was recrystallized from methanol/water (colorless crystals); yield and mp are given in Table I.

In a similar manner, **1-phenyl-3-(5-benzamidopentyl)imidazolidine-2,4,5-trione (13d)** was obtained from *N*-phenyl-*N'*-(5-benzamidopentyl)urea[15] and oxalyl chloride in refluxing chloroform (45% yield).

Hydrolytic cleavage of **13d** in aqueous potassium hydroxide–methanol (1:3) at room temperature yielded the corresponding *N*-phenyl-*N'* (5-benzamidopentyl)urea in 90% yield.

Registry No.—**1a**, 96-31-1; **1b**, 120-93-4; **1c**, 1852-17-1; **1d**, 19055-93-7; **8**, 67488-36-2; **10**, 67488-37-3; *N*-phenyl-*N'*-(β-benzamidoethyl)urea, 67488-38-4; oxalyl chloride, 79-37-8; *N*-phenyl-*N'*-(5-benzamidopentyl)urea, 67488-39-5; benzoyl chloride, 98-88-4; benzenesulfonyl chloride, 98-09-9; *p*-toluenesulfonyl chloride 98-59-9; aniline, 62-53-3; 1,3-dimethylimidazolidine-2,4,5-trione, 5176-82-9; 1,5-diaminopentane, 462-94-2; *N*-(5-aminopentyl)-*N'*-phenylurea, 67488-40-8.

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Pteridines. 45. Synthesis and Properties of Some Isothiazolo[4,5-*b*]pyrazines and Isothiazolo[4,5-*g*]pteridines[1,2]

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Several isothiazolo[4,5-*b*]pyrazines and isothiazolo[4,5-*g*]pteridines were prepared utilizing 3-methyl- and 3-methylmercapto-4-nitroso-5-acetamidoisothiazole (**5a,b**) as key starting materials. All attempts to desulfurize these fused isothiazoles were uniformly unsuccessful. Reaction of 3-methylmercapto-5-cyano-6-aminoisothiazolo[4,5-*b*]pyrazine (**6b**) with diethyl malonate in the presence of base unexpectedly resulted in the formation of the pyrido[2,3-*b*]isothiazolo[4,5-*e*]pyrazine **14** rather than cleavage of the isothiazole ring.

The classical synthetic route to pteridines involves condensation of a preformed 4,5-diaminopyrimidine with an appropriately functionalized two-carbon unit (e.g., an α-keto, α-hydroxy, or α-bromocarbonyl compound).[3] This so-called Isay route to pteridines, despite its attractive simplicity, suffers from the serious disadvantage that a mixture of structural isomers is formed when the two-carbon reaction component is itself unsymmetrical.[4] In addition, however, the requisite pyrimidine intermediates are often extremely insoluble and difficult to manipulate, and there are obvious structural limitations in the other reaction component which provides carbons 6 and 7 of the pteridine ring along with their associated substituents. Furthermore, pteridines are notoriously insoluble and chemically recalcitrant compounds whose chemical manipulation by the usual methods of synthetic organic chemistry poses severe problems. We have developed and exploited over the past few years an alternative synthetic pathway to pteridines which involves the prior synthesis of pyrazine (as opposed to pyrimidine) intermediates, followed by final annelation of the fused pyrimidine ring. This procedure possesses many chemical and manipulative advantages which have been summarized elsewhere.[5] However, since certain types of pteridine derivatives have thus far not been directly accessible by this latter pathway (e.g., acyl derivatives), we have a continuing interest in exploring new synthetic methodologies. The present paper describes a projected strategy for the preparation of 6-acyl derivatives via isothiazolo[4,5-*b*]pyrazines and isothiazolo[4,5-*g*]pteridines, both

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