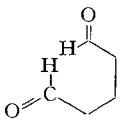
28. Synthesis of δ-Lactones from Glutaraldehyde

by **M. Rosenberger, D. Andrews**[1]**, F. DiMaria, A. J. Duggan** and **G. Saucy**
Chemical Research Department, *Hoffmann-La Roche Inc.*, Nutley, N.J. 07110

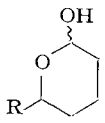
(29.XI.71)

Summary. A novel and general synthesis of δ-lactones from glutaraldehyde is described. The dialdehyde is first reacted with an alkyl or substituted alkyl *Grignard* reagent to afford a δ-hydroxyaldehyde in good yield. These aldehydes exist preferentially in the cyclic hemiacetal form (δ-lactols). Oxidation of the latter compounds to give δ-lactones is readily achieved with silver oxide or bromine. The δ-lactols and δ-lactones serve as intermediates for the total synthesis of steroids.

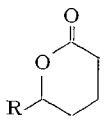
In the course of our work on the total synthesis of steroids[2], it became desirable to develop a simple and efficient route to suitably substituted δ-lactols **A** and δ-lactones **B**. Specifically, we were interested in a method permitting the introduction of acid-labile substituents containing, e.g., the *t*-butyl ether moiety or various cyclic acetals. The use of glutaraldehyde **1** for the construction of the five-carbon-atoms moiety of the δ-lactones had not been reported[3] previously. We hoped that a *Grignard* reagent would add selectively to glutaraldehyde[4] to give the hemiacetal **A**, which is ideally suited for oxidation to the δ-lactone **B**. Fortunately, mono-addition of alkyl *Grignard* reagents to the aldehyde **1** was found to predominate, provided that the reaction was run in the cold. As expected, double *Grignard* addition was the major side reaction. It is conceivable that the observed high selectivity of mono-addition (up to 80% in some cases) was due to 'trapping' of the primary (mono) adduct as the relatively unreactive magnesium alkoxide of lactol **A**.



1



A



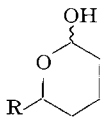
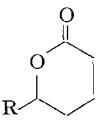
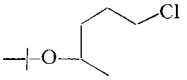
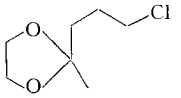
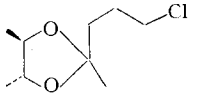
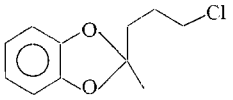
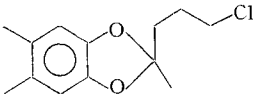
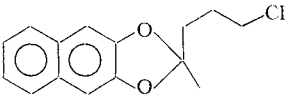
B

The preparation of the *Grignard* reagents derived from **6**[5] and from the chloroacetals **9** [4] and **12**[5] caused no difficulties. In contrast, the catechol acetal moiety was found to suffer internal attack (*cf.* [4] [5]) when the chloroacetal **15** was reacted with magnesium in tetrahydrofuran (THF). Fortunately, this side reaction could be minimized by careful temperature control (<40°) during the preparation of the *Grignard* reagent. The same technique was applied to the reaction between magnesium (in THF) and the chloroacetals **18** and **20**.

---

[1] Technical Development Department, *Hoffmann-La Roche Inc.*
[2] See [1] and further references cited therein.
[3] See [2] for a discussion of presently available methods.
[4] *Cf.* [3] regarding the structure of **1** in aqueous solution.
[5] See experimental.

Preparation of δ-Lactols **A** *and δ-Lactones* **B**

Alkyl Halides R-Hal		δ-Lactols **A**, yield 	δ-Lactones **B**, yield 
		**2** 68.5%[a]	**3** [8] 50%[b,c]
		**4**	**5** [9] 41%[b,c]
	**6**	**7** 66%[d]	**8** 83%[e]
	**9** [4]	**10** 52%[d]	**11** 77%[e]
	**12**[f]	**13** 64%[d,f]	**14** 88%[e,f]
	**15**	**16** 78%[g]	**17** 86%[c]; 60%[h]
	**18**	**19** 45%[g]	
	**20**	**21** 63%[g]	

a) Crude product.
b) Overall yield from akylchloride.
c) Oxidation with silver oxide.
d) Purified *via* the hydrogensulfite adduct.
e) Oxidation with bromine.
f) Acetal derived from D(–)–2,3–dihydroxybutane.
g) Chromatographically pure.
h) Oxidation with sodium dichromate in acetic acid.

The *Grignard* reaction with glutaraldehyde was found to work well for all the examples tried, as shown in the table. In most cases, the hemiacetals **A** thus produced could conveniently be purified via hydrogensulfite complex formation.

Of the various methods [6] for oxidation of the hemiacetals to the corresponding δ-lactones, silver oxide in methanolic caustic soda [7] proved to be the most general. It had the added advantage that it could be used with crude hemiacetals since the

hydroxy acids generated in the reaction were readily separable from neutral impurities. Thus, δ-heptanolide **3** [8] and δ-decanolide **5** [9] were obtained conveniently in 50% and 41% yield respectively (based on the alkyl halide) without purification of the intermediates **2** and **4**. Oxidation of the pure lactol **16** with silver oxide gave 86% of the desired lactone **17**. Except for the case of the aromatic compound **16**, bromine in an aqueous acetic acid – sodium acetate buffer mixture was also found to be satisfactory (*cf.* [10]). This method gave the δ-lactones **8**, **11** and **14** in good yields (see table) from the corresponding lactols.

A preliminary check of other oxidation procedures gave the following results: Sodium dichromate in acetic acid afforded 60% (from **16**) of the lactone **17**. Activated manganese dioxide [11] in benzene was found to oxidize the δ-lactols **13** and **16** to the δ-lactones **14** and **17** in 45% and 35% yield respectively. The silver carbonate reagent [12] in refluxing toluene, tried with the lactol **16**, gave the lactone **17** in about **33**% yield, the corresponding dihydropyran (dehydration of **16**) being the major by-product (~25%). Oxidation of **16** with air in ethyl acetate in the presence of platinum [13] (equal weight) afforded over 90% of **17**. Reducing the amount of platinum to $^1/_{10}$ or less gave much lower yields.

Experimental Section

General. Boiling points (b.p.) are uncorrected. Thin-layer chromatography (TLC) was carried out on *Brinkmann* F 254 silica plates, using a 1:1-mixture of ethyl acetate and benzene. The plates were first viewed under short-wavelength UV. light. The spots were developed by spraying with 50% aqueous *p*-toluenesulfonic acid and heating to 120° for 1–3 minutes, followed by exposure to iodine vapors. Infrared (IR.) spectra were determined with a *Beckman* IR. 9 spectrophotometer. Nuclear magnetic resonance (NMR.) spectra were recorded with *Varian* A-60 and HA-100 spectrometers. Chemical shifts were determined using tetramethylsilane (TMS) as an internal standard. Mass spectra were determined on *CEC* 21-110 or *Jeolco* 015G spectrometers.

Removal of solvents 'in vacuo' refers to removal at 20 Torr and 45° with a rotavapor and finally at 0.5 Torr.

Glutaraldehyde (**1**). A commercially available aqueous solution of glutaraldehyde (150 ml; 50%) was combined with benzene (500 ml) and treated with anhydrous magnesium sulfate (100 g) in an ice bath. After standing for 30 min at room temperature, the solids were filtered off and the last traces of water were removed by azeotropic distillation using a water-cooled *Dean-Stark* trap. After one hour at reflux, the solvent was removed at 20 Torr at 40°. The residue was distilled to afford the pure dialdehyde (60 g): b.p. 69–70° at 8 Torr. Freshly distilled aldehyde was used for the *Grignard* reactions described below. In some runs (preparation of lactones **3** and **5**) the crude residue was used directly.

(±)-*5-Hydroxyheptanoic acid lactone* (**3**) [8]. Crude glutaraldehyde (residue obtained from 240 ml of the 50% aqueous solution, see above) was dissolved in THF (1000 ml) and cooled to –70°. A solution of ethylmagnesium bromide (from 96 g of ethyl bromide) in THF (545 ml) was added rapidly with stirring, the temperature being maintained between – 50 and – 60°. After complete addition (5–10 min) the mixture, which had become difficult to stir, was warmed to room temperature within 60 min and stirred for an additional 16 hours. The reaction mixture was then cooled to 5° and treated with a saturated solution of ammonium chloride (65 ml). The supernatant liquid was decanted off and the residue was washed with more THF (2 × 150 ml). The combined extracts were died over anhydrous magnesium sulfate and taken to dryness 'in vacuo' to yield the crude *hemiacetal* **2** (89 g).

For the oxidation, a slurry of silver oxide was first prepared as follows: A solution of silver nitrate (611.3 g) in water (600 ml) was treated at 15° with a solution of sodium hydroxide (286 g) in a mixture of water (468 ml) and methanol (613 ml) (exothermic reaction!). To the resulting warm slurry was added with stirring the crude hemiacetal (89 g) dissolved in methanol (265 ml), the temperature being maintained at 55° (exotherm). The mixture was then stirred for 1 h at 55° and

cooled to room temperature. The solids were filtered off and washed with methanol/water 1:1 (3 × 400 ml) and toluene (2 × 300 ml). The aqueous part of the filtrate was concentrated at 40°/20 Torr (removal of methanol) and then acidified with sulfuric acid (10N) at 10°. Extraction with dichloromethane, removal of the solvents at 22 Torr and distillation of the residue gave the pure *lactone* **3** [8] (64 g): b.p. 102–105°/9 Torr. IR ($CHCl_3$): 1720 and 1230 cm^{-1} (δ-lactone). NMR. ($CDCl_3$): δ 4.2 (*m*, 1H, >C*H*—O), 2.43 (*m*, 2 H, —CH_2—CO) and 1.0 ppm (*t*, 3 H, J = 6 Hz; CH_3—CH_2).

(±)-*5-Hydroxydecanoic acid lactone* (**5**) [9]. Using the procedure described above, crude glutaraldehyde (55 g) was reacted with *n*-pentylmagnesium bromide (0.5 mole) in THF to afford the crude *lactol* **4**. This, upon oxidation with silver oxide, followed by working up and distillation, gave the known [9] *lactone* **5** (35 g): b.p. 111–113°/1.5 Torr. IR. ($CHCl_3$): 1715 and 1230 cm^{-1} (δ-lactone). NMR. ($CDCl_3$): δ 4.2 (*m*, 1H, >C*H*—O), 2.46 (*m*, 2 H, CH_2—CO—) and 0.88 ppm (*m*, 3 *H*, CH_3—CH_2—).

(±)-*1-Chloro-4*-t-*butoxy-pentane* **6**. A solution of 5-chloro-2-pentanone [14] (236 g) in ether (825 ml) was added slowly to a slurry of lithium aluminium hydride (39.6 g) in ether (1000 ml) at −40° (2½ h). The mixture was then warmed to −30°, a saturated solution of sodium sulfate (495 ml) was added and after the solids had been filtered off the solvents were removed at 30°/20 Torr to give crude (±)-*5-chloro-2-pentanol* [15] (238.4 g). IR. analysis (film) showed no characteristic tetrahydrofuran bands at 1080 and 1380 cm^{-1}. This crude alcohol (238 g) was dissolved in dichloromethane (1000 ml) containing concentrated sulfuric acid (24 ml) and then reacted with liquid isobutylene (1000 ml) at room temperature for 20 h in a sealed flask. Removal of the excess isobutylene and washing the resulting solution with brine gave crude 1-chloro-4-*t*-butoxy-pentane (294 g; approximately 95% pure by GC.). A sample was distilled for analysis: b.p. 65–66°/9 Torr. NMR. ($CDCl_3$): δ 3.5 (*m*, 3 H, >C*H*O— and —CH_2Cl), 1.67 (*m*, 4 H, —CH_2—CH_2—), 1.18 (*s*, 9 H, O—C(CH_3)$_3$), and 1.12 ppm (*d*, 3 H, J = 6 Hz; —CH—CH_3).

$C_9H_{19}ClO$ (180.7) Calc. C 60.6 H 10.72 Cl 19.85%, Found C 60.92 H 10.75 Cl 19.92%.

(±)-*6-(4*-t-*Butoxy-pentyl)-tetrahydropyran-2-ol* (**7**). A solution of the crude chloroether **6** (67.4 g) in THF (250 ml; distilled from sodium hydride) was added to magnesium turnings (10 g) which had been activated with iodine. This mixture was heated at reflux for 30 min and then treated with 1,2-dibromoethane [16] (0.1 ml). A vigorous reaction generally occurred at this stage and the *Grignard* reagent started to form. The mixture was stirred for 60 min at reflux, cooled and added over 10 min to a solution of freshly distilled glutaraldehyde (39.2 g) in THF (400 ml) at −25°. The mixture was stirred for 15 min at −25°, followed by 60 min at 0°, aqueous ammonium chloride solution (200 ml; 30%) then added, and the supernatant layer was decanted off. The aqueous phase was washed with ether (250 ml) and the combined extracts were taken to dryness 'in vacuo' to yield crude **7** (91 g), which was treated with a solution of sodium sulfite (20%; 650 ml), brought to pH 7.5 with caustic soda solution (1N), and heated at 40° for 60 min. The resulting mixture, after cooling, was extracted with ether to yield the bis-addition product (15.4 g). The pure hemiacetal **7** (61.6 g) was readily obtained from the aqueous phase by extraction with ether after addition of aqueous sodium hydroxide (to pH 12). A sample of **7** was distilled for analysis: b.p. 100°/0.005 Torr (bulb tube). IR. ($CHCl_3$): 3600 and 3375 (hydroxyl), and 1200 cm^{-1} (*t*-butoxy). NMR. ($CDCl_3$): δ 5.32 (*m*, equatorial C(2) proton), 4.78 (*m*, axial C(2) proton), 4.17, 4.05 (axial and equatorial C(2)—O*H*), 3.4 (*m*, 1 H, —C*H*—O—), 1.18 [*s*, 9 H, (CH_3)$_3$C—] and 1.12 ppm (*d*, 3 H, J = 6 Hz, CH_3—CH).

$C_{14}H_{28}O_3$ (244.36) Calc. C 68.81 H 11.55%; Found C 68.40 H 11.38%

(±)-*9*-t-*Butoxy-5-hydroxy-decanoic acid lactone* (**8**). A solution of sodium acetate (30 g) in water (50 ml) containing acetic acid (25 ml) was prepared and 55 ml of it (pH 5.5) were added to the hemiacetal **7** (5.4 g). This mixture was treated at room temperature with bromine (0.8 ml), the solution stirred for 1 h at room temperature, water added, and the products isolated with ether. Removal of the solvents and distillation yielded pure lactone **8** (4.5 g): b.p. 110–115°/0.1 Torr; IR. ($CHCl_3$): 1725 cm^{-1} (δ-lactone).

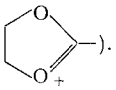
$C_{14}H_{26}O_3$ (242.35) Calc. C 69.38 H 10.81% Found C 69.14 H 10.95%

(±)-6-(*4,4-Ethylenedioxypentyl*)-*tetrahydropyran-2-ol* (**10**). From glutaraldehyde and the *Grignard* reagent [4] formed at room temperature from 1-chloro-4,4-ethylenedioxy-pentane (**9**)

(52% yield based on the chloroacetal) as described above. Properties: b.p. 130–132°/0.1 Torr. IR. ($CHCl_3$): 3600 and 3400 cm^{-1} (hydroxyl). NMR. ($CDCl_3$): δ 3.92 (*s*, 4 H, O–CH_2–CH_2–O) and 1.3 ppm (*s*, 3 *H*, CH_3–C<).

$C_{12}H_{22}O_3$ (230.3) Calc. C 62.58 H 9.63% Found C 62.66 H 9.77%

(±)-*9,9-Ethylenedioxy-5-hydroxy-decanoic acid lactone* (**11**). The hemiacetal **10** (25 g) dissolved in dimethylformamide (120 ml) was added to a mixture of sodium acetate (30 g), water (120 ml) and acetic acid (40 ml) and cooled to 5°. Bromine (7 ml) was added over 5 min and the mixture was then warmed to room temperature and stirred for 1 h. Solid sodium hydrogensulfite (2.5 g) was added, followed by brine (250 ml). The lactone was extracted with benzene and the benzene extracts were washed with water and taken to dryness 'in vacuo'. Distillation of the residue yielded pure **11** (19 g): b.p. 138–140°/0.2 Torr. IR. ($CHCl_3$): 1730 and 1255 (δ-lactone), and 1040 cm^{-1} (ethylene-acetal). NMR. ($CDCl_3$): δ 3.94 (*s*, 4 H, OCH_2–CH_2O) and 1.3 (*s*, 3 *H*, CH_3–C<).

MS.: *m/e* 37 (base peak, ).

$C_{12}H_{20}O_4$ (228.28) Calc. C 63.13 H 8.83% Found C 63.24 H 8.80%

1-Chloro-4,4-(R)*-2,3-butylenedioxy)-pentane* (**12**). Reaction of 5-chloro-2-pentanone [14] (68.3 g) with (*R*)-2,3-dihydroxy-butane (65.3 g) in refluxing benzene (120 ml) (*Dean-Stark* trap) in the presence of *p*-toluenesulfonic acid (0.45 g) gave the corresponding acetal in the usual manner (90% yield based on chloroketone). The product had the following properties: b.p. 77°–83°/10 Torr; $[\alpha]_D^{25} = -20.49°$ ($c = 1.449$, $CHCl_3$).

$C_9H_{17}ClO_2$ (192.68) Calc. C 56.08 H 8.90 Cl 18.41%
Found C 56.30 H 8.77 Cl 18.42%

(*2,6-*RS)*-6-[4,4-*(R)*-(2,3-butylenedioxy)-pentyl]-tetrahydropyran-2-ol* (**13**). Transformation of the chloride **12** into the *Grignard* complex, followed by reaction with glutaraldehyde as described for compound **10** afforded the lactol **13** (64% yield, based on acetal): $[\alpha]_D^{25} = -14.47°$ ($c = 1.6512$, $CHCl_3$).

$C_{14}H_{26}O_4$ (258.35) Calc. C 65.08 H 10.14% Found C 64.89 H 10.34%

9,9-(R)*-(2,3-Butylenedioxy)-5-*(RS)*- hydroxy-decanoic acid lactone* (**14**). Oxidation of the hemiacetal **13** with bromine as described for **11** gave the lactone **14** in 88% yield: b.p. 119°/0.01 Torr; $[\alpha]_D^{25} = -12.89°$ ($c = 1.0$, $CHCl_3$).

$C_{14}H_{24}O_4$ (258.33) Calc. C 65.59 H 9.44% Found C 65.58 H 9.51%

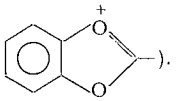
*1-Chloro-4,4-*O*-phenylenedioxy-pentane* (**15**). A mixture of 5-chloro-2-pentanone (100 g), pyrocatechol (100 g), *p*-toluene-sulfonic acid (2 g) and benzene (600 ml) was heated at reflux for 24 h in conjunction with a water-cooled *Dean-Stark* trap. The dark solution was cooled to room temperature, washed with aqueous sodium hydroxide (1N) and dried over neutral alumina (activity I). Removal of the solvents 'in vacuo' and distillation of the residue yielded pure pyro-catechol acetal **15** (99.5 g): b.p. 82°/Torr.

$C_{11}H_{13}O_2Cl$ (212.7) Calc. C 62.12 H 6.16% Found C 61.52 H 6.11%

(±)-*6-(4,4-*o*-Phenylenedioxy-pentyl)-tetrahydropyran-2-ol* (**16**). Magnesium (28 g) was activated with a trace of iodine in an atmosphere of nitrogen. A portion (100 ml) of a solution of the chloroacetal **15** (213 g), dissolved in dry THF (1400 ml), was added and the mixture was heated at 38° for 5 min and then treated with 1,2-dibromoethane (0.5 ml) [16]. This initiated formation of the *Grignard* reagent and resulted in a mild exothermic reaction. The reaction temperature was held at 36–38° with cooling, to minimize rearrangement of the *Grignard* reagent, and after a further 15–20 min the rest of the chloroacetal solution was added over 1 hour. After the exothermic reaction had subsided (~1 h after addition was complete) the mixture was heated at 36–38° for 2 hours. The progress of the reaction was readily monitored by quenching an aliquot with ammonium chloride solution and analysing the organic phase by GC. (the above run showed a 96% conversion).

Freshly distilled glutaraldehyde (100 g) was dissolved in dry THF (700 ml). To this solution, cooled to –65°, the above *Grignard* reagent, cooled to –20°, was rapidly added (~30 min; temperature held between –60 and –50°). The mixture was then warmed to room temperature over

1 h, stirred a further $1^1/_2$ h at room temperature, cooled to 5°, treated with an aqueous solution of ammonium chloride (25%; 150 ml), and filtered. Removal of the solvents 'in vacuo' yielded the crude hemiacetal **16** (270 g). Chromatography of a sample on silica gel yielded pure **16** on elution with ethyl acetate – benzene mixtures (10–15%) (2 g crude gave 1.45 g pure **16**). IR. (film): 3625 and 3375 (—OH), 1500 and 1250 cm^{-1} (pyrocatechol acetal). NMR. ($CDCl_3$): δ 6.73 (*s*, 4 H, phenyl protons) and 1.58 ppm (*s*, 3 H, CH_3—C<). This material also showed multiple bands due to the axial and equitorial hydroxyl). MS:

$M^{\oplus}$ *m/e* 135 (base peak, ).

$C_{16}H_{22}O_4$ (278.34) Calc. C 69.04 H 7.97% Found C 69.00 H 8.04%

(±)-*9,9-o-Phenylenedioxy-5-hydroxy-decanoic acid lactone* (**17**). -(a) *By oxidation with silver oxide.* A solution of silver nitrate (22 g) in water (75 ml) at room temperature was treated with a solution of sodium hydroxide (10.2 g) in water (25 ml) and warmed to 55°. Methanol (150 ml) was then added, followed by the lactol **16** (14 g) dissolved in methanol (25 ml). The mixture was stirred 60 min at 50–55°, cooled to room temperature and filtered. The residue was washed with aqueous methanol (1:1; 50 ml), water (2 × 50 ml) and benzene (2 × 50 ml). The aqueous layer separated from the combined filtrates, yielded by acidification with aqueous sulfuric acid (2N) to pH 1 a mixture of lactone and hydroxy acid (14.15 g), extracted with dichloromethane. Distillation of the extracted material from an oil-jacketed flask gave pure **17** (12 g): b.p. 180–195°/Torr 0.1. IR. ($CHCl_3$); 1730 and 1220 (δ-lactone), 1490 and 1240 cm^{-1} (pyrocatechol acetal). NMR. ($CDCl_3$): δ 6.72 (*s*, 4 H, phenyl protons, 4.2 (*m*, 1 H, —C*H*—O) and 1.58 ppm (*s*, 3 H, CH_3—). MS.: $M^{\oplus}$ *m/e* 276, *m/e* 135 (base peak; see above).

$C_{16}H_{20}O_4$ (276.32) Calc. C 69.54 H 7.30% Found C 69.84 H 7.84%

b) *By oxidation with dichromate.* A solution of the crude hemiacetal **16** (75% purity; 233 g) in toluene (1200 ml) was added to a mixture of sodium dichromate dihydrate (315 g) and acetic acid (1200 ml). The mixture was kept at 35° for 2 h and then stirred for 16 h at room temperature. Water (2500 ml) was then added, the products were isolated with toluene and the toluene phase was taken to dryness 'in vacuo'. Distillation of the residue gave the lactone **17** (105 g; 60% based on hemiacetal content).

1-Chloro-4,4-dimethyl-1,2-phenylenedioxy)-pentane (**18**). Prepared from 4,5-dimethyl-pyrocatechol and 5-chloro-2-pentanone as in the case of compound **15**, and isolated in pure form by distillation: b.p. 110–120°/0.1 Torr. NMR. ($CDCl_3$): δ 6.66 (*s*, 2 H, aromatic protons), 3.65 (*t*, 2 H, J = 5 Hz, —CH_2—Cl), 2.2 (*s*, 6 H, aromatic methyls) and 1.66 ppm (*s*, 3 H, CH_3—C<). UV. max (EtOH): 243, 293 nm (ε = 3590, 4890).

$C_{13}H_{17}ClO_2$ (240.72) Calc. C 64.86 H 7.12 Cl 14.73%
Found C 64.66 H 7.30 Cl 14.74%

(±)-*6-[4,4-(4,5-Dimethyl-1,2-phenylenedioxy)-pentyl-tetrahydropyran-2-ol* (**19**). Conversion of the chloroacetal **18** to the *Grignard* reagent and subsequent reaction with glutaraldehyde as described for **16** yielded the pure hemiacetal **19** as an oil after chromatography on silica gel. IR. ($CHCl_3$): 3600 (—OH), 1500 and 1260 cm^{-1} (phenylenedioxy).

$C_{18}H_{26}O_4$ (306.36) Calc. C 70.56 H 8.55% Found C 69.73 H 8.27%

1-Chloro-4,4-(2,3-naphtalenedioxy)-pentane (**20**). This material was prepared from 2,3-dihydroxynaphthalene and 5-chloro-2-pentanone in benzene with *p*-toluenesulfonic acid as described for **15**: b.p. 139–141°/0.07 Torr.

$C_{15}H_{15}ClO_2$ (262.72) Calc. C 68.57 H 5.75 Cl 13.49%
Found: C 68.41 H 5.67 Cl 13.49%

(±)-*6-[4,4-(2,3-Naphtalenedioxy)-pentyl]-tetrahydropyran-2-ol* (**21**). Addition of the *Grignard* reagent formed from **20** to glutaraldehyde, as described for **16** yielded crude hemiacetal **21** which by chromatography on silica gel yielded pure **21**. IR. ($CHCl_3$): 3600 (—OH), 1470 and 1250 cm^{-1} (naphtalenedioxy). NMR. ($CDCl_3$): δ 7.5 (*m*, 4 H, aromatic protons), 7.0 (*s*, 2 H, aromatic protons) and 1.61 ppm (*s*, 3 H, CH_3—C<). UV. max (EtOH): 230 nm (ε = 55600).

$C_{20}H_{24}O_4$ (328.39) Calc. C 73.14 H 7.37% Found C 72.84 H 7.67%

BIBLIOGRAPHY

[1] *G. Saucy & R. Borer,* Helv. *54,* 2121, 2517 (1971); *M. Rosenberger, T. P. Fraher & G. Saucy,* Helv. *54,* 2857 (1971), and forthcoming publications.
[2] *G. Lardelli, V. Lamberti, W. T. Weller & A. P. De Jonge,* Rec. Trav. chim. Pays-Bas. *86,* 481 (1967); *cf. G. Baumeyer, G. Dittus & E. Müller* in *Houben-Weyl,* «Methoden der organischen Chemie», *6*/4, 329 (1966).
[3] *P. M. Hardy, A. C. Nicholls & H. N. Rydon,* J. chem. Soc., Sect. D, *1969,* 565.
[4] *C. Feugeas,* Bull. Soc. chim. France *1963,* 2568.
[5] *C. Feugeas & H. Normant,* Bull. Soc. chim. France *1963,* 1441.
[6] *H. Kröpper* in *Houben-Weyl,* Methoden der organischen Chemie, *6*/2, 715 (1963).
[7] *L. F. Fieser & M. Fieser,* 'Reagents for Organic Synthesis', p. 1012, J. Wiley & Sons. Inc., New York 1967.
[8] *H. D. Zook & J. A. Knight,* J. Amer. chem. Soc. *76,* 2302 (1954).
[9] *K. W. Rosenmund & H. Bach,* Chem. Ber. *94,* 2401 (1961).
[10] *N. C. Deno & N. H. Potter,* J. Amer. chem. Soc. *89,* 3555 (1967).
[11] *R. J. Highet & W. C. Wildman,* J. Amer. chem. Soc. *77,* 4399 (1955).
[12] *M. Fétizon & M. Golfier,* C.r. hebd. Seances Acad. Sci. *267* (C), 900 (1968).
[13] *M. Shamma & H. R. Rodriguez,* Tetrahedron *24,* 6583 (1968).
[14] *G. W. Cannon, R. C. Ellis & J. R. Leal,* 'Organic Synthesis', Coll. vol. IV, p. 597 (1963).
[15] *R. C. Elderfield & F. Brody,* U.S. Pat. 2464199 (1949) [Chem. Abstr. *43,* 4684b (1949)].
[16] *D. E. Pearson, D. Cowan & J. D. Beckler,* J. org. Chemistry, *24,* 504 (1959).

29. Photoelectron Spectra of Azabenzenes and Azanaphthalenes: I. Pyridine, Diazines, *s*-Triazine and *s*-Tetrazine[1])

by **R. Gleiter, E. Heilbronner** and **V. Hornung**
Physikalisch-Chemisches Institut der Universität Basel

(8. XI. 71)

Summary. The experimental and theoretical basis of a recently proposed reassignment of the bands in the PE. spectra of pyridine, pyridazine, pyrimidine and pyrazine is discussed in detail. A characteristic feature of the derived orbital sequence is that it takes the 'through-space' and 'through-bond' interaction between the 'lone pair' basis orbitals explicitly into account. A simple parametrization of the orbital energies, based on HMO-type models for the π-orbitals and for the 'lone pair' linear combinations, yields excellent agreement with the observed band positions in the PE. spectra of *s*-triazine and *s*-tetrazine. Our new assignment is compared to those proposed previously.

The interaction between nitrogen or oxygen non-bonding 'lone pair' orbitals has been extensively discussed [2] [3]. In some cases predictions, derived from model MO.-calculations, could be verified by high-resolution photoelectron spectroscopy (*e.g.* [4]). In this connection the diazines II, III, and IV are of special interest, insofar as the recognition of substantial coupling between the non-adjacent nitrogen lone pair orbitals in pyrimidine (III) and pyrazine (IV) leads to a reassignment of the bands in their photoelectron spectra (PE. spectra) [1] [5].

[1]) Part 28 of: 'Applications of Photoelectron Spectroscopy'. Part 27: [1].