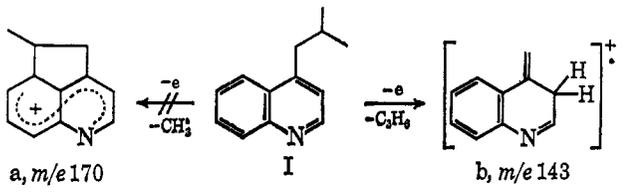
b), while $m/e$ 142 is associated with benzylic fission with loss of a propyl radical and $m/e$ 115 with subsequent expulsion of the elements of hydrogen cyanide (appropriate metastable peak observed). *peri* interactions thus do not exist in 1-alkylnaphthalenes or 4-alkylquinolines.




a, $m/e$ 170 I b, $m/e$ 143

### Experimental Section[5]

**Butylnaphthalenes.**—The three butylnaphthalenes were prepared by a Wurtz–Fittig coupling reaction[6] and purified by vpc.

**4-Isobutylquinoline.**—The synthesis was based on a modification[7] of the Blaise–Maire synthesis[8] of 4-alkylquinolines, which involves as a precursor a 2-chloroethylalkylketone obtained by condensation of a dialkycadmium reagent with the appropriate acid chloride.[9]

Isobutylmagnesium bromide was prepared from 7.9 ml of isobutyl bromide (0.073 mol) and 1.77 g of magnesium turnings (0.073 g-atom) in dry ether. This Grignard reagent was treated with 7.36 g of finely powdered dry cadmium chloride (0.040 mol) to produce diisobutylcadmium. The ether was removed by heating and replaced with benzene. After cooling of the vigorously stirred suspension in an ice bath, a solution of 5.7 ml of 3-chloropropionyl chloride (0.059 mol) in benzene was added slowly with continuous stirring. Ice-bath temperature was maintained for 0.5 hr and was followed by a 45-min reflux. The reaction mixture was then cooled and filtered, and the precipitate washed with benzene. After extraction with 10% aqueous sodium bicarbonate and drying with magnesium sulfate, the benzene solvent was evaporated under water aspiration, leaving 1-chloro-5-methyl-3-hexanone (1.1 g) as a sweet-smelling oil which was used directly in the next step.

To an absolute ethanol solution of 35.1 g of stannic chloride pentahydrate (0.10 mol) and 1.45 ml of distilled aniline (0.155 mol) was added 1.1 g of above described chloro ketone. The solution was then heated under reflux for 4 hr. Upon cooling, the ethanol solution was poured into water; the pH was adjusted to neutral by the addition of solid sodium bicarbonate; and the product was extracted with ether. The ether was then partially evaporated and extracted three times with 10% aqueous hydrochloric acid. The aqueous extract was neutralized with aqueous ammonia and extracted three times with ether. The residue after removal of the ether was heated with excess acetic anhydride at steam-bath temperature for 2 hr in order to facilitate separation of unreacted aniline.

The acetic anhydride solution was mixed with ether and extracted three times with 10% aqueous hydrochloric acid; the aqueous extract was then neutralized and extracted with ether as above, giving in poor yield a solution of tertiary amine in ether. This ether solution was dried with magnesium sulfate, filtered, and evaporated. The resultant red, viscous oil was purified by vpc and shown to contain two components, only one of which was of low enough volatility to be the desired product. The structure was confirmed by proton nmr spectroscopy and the compound was characterized as its picrate (yellow needles, mp 168.5–170°, with sintering at 165° after three recrystallizations from 95% ethanol).

*Anal.* Calcd for $C_{19}H_{18}O_7N_4$: C, 55.03; H, 4.39; N, 13.53. Found: C, 55.24; H, 4.41; N, 13.59.

**Registry No.**—I, 7661-51-0; picrate of I, 16727-90-5; 1-isobutylnaphthalene, 16727-91-6.

(5) The mass spectral data were obtained by Mr. R. G. Ross on an MS-9 mass spectrometer at 70 eV, utilizing a heated glass inlet system at 180° with steel manifolding.

(6) E. Vogel, "Practical Organic Chemistry," 3rd ed, John Wiley and Sons, Inc., New York, N. Y., 1966, pp 511–512.

(7) J. Kenner and F. S. Statham, *Ber.*, **69**, 16 (1936).

(8) E. E. Blaise and M. Maire, *Bull. Soc. Chim. Fr.*, **3**, 658 (1908).

(9) J. Cason, *Chem. Rev.*, **40**, 15 (1947).

## Quinazolines and 1,4-Benzodiazepines. XLI.[1] 1,3-Dihydro-2H-1,4-benzodiazepin-2-one 4-Oxide Previously Described as 1,3-Dihydro-2H-4,1,5-benzoxadiazocin-2-one

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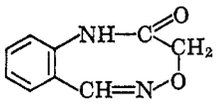
In a recent publication,[2] we reported the synthesis of a series of 5-substituted 4,1,5-benzoxadiazocin-2-ones by cyclization of 2′-aroyl- (or alkanoyl-) 2-haloacetanilide *syn*[3]-oximes in an alkaline medium. A similar mild alkaline treatment of 2-chloro-2′-formylacetanilide oxime **1** of unspecified configuration was reported by v. Auwers[4] to yield a compound described as 1,3-dihydro-2H-4,1,5-benzoxadiazocin-2-one (A). Since the steric configuration of the oxime is believed to determine the site of attack in intramolecular alkylation,[2] a 4,1,5-benzoxadiazocin-2-one resulting from the *syn*-oximes and a 1,4-benzodiazepin-2-one 4-oxide from the *anti* isomer, a study of the structure of the compound reported by v. Auwers was undertaken.[5]




A

A sample of **3**,[6] prepared as described by v. Auwers, when submitted to mass spectroscopy showed a strong peak at M − 16 indicating the loss of oxygen. This phenomenon is characteristic for nitrones but has not been seen with 4,1,5-benzoxadiazocin-2-ones.[2] The nitrone structure was corroborated by preparation of the nitrone **3**, identical with the material prepared directly from **1**, by rearrangement of 2-chloromethylquinazoline 3-oxide (**2**)[7] on treatment with dilute alkali. Catalytic reduction of the nitrone with Raney nickel catalyst removed the N-oxide oxygen and also reduced the 4,5 double bond resulting in the formation of the 1,3,4,5-tetrahydro-1,4-benzodiazepin-2-one (**5**). This compound was identical with the product prepared by reduction of the corresponding 1,3-dihydro-1,4-benzodiazepin-2-one (**8**) which had been synthesized from **7** according to the classical method shown. When

(1) Paper XL: J. V. Earley, R. I. Fryer, D. Winter, L. H. Sternbach, *J. Med. Chem.*, in press.

(2) A. Stempel, I. Douvan, E. Reeder, and L. H. Sternbach, *J. Org. Chem.*, **32**, 2417 (1967).

(3) The terms *syn* and *anti* are used as defined in ref 2, footnote 7. This is particularly important in a discussion of benzaldehyde oximes since these terms are then in conflict with the traditional definition in which the position of the oxime hydroxyl is considered in reference to the aldehydic hydrogen. To be consistent, in this report the configuration will be named based on the relationship of the oxime hydroxyl to the amino-substituted phenyl ring in both aldehydic and ketonic oximes.

(4) K. v. Auwers and E. Frese, *Ann. Chem.*, **450**, 273 (1926). These authors named the compound 4,5-benzo-7-oxy-oct-1,2,6-oxdiazin.

(5) While our work was in progress, the product of an analogous reaction carried out with 2,4′-dichloro-2′-formylacetanilide oxime, again of unspecified configuration, was reported in a Dutch patent to be 7-chloro-1,3-dihydro-2H-1,4-benzodiazepin-2-one 4-oxide but no proof of structure was offered: Grindstedvarket, A.S., Netherlands Patent 6,608,039 (Dec 12, 1966).

(6) In view of the evidence discussed below we shall present this compound as the N-oxide **3** rather than the earlier incorrect structure A.

(7) L. H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 4936 (1961).

compound **3** was reduced in acetic acid using palladium on charcoal as catalyst, in addition to **5**, a small amount of the hydroxylamino compound **6** was also obtained. The reactions discussed above show beyond any doubt that the structure of the compound described by v. Auwers is that of the nitrone (**3**) and not a benzoxadiazocin-2-one.

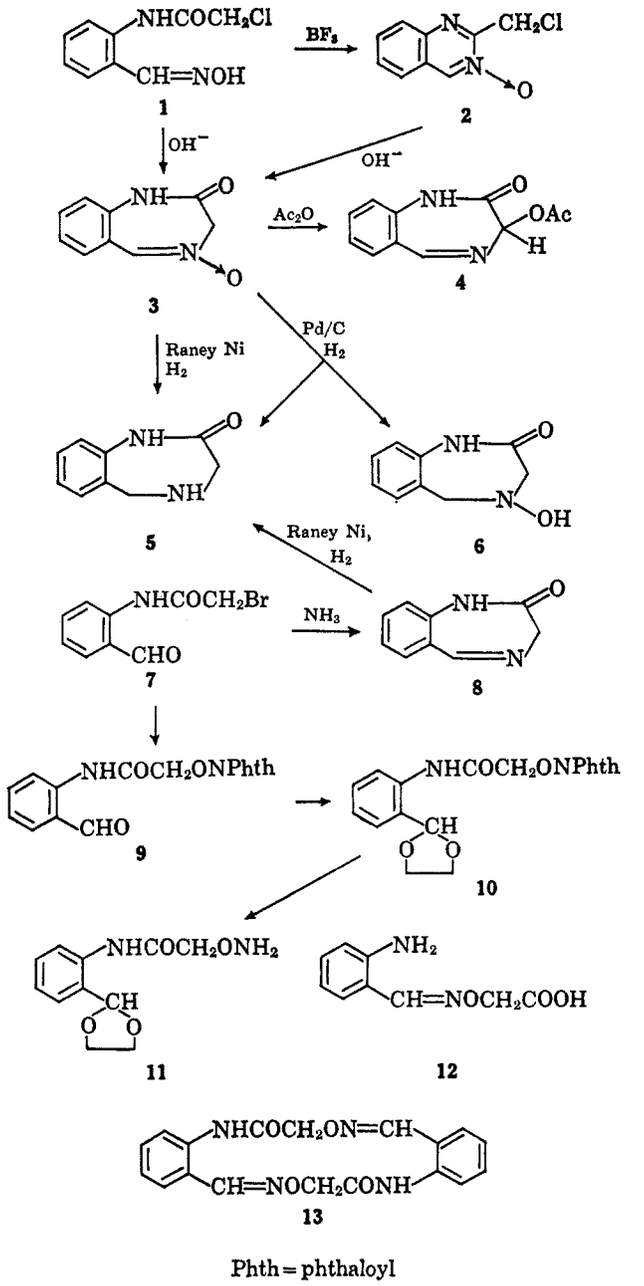
The "monoacetyl derivative" prepared by v. Auwers[4] by reaction of the compound described as A with acetic anhydride is then the product of the Polonovski rearrangement of the nitrone **3** and has the structure **4**. This was confirmed by the infrared spectrum which showed two carbonyl bands, at 1750 (ester) and 1690 $cm^{-1}$ (amide CO) and the nmr spectrum with one proton each at $C_3$ and $C_5$. These two protons exhibited an "allylic" coupling ($J$ = 3 cps) similar to that reported recently[8a] in a closely related system.[8b]

If the rules for intramolecular alkylation of oximes stated earlier[2] are valid then the configuration of the oxime **1** should be *anti*. The infrared spectrum of **1** in very dilute solution showed hydrogen bonding in the NH region. This had been observed in corresponding acylated aminobenzophenone *anti*-oximes but not in the *syn* isomers.[9] Nevertheless, it would be difficult to assign a definite configuration based on the infrared spectra since only one isomer of **1** was obtained. For the same reason interpretation of the nmr spectra cannot be used for structural assignment.

Since it is known[10] that the *syn* and *anti* forms of aldoximes are not very stable and are readily convertible into each other, it is reasonable to assume that the oxime would react in a manner as to yield the thermodynamically most favored product. It is, therefore, not astonishing and in good agreement with our former findings that the seven-membered benzodiazepine N-oxide and not the eight-membered benzoxadiazocine is formed.

In order to be able to study the properties and stability of this latter compound, we attempted the synthesis of the 4,1,5-benzoxadiazocin-2-one (A) but were not successful. Compound **9** was prepared as outlined from **7** (Chart I) and attempts were made to convert it into A as described for the benzophenone derivatives.[2] On treatment of **9** with hydrazine hydrate or **11** with dilute acid or pyridine hydrochloride, the product obtained was shown by mass spectroscopy to be predominantly a dimer (*m/e* 352, possibly **13**). Similar results were also obtained in an attempted cyclization of **12** with dicyclohexylcarbodiimide.

CHART I




Phth = phthaloyl

### Experimental Section[11]

**1,3-Dihydro-2H-1,4-benzodiazepin-2-one 4-Oxide (3). Method A.**—To a solution of 5.0 g (23.5 mmol) of 2-chloro-2′-formylacetanilide oxime (**1**) in 150 ml of dioxane, 25 ml of 2 *N* sodium hydroxide was added. After stirring at room temperature for 4 hr, the reaction mixture was diluted with 100 ml of water (pH 11.9) and acidified to pH 1.5 by addition of 3 *N* hydrochloric acid. On concentration under reduced pressure to remove dioxane, a crystalline product formed which was separated by filtration to give 2.1 g of **3** (50%, mp 252–255° dec). Recrystallization from dilute ethanol gave colorless needles melting at 259–260° dec (lit.[4] mp 251–252°): ir (KBr disk) 3205 (NH), 1675 $cm^{-1}$ (amide C=O); (nmr (DMSO-$d_6$), $\delta$ 4.50 (s, 2, $CH_2$), 8.12 (s, 1, CH=N), 10.2 (s, 1, NH).

*Anal.* Calcd for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.41; H, 4.36; N, 15.78.

**Method B.**—A stirred solution of 21.7 g (0.16 mol) of 2-aminobenzaldoxime in a mixture of 500 ml of ether and 300 ml of water was cooled to 5° and 19.5 g (13 ml, 0.17 mol) of chloroacetyl chloride was added slowly while keeping the reaction mixture slightly alkaline by the addition of 10% sodium hydroxide. After stirring for 1 hr in an ice bath, the reaction mixture was allowed to warm to room temperature; the solid that had sepa-

(8) (a) R. I. Fryer, D. Winter, and L. H. Sternbach, *J. Heterocycl. Chem.*, **4**, 355 (1967). (b) One of the referees has suggested that the Polonovski rearrangement could occur at $C_5$. This would be inconsistent with the nmr data unless isomerization to the $\Delta^{3,4}$ compound had occurred. A comparison of the uv spectra of **4** and **8** showed only minor differences. A similar comparison of the uv spectra (unpublished) of the $\Delta^{3,4}$ and $\Delta^{4,5}$ compounds reported in ref 8a showed major differences in the spectra.

(9) A. Stempel, E. Reeder, and L. H. Sternbach, *J. Org. Chem.*, **30**, 4267 (1965).

(10) J. Meisenheimer in "Stereochemistry," K. Freudenberg, Ed., Franz Deuticke, Leipzig, 1933, pp 987–990.

(11) All melting points were taken in a Thomas–Hoover melting point apparatus and are corrected. Infrared spectra were determined using a Beckmann IR-5 or IR-9 grating spectrophotometer, mass spectra with a CEC 21-110 spectrometer, and nmr spectra with a Varian A-60 spectrometer. Identity of compounds was established by comparison of spectra and mixture melting point. In reporting infrared and nmr data, only the significant peaks are noted.

rated dissolved upon addition of 10% sodium hydroxide. The aqueous layer was separated, cooled, and acidified with concentrated hydrochloric acid. Compound **3** crystallized and was filtered to separate 19.7 g of product (70%, mp 255–257° dec) identical with material prepared by method A.

**Method C.**—A solution of 1.0 g (5 mmol) of 2-chloromethylquinazoline 3-oxide (**2**) in 25 ml of 1 *N* sodium hydroxide was stirred for 45 min at room temperature then acidified by the addition of 3 *N* hydrochloric acid. The solid that formed was separated by filtration to give 0.5 g of crude **3** (mp 235–240°). Recrystallization from ethanol gave 0.1 g of **3** (mp 258–259 dec) identical with material prepared by method A.

**2-Chloromethylquinazoline 3-Oxide (2).**—A mixture of 14 g of **1** and 13 ml of boron trifluoride etherate in 500 ml of benzene was stirred and heated to reflux for 8 hr. After cooling, water was added, the mixture was stirred, and the organic phase was separated and washed with dilute sodium bicarbonate. An oily brown residue that remained in the flask was dissolved in methylene chloride, washed with 5% sodium bicarbonate, and combined with the benzene layer. The mixture was dried ($Na_2SO_4$) and concentrated to dryness under reduced pressure. Crystallization of the residue from a mixture of benzene and hexane gave 4.4 g of **2**, mp 148.5–149°. A second crop (1.7 g, mp 145–146.5°) was obtained from the mother liquors (total yield 48%). Further crystallization from a mixture of benzene and hexane gave yellow needles of **2**: mp 150–151.5°; ir ($CHCl_3$) 1613 (w), 1563 (m), 1488 $cm^{-1}$ (m); nmr (DMSO-$d_6$), $\delta$ 5.07 (s, 2, $CH_2$) and 9.50 (s, 1, CH=N).

*Anal.* Calcd for $C_9H_7ClN_2O$: C, 55.54; H, 3.62; N, 14.39. Found: C, 55.34; H, 3.68; N, 14.14.

**3-Acetoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (4).**—A stirred mixture of 5.0 g of **3** in 20 ml of acetic anhydride was warmed on a steam bath for 15 min. After 10 min, the temperature rose to 108° and a clear solution resulted. On cooling, **4** crystallized and was separated by filtration (3.2 g, mp 199–200° dec, 51%), lit.[4] mp 197–198° dec. Crystallization from tetrahydrofuran gave colorless plates of unaltered melting point: uv (*i*-PrOH) max 227 ($\epsilon$ 37,500), infl 255 ($\epsilon$ 4750), max 312 ($\epsilon$ 1800); ir (KBr disk) 1750 (ester CO) and 1690 $cm^{-1}$ (amide CO); nmr (DMSO-$d_6$), $\delta$ 2.22 (s, 3, $CH_3COO$), 5.72 (d, 1, $J$ = 3 cps, -CHOAc-N=), 8.63 (d, 1, $J$ = 3 cps, -CH=N).

*Anal.* Calcd for $C_{11}H_{10}N_2O_3$: C, 60.54; H, 4.62; N, 12.84. Found: C, 60.41; H, 4.68; N, 12.89.

**1,3,4,5-Tetrahydro-2H-1,4-benzodiazepin-2-one (5). A. From 3.**—A solution of 1.8 g (10 mmol) of **3** in 250 ml of dimethylformamide containing a suspension of *ca.* 5 g of Raney nickel was reduced at atmospheric pressure and room temperature. The uptake of hydrogen stopped when slightly more than 20 mmol had been absorbed. Solvent was removed by distillation under reduced pressure and the residue crystallized from acetonitrile to give colorless needles of **5** (1.2 g, 67%, mp 151–154°). Further crystallization from a mixture of methylene chloride and hexane gave a pure product melting at 150–151°: ir ($CHCl_3$) 3350 (NH), 3215 (NH) and 1660 $cm^{-1}$ (amide CO); nmr ($CDCl_3$), $\delta$ 2.0 (s, 1, NH), 3.83 (s, 2, $CH_2$), 4.02 (s, 2, $CH_2$) and 9.03 (s, 1, NH).

*Anal.* Calcd for $C_9H_{10}N_2O$: C, 66.65; H, 6.22; N, 17.27. Found: C, 66.48; H, 6.24; N, 17.23.

**B. From 8.**—A solution of 1.6 g (10 mmol) of **8** in 100 ml of dimethylformamide containing *ca.* 5 g of Raney nickel catalyst was reduced as above. Reduction stopped when about 10 mmol of hydrogen was absorbed. Following removal of solvent by distillation under reduced pressure, the residue was crystallized from a mixture of chloroform and hexane to give **5** (1.0 g, 62%, mp 150–151°) which was identical with material prepared from **3**.

**4-Hydroxy-1,3,4,5-2H-1,4-tetrahydrobenzodiazepin-2-one (6) and 5.**—A solution of 1.8 g (10 mmol) of **3** in 200 ml of acetic acid containing 0.5 g of 10% palladium on charcoal was reduced at atmospheric pressure and room temperature. The reduction stopped when about 16 mmol of hydrogen had been absorbed. After filtration to remove the catalyst and distillation under reduced pressure to remove solvent, the residue was stirred with methylene chloride. The solid that formed was separated by filtration to give 300 mg of crude **6**, mp 190–192°. Recrystallization from acetonitrile gave a product melting at 207–208°: ir (KBr disk) 3200 (NH) and 1660 $cm^{-1}$ (amide CO); nmr peaks (DMSO-$d_6$), $\delta$ 3.40 (s, 2, $CH_2$), 3.93 (s, 2, $CH_2$), 8.40 (s, 1, OH), 9.88 (s, 1, NH). The mass spectrum showed the molecular ion at 178.

*Anal.* Calcd for $C_9H_{10}N_2O_2$: C, 61.00; H, 5.52; N, 15.72. Found: C, 60.67; H, 5.66; N, 15.72.

Addition of hexane to the methylene chloride filtrate obtained above gave a crystalline material melting sharply at 109–111°. This was **5** containing solvent of crystallization since on prolonged drying at 78° under reduced pressure, the melting point became 149–151° and the product was identical with **5** prepared as described above.

**2-Bromo-2′-formylacetanilide (7).**[12]—A solution of 36.4 g (0.22 mol) of 2-aminobenzaldehyde dimethyl acetal in 1200 ml of ether was stirred with 700 ml of water at 0–5° and 48.2 g (20.8 ml, 0.24 mol) of bromoacetyl bromide dissolved in 50 ml of ether was added slowly while maintaining the reaction mixture slightly alkaline by addition of 10% sodium hydroxide. The organic layer was washed with water, dried over sodium sulfate, and concentrated under reduced pressure. The residue was extracted with two 250-ml portions of hot hexane. On cooling, 16.3 g of **7** crystallized, mp 68–71°. From the mother liquors an additional 3.3 g (mp 72–74°) separated. A methylene chloride solution of the hexane insoluble material, after filtration through Florisil, gave 3.3 g of **7** for a total of 22.9 g (43%). Recrystallization of a sample from hexane gave colorless prisms: mp 73–75°; ir ($CHCl_3$) 3250 (NH), 2850, 2755 (CHO), 1690 (infl, aldehyde), 1670 (amide CO), 1525 $cm^{-1}$ (amide II); nmr (DMSO-$d_6$), 4.25 (s, 2, $CH_2$), 10.03 (s, 1, CHO), 11.27 (s, 1, NH).

*Anal.* Calcd for $C_9H_8BrNO_2$: C, 44.65; H, 3.33; N, 5.79. Found: C, 44.92; H, 3.15; N, 5.59.

**1,3-Dihydro-2H-1,4-benzodiazepin-2-one (8).**—A solution of 9.1 g (37.6 mmol) of 2-bromo-2′-formylacetanilide (**7**) in 150 ml of tetrahydrofuran was added slowly to 300 ml of liquid ammonia while stirring and allowed to reflux for 5 hr. The ammonia was then evaporated slowly. The solid that formed was separated by filtration, stirred with water and again filtered to give 4.0 g of **8**, mp 216–218°. An additional 1.0 g was obtained from the filtrate after addition of water and evaporation of tetrahydrofuran under reduced pressure (total yield, 5.0 g, 83%). Recrystallization from acetonitrile gave colorless rods: mp 225–227°; uv (*i*-PrOH) max 228 m$\mu$ ($\epsilon$ 43,000), 254 (8400), 320 (3100); ir (KBr disk) 3300 (NH) and 1670 $cm^{-1}$ (amide CO); nmr (DMSO-$d_6$), $\delta$ 4.07 (s, 2, $CH_2$), 8.75 (s, 1, CH=N), 10.75 (s, 1, NH).

*Anal.* Calcd for $C_9H_8N_2O$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.33; H, 5.11; N, 17.61.

**2′-Formyl-2-phthalimidoxyacetanilide (9).**—A solution of 6.3 g (26 mmol) of **7** and 4.25 g (26 mmol) of N-hydroxyphthalimide in 60 ml of tetrahydrofuran containing 4.4 ml of triethylamine was stirred and heated to reflux for 75 min. The solid, which formed after 5 min, was separated by filtration, after cooling, and stirred for 10 min with 200 ml of water. Filtration gave 6.3 g of crude **9**, mp 193–205°. An additional 1.4 g (mp 195–198°) was obtained from the tetrahydrofuran filtrate after concentration under reduced pressure and addition of water. Recrystallization from benzene gave 5.4 g (65%): mp 200–201° (further recrystallization did not alter the melting point); ir ($CHCl_3$) 3250 (NH), 2850, 2755 (CHO), 1790, 1740 (phthalimide CO), 1715 (infl, CHO), 1690 $cm^{-1}$ (amide CO).

*Anal.* Calcd for $C_{17}H_{12}N_2O_5$: C, 62.96; H, 3.73; N, 8.64. Found: C, 63.20; H, 3.52; H, 8.82.

**2′-(1,3-Dioxolan-2-yl)-2-phthalimidoxyacetanilide (10).**—To a solution of 5 g (15 mmol) of **9** in 500 ml of benzene, 1.1 ml of ethylene glycol and several crystals of *p*-toluenesulfonic acid were added, and the mixture was stirred and refluxed for 2 hr while separating water in a Dean–Stark tube. The benzene solution was washed with dilute sodium bicarbonate, dried ($Na_2SO_4$), and concentrated to dryness under reduced pressure. Warming the residue with ethanol gave 0.7 g of unreacted starting material (**9**), mp 191–192°. The ethanol filtrate was concentrated to dryness and, on trituration of the residue with ether, 3.8 g of **10** (mp 112–115°) was obtained. Recrystallization from ethanol gave colorless rods: mp 118–120°; ir ($CHCl_3$) 3350 (NH), 1800, 1750 (phthalimide CO), 1690 (amide CO), 1540 $cm^{-1}$ (amide II).

*Anal.* Calcd for $C_{19}H_{16}N_2O_6$: C, 61.95; H, 4.38; N, 7.61. Found: C, 62.16; H, 4.39; N, 7.52.

**2-Aminoxy-2′-(1,3-dioxolan-2-yl)acetanilide (11).**—A solution of 3.2 g (9 mmol) of **10** in a mixture of 100 ml of chloroform and 100 ml of ethanol containing 0.9 ml of water and 0.9 ml (18 mmol) of hydrazine hydrate was kept at room temperature for 17 hr.

(12) First prepared in these laboratories by Dr. W. Metlesics from 2-aminobenzaldehyde and bromoacetyl bromide (unpublished).

The phthalhydrazide that formed was separated by filtration. The filtrate was concentrated to a small volume under reduced pressure and partitioned between methylene chloride and water. After drying the organic phase ($Na_2SO_4$), it was concentrated to dryness and the residue crystallized from a mixture of benzene and hexane to give 1.1 g of **11**, mp 47–51°. An additional 0.25 g (mp 51–54°) was obtained from the filtrate. Recrystallization of a sample from a mixture of ether and hexane gave colorless prisms: mp 51–54°; ir ($CHCl_3$) 3360 (NH), 1690 (amide CO), 1520 $cm^{-1}$ (amide II).

*Anal.* Calcd for $C_{11}H_{14}N_2O_4$: C, 55.45; H, 5.92; N, 11.76. Found: C, 55.47; H, 6.14; N, 11.44.

**2-(2-Aminobenzylideneaminoxy)acetic Acid (12).**—To a solution of 13.6 g (0.1 mol) of 2-aminobenzaldoxime in 300 ml of ethanol containing 10.8 g (0.2 mol) of sodium methoxide, 9.5 g (0.1 mol) of chloroacetic acid was added. The mixture was stirred and heated to reflux for 2 hr and filtered to remove the solid that formed; the filtrate was concentrated to dryness under reduced pressure. On addition of water, **12** crystallized (2.0 g, mp 136–139°) and an additional 8.6 g (mp 134–138°, total yield 55%) was obtained on acidification of the mother liquor with acetic acid. Recrystallization from a mixture of methylene chloride and hexane gave a product melting at 137–139°: ir (KBr disk) 3460, 3450, 3340, 3360 ($NH_2$), 3200–2600 (associated COOH), 1710 $cm^{-1}$ (carboxyl CO).

*Anal.* Calcd for $C_9H_{10}N_2O_3$: C, 55.66; H, 5.19; N, 14.43. Found: C, 55.46; H, 5.18; N, 14.49.

**Cyclization of 11 to 13. A.**—To a solution of 1 g (4 mmol) of **11** in 50 ml of ethanol, 16 ml of 1 *N* hydrochloric acid was added. Within 5 min, a white solid formed. After 16 hr at room temperature, the solid was separated by filtration (0.5 g, mp 263–266 dec). Recrystallization from a mixture of methanol and chloroform gave a product melting at 281–282°: ir (KBr) 3280 (NH), 1695 (amide CO), 1613, 1585, 1540 $cm^{-1}$; mass spectrum *m/e* 352, 176, 147, 118. The peak at *m/e* 176 could indicate the presence of the monomer.

*Anal.* Calcd for $(C_9H_8N_2O_2)_n$ C, 61.36; H, 4.58; N, 15.90. Found: C, 61.08; H, 4.77; N, 15.78.

**B.**—A solution of 2.35 g of **11** in 50 ml of pyridine was added during 1 hr to a refluxing solution of 2.35 g of pyridine hydrochloride in 200 ml of pyridine and the mixture refluxed for 4 more hr. Solvent was removed by distillation at reduced pressure and the residue was partitioned between methylene chloride and water. The organic phase was washed with water, dried ($Na_2SO_4$), and concentrated to dryness. Trituration of the residue with methylene chloride gave 200 mg of solid (mp 270–275°). Recrystallization from a mixture of methanol and chloroform gave a product melting at 269–270°: ir (KBr) 3270 (NH), 1690 (amide CO), 1660, 1620, 1580, 1540, 1500 $cm^{-1}$, mass spectrum *m/e* 352, 321, 305, 294, 176, 147, 131, 118.

*Anal.* Found: C, 61.13; H, 4.47; N, 15.83.

**Registry No.**—**2**, 16780-56-6; **3**, 16780-57-7; **4**, 16780-58-8; **5**, 1824-72-2; **6**, 16780-60-2; **7**, 16780-61-3; **8**, 16780-62-4; **9**, 16780-63-5; **10**, 16780-64-6; **11**, 16780-65-7; **12**, 16780-66-8; **13**, 16780-55-5.

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## 5-Aroyl- (or -Acyl-) 4-hydroxycoumarins

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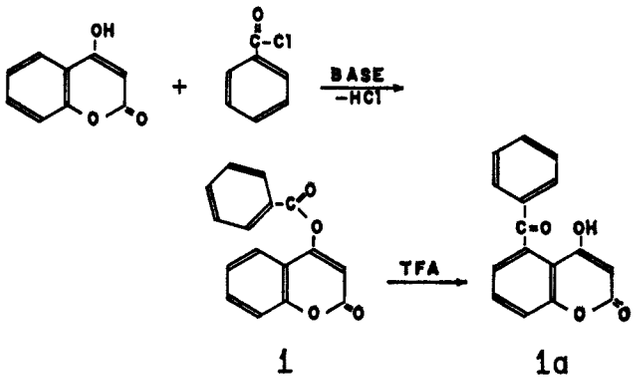
In this Note we present a novel rearrangement of 4-acyloxy- or 4-aroyloxycoumarins (see Table I) given as the **1–5** series, to give 5-aroyl- (or -acyl-) 4-hydroxy coumarin in good yield. This is the only rearrangement, to our knowledge, involving oxygen heterocycles in which a group has migrated from one ring to another and in this respect is quite different from the recorded instances of the Fries reaction[2] involving coumarins.

The rearranged compounds described in Table II as **1a–5a**, are considered by us to be produced by the reaction for **1a** given in Chart I and may be visualized as the general course of the reaction for the production of all the other members of the series.

CHART I

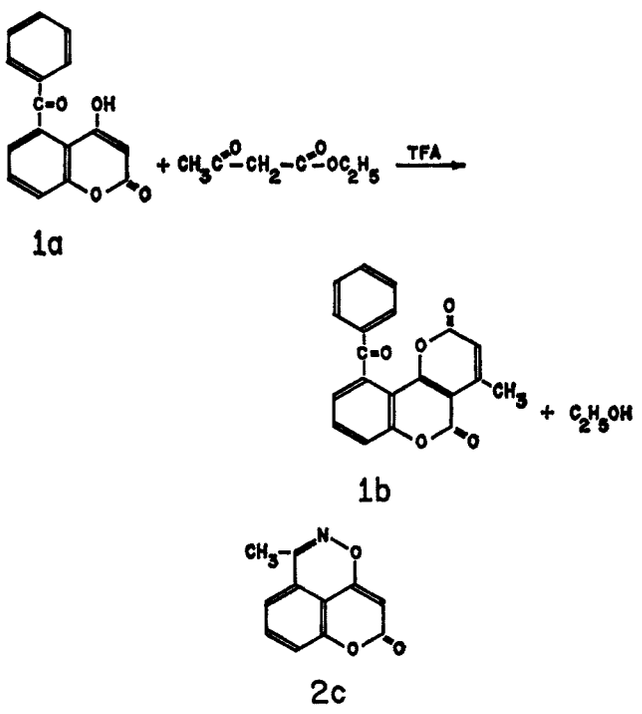



Compound **2a** is the only member of the series which formed a 2,4-dinitrophenylhydrazone.

The failure of the compounds to form dinitrophenyl hydrazones showed that the ketones were hindered and the infrared spectra showed that they were hydrogen bonded. Therefore, the migrating aroyl or acyl group must have taken up positions 3 or 5 on the ring system.

A comparison of the properties of **2a** with 3-acetyl-4-hydroxycoumarin, which had been very carefully

CHART II

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(2) R. C. Elderfield, "Heterocyclic Compounds," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1951, p 195.