ether layer was extracted with two 100-ml. portions of 10% sodium hydroxide, dried, and concentrated. Distillation of the residue yielded 7.53 g. (72%) of 5-benzylthio-1-pentanol, b.p. 144° (0.5 mm.), $n^{26}D$ 1.5488.

Anal. Calcd. for $C_{12}H_{18}OS$: C, 68.52; H, 8.63. Found: C, 68.42; H, 8.50.

The infrared spectrum of the material was identical with that of the cleavage product of 2-benzylthiotetrahydropyran (Table III).

Other Compounds.—Also synthesized in the course of this work was the 2-tetrahydropyranyl derivative of ethyl mercaptoacetate, b.p. 98–99° (2 mm.).

Anal. Calcd. for $C_9H_{16}O_3S$: C, 52.91; H, 7.90. Found: C, 53.01; H, 7.83.

The bis-2-tetrahydropyranyl derivative of mercaptoethanol, b.p. 136–138° (3 mm.), was also synthesized.

Anal. Calcd. for $C_{12}H_{22}O_3S$: C, 58.50; H, 9.00. Found: C, 58.60; H, 8.90.

Notes

Reductions with Metal Hydrides. XVI. Reduction of Some 2-Tetrahydropyranylamines

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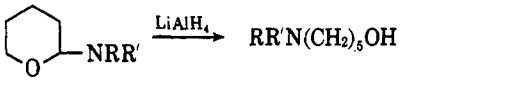
Having studied the reduction of 2-tetrahydropyranyl ethers[1] and 2-tetrahydropyranyl thioethers[2] with lithium aluminum hydride–aluminum chloride, we were interested in the reduction of the corresponding 2-tetrahydropyranyl-N,N-dialkylamines. As was to be expected on the basis of the fact[3] that oxazolidines, unlike ketals and monothioketals, are hydrogenolyzed by lithium aluminum hydride alone, without the need for added Lewis acids, 2-piperidinotetrahydropyran, 2-morpholinotetrahydropyran, and 2-benzylaminotetrahydropyran were similarly reduced to substituted 5-aminopentanols. The starting materials (which are



simple models for nucleosides) are readily prepared from 2-chlorotetrahydropyran and the appropriate amine. The reduction product from 2-piperidinotetrahydropyran was identical in infrared spectrum and other physical properties with an authentic sample of 5-piperidino-1-pentanol prepared from pentamethylene chlorohydrin and piperidine.

Hydride reduction of 2-alkylaminotetrahydropyrans provides an alternative to the previously described[4,5] catalytic hydrogenation which also yields 5-alkylamino-1-pentanols.

Experimental

2-Chlorotetrahydropyran.[6]—Hydrogen chloride gas was bubbled into a solution of 33.6 g. (0.4 mole) of dihydropyran and 100 ml. of anhydrous ether at 0° until no more was absorbed. Concentration and distillation at reduced pressure gave 28.8 g. (60%) of 2-chlorotetrahydropyran, b.p. 40–42° (16 mm.), lit.[6] b.p. 40° (15 mm.). The product was stored in a refrigerator over anhydrous potassium carbonate until used.

2-Piperidinotetrahydropyran.—In a 500-ml. three-necked flask equipped with a magnetic stirrer and condenser was placed 27.6 g. (0.2 mole) of anhydrous potassium carbonate, 20.8 g. (0.25 mole) of piperidine, and 100 ml. of anhydrous ether. A solution of 12.7 g. (0.1 mole) of 2-chlorotetrahydropyran in 100 ml. of ether was slowly added from a dropping funnel. After addition was complete, the turbid solution was boiled for 6 hr., cooled, and 100 ml. of water was added to dissolve the salts. The ether layer was separated and the aqueous layer was extracted three times with 100-ml. portions of ether. The combined ethereal extracts were dried over potassium carbonate, decanted, and concentrated. Vacuum distillation of the residue gave 11.9 g. (71%) of 2-piperidinotetrahydropyran, b.p. 93–94° (7 mm.). The infrared spectrum was compatible with the assigned structure.

Anal. Calcd. for $C_{10}H_{19}NO$: C, 70.93; H, 11.32; N, 8.27. Found: C, 71.00; H, 11.28; N, 8.00.

2-Morpholinotetrahydropyran was similarly prepared from 9.6 g. (0.11 mole) of morpholine in 48% yield (8.2 g.): b.p. 88–89° (7 mm.), $n^{20}D$ 1.4776; lit.[5] b.p. 111.5° (12 mm.), $n^{20}D$ 1.4809. The infrared spectrum indicated absence of starting materials.

2-Benzylaminotetrahydropyran was analogously prepared from 11.8 g. (0.11 mole) of benzylamine in 47% yield (9.0 g.) and boiled at 114° (5 mm.). The infrared spectrum indicated substantial absence of benzylamine.

Anal. Calcd. for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.19; H, 9.27; N, 7.01.

Reduction of 2-Piperidinotetrahydropyran.—Lithium aluminum hydride (0.1 mole) in the form of a clear ethereal solution (*ca.* 1 *M*) was placed in a three-necked flask equipped with a condenser, drying tube, stirrer, and dropping funnel. The solution was diluted with 50 ml. of ether, and 8.5 g. (0.05 mole) of 2-piperidinotetrahydropyran in 100 ml. ether was added dropwise. The solution was boiled for 2 hr., cooled, and decomposed by the addition of 4 ml. of water, 4 ml. of 15% aqueous sodium hydroxide, and again 12 ml. of water. The precipitated solid was removed by suction filtration and washed with several portions of ether, and the combined ether filtrate was dried over potassium carbonate and concentrated. Distillation of the residue at reduced pressure gave 7.0 g. (82%) of 5-piperidino-1-pentanol: b.p. 99–101° (0.75 mm.), $n^{18}D$ 1.4804; lit.[7] b.p. 140° (13 mm.), $n^{16.5}D$ 1.4820. The infrared spectrum showed the expected presence of OH and was identical with that of an authentic specimen (see below).

Reduction of 2-Morpholinotetrahydropyran.—From 6.0 g. (0.05 mole) of 2-morpholinotetrahydropyran was obtained 5.5 g. (92%) of 5-morpholino-1-pentanol: b.p. 116–118° (3 mm.), $n^{18}D$ 1.4750; lit.[5] b.p. 151° (10 mm.), $n^{19}D$ 1.4780. The infrared spectrum showed a prominent band at 2.95 μ and was different from that of the starting material.

Reduction of 2-Benzylaminotetrahydropyran.—2-Benzylaminotetrahydropyran was reduced on a 0.031 *M* scale (6.0 g.) by proportionally diminishing the amounts of reagents given above.

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(4) I. Scriabine, *Bull. soc. chim. France*, **14**, 454 (1947).

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Distillation of the product gave 0.66-g. forerun, b.p. 42–50° (6 mm.), identical in infrared spectrum with benzylamine, and 4.05 g. (67%) of 5-benzylamino-1-pentanol, b.p. 152–168° (6 mm.), lit.[4] b.p. 174–178° (11 mm.). The infrared spectrum was compatible with the assigned structure.

5-Piperidino-1-pentanol from Pentamethylene Chlorohydrin.—In a 250-ml. three-necked flask equipped with a condenser, magnetic stirrer, dropping funnel, and thermometer were placed 25.5 g. (0.3 mole) of piperidine and a pellet of potassium hydroxide in 100 ml. of water. Pentamethylene chlorohydrin (13.9 g., 0.1 mole) was added dropwise at room temperature. The mixture was then heated at about 78° for 2 hr. and cooled. Potassium hydroxide pellets were added until two layers formed. These were separated, and the aqueous layer was extracted with three 100-ml. portions of diethyl ether. The ether extracts were combined with the original organic material, dried over potassium carbonate, and concentrated. Distillation at 175 mm. led to removal of excess piperidine. The residue distilled at 100–112° (5.5 mm.), $n^{18}D$ 1.4799, and weighed 12.7 g. (74%); lit.[7] b.p. 140° (13 mm.), $n^{15.5}D$ 1.4820.

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The Gomberg-Bachmann Reaction with Benzene-*d*

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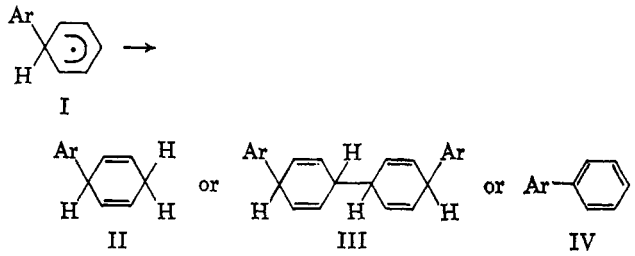
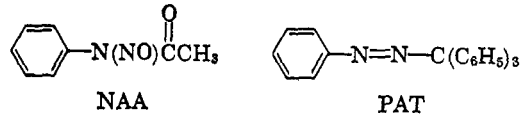
Previous work[2,3] has shown that free-radical arylation[4] of benzene with diaroyl peroxides involves arylcyclohexadienyl radicals (I) as intermediates. Among the criteria employed to demonstrate the intermediacy of these radicals has been isolation of their disproportionation and dimerization products[2] [dihydrobiaryls (II) and tetrahydroquateraryls (III)], an apparent



isotope effect in the formation of arylbenzene (IV) when benzene-*d* is the substrate,[3] and the appearance of dideuterated biaryls with the same starting material.[3] The apparent isotope effect is due to a discrimination between 1-deuterated 1-arylcyclohexadienyl radicals and undeuterated arylcyclohexadienyl radicals in regard to hydrogen abstraction (to give IV) *vs.* hydrogen acceptance or dimerization (to give II or III). Dideuterated biaryls result from dehydrogenation[5] of dideuterated dihydrobiaryls which arise in the disproportionation process when the substrate is benzene-*d*.

The failure of the above three criteria in the case of arylation with nitrosoacetanilide (NAA) and phenylazotriphenylmethane (PAT)[6] was originally interpreted



to indicate that free arylcyclohexadienyl radicals (I) are not intermediates in arylation with these reagents. Instead, the intervention of certain caged radicals was postulated.[6] Subsequently, however, it was pointed out[7–9] that the absence of disproportionation or dimerization products does not rule out the intervention of arylcyclohexadienyl radicals. Rather, this failure may be ascribed to the presence, in relatively high stationary-state concentrations, of radicals that can act as efficient hydrogen abstractors. With such radicals present, the arylcyclohexadienyl radicals (I) give hydrogen to yield IV before they have an opportunity to disproportionate or dimerize to give II or III. In the case of PAT,[7,8] the relatively stable hydrogen abstractor is the triphenylmethyl radical $Ph_3C\cdot$. With benzoyl peroxide as the radical source, there is no corresponding stable hydrogen abstractor (benzoate radicals being rather fleeting), and so dimerization and disproportionation become important side reactions to arylation.

It was less clear why there is little or no disproportionation or dimerization when the arylating reagent is NAA. Clearly, assuming a high stationary state concentration of acetate radicals as hydrogen abstractors is unreasonable in view of the known[10] instability of these radicals. Nevertheless, "cage effects" are not involved.[11]

The long-standing mystery of the NAA reaction has now been elegantly solved by Rüchardt and coworkers,[12,13] who have presented convincing evidence[13] that NAA is converted to a diazoanhydride, ArN=N—O—N=NAr, prior to arylation. The diazoanhydride then gives rise to Ar· (the arylating agent), nitrogen, and Ar—N=N—O·. The latter radical is rather stable and thus, like $Ph_3C\cdot$, accumulates in quite high stationary-state concentration and acts as an efficient scavenger for the arylcyclohexadienyl radicals I, preventing their dimerization and disproportionation and converting them, instead, to arylbenzene IV and ArN=N—OH. The latter then reacts

(1) The Radiation Laboratory is operated under contract with the Atomic Energy Commission. This is AEC Document No. COO-38-413.

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