[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEW HAMPSHIRE]

# MOLECULAR REARRANGEMENTS. VI.[1] THE REARRANGEMENT OF OXIMES ON REDUCTION WITH LITHIUM ALUMINUM HYDRIDE

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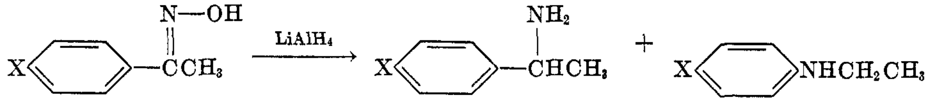
Reductions with lithium aluminum hydride have been characterized by the high degree of predictability of the products (1). In a few instances groups were anomalously reduced due to the structure of the compound treated with this reagent (1). Recently, however, three interesting molecular rearrangements have been reported to occur with lithium aluminum hydride indicating a new type of reaction with this reagent. Cram (2) has shown that the phenyl groups of the *p*-toluenesulfonic acid esters of either 2-phenyl-3-pentanol or 3-phenyl-2-pentanol undergo rearrangement by a Wagner- Meerwein reaction to form a mixture of 2- and 3-phenylpentane on treatment with lithium aluminum hydride. Cope (3) reported the formation of bicyclo[3.3.0]octane-1-methanol by a reductive rearrangement, resembling a Favorski rearrangement, of bicyclo[3.3.1]nonan-9-one. N-Ethyl- and N-propyl-aniline have been isolated in addition to the expected primary amines from the reduction of acetophenone and propiophenone oximes with lithium aluminum hydride (4a, b). This last rearrangement would appear to be related to the Beckmann rearrangement; however, it is not as general as the Beckmann rearrangement, for many oximes have been reduced without rearrangement with lithium aluminum hydride (5). Since only oximes of phenyl ketones had been found to undergo rearrangement, substituted acetophenone oximes seemed to be the most promising series of compounds to use for the study of this reaction. The results of the reduction of *para*-substituted acetophenone oximes with lithium aluminum hydride are contained in this report.



I II

Every acetophenone studied gave, in addition to the normal reduction product—the 1-(*p*-substitutedphenyl)-1-ethylamine (I), a significant yield of the product of rearrangement, *p*-substituted- N-ethylaniline (II); see Table I. The non-identity of the amines was established by refractive index and melting point of the hydrochloride, see Table II.

A comparison of the yields of the secondary amines (II) isolated from the reduction of the acetophenones, expressed as percentage rearrangement, with the Hammett's substitutent constant, *sigma*, (6) or with the "migratory aptitude" of

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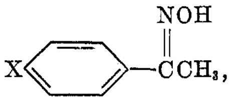
[2] Abstracted from the Thesis of H. J. Trosciániec presented to the Graduate School of the University of New Hampshire in partial fulfillment of the Degree of Master of Science, 1955.

TABLE I

PRODUCTS OF THE REDUCTION OF THE OXIMES, , WITH LITHIUM ALUMINUM HYDRIDE

| X | Oxime m.p., °C | Lit. m.p., °C. | Ref. | Amine (type) | Yield | | Obsv'd | | Lit. | | Ref. | Obsv'd $n_D^{26}$ | Lit. $n_D^{25}$ | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Crude % | Distilled % | b.p., °C. | press. mm. | b.p., °C. | press. mm. | | | | |
| $CH_3O$ | 85–87 | 86–87 | (8) | I | 16 | 4 | 100–101 | 9 | 126 | 20 | (9) | 1.5238 | 1.5280 | (9) |
| | | | | II | 76 | 59 | 120–122 | 9 | 135–140 | 20 | (10) | 1.5494 | 1.5444 | (10)[f] |
| $CH_3$ | 84–86 | 88 | (8) | I | 25 | 17 | 82–83 | 4 | 204–205 | Atm. | (9) | 1.5180 | | |
| | | | | II | 44 | 30 | 91–92 | 7 | 100 | 11 | (11) | 1.5410 | | |
| H | 58–59 | 60 | (8) | I | 50 | 30 | 67–68 | 9 | 77–78 | 16 | (12) | 1.5245 | | |
| | | | | II | 25 | 9 | 79–81 | 9 | 84 | 10 | (8) | 1.5500 | 1.5559 | (8)[f] |
| F | 74–76 | [a] | | I | 53 | 35 | 75–76 | 12 | [b] | | | 1.4988 | | |
| | | | | II | 24 | 8 | 93–94 | 12 | [c] | | | 1.5200 | | |
| Cl | 94–95 | 95 | (8) | I | 64 | 50 | 100–102 | 10 | 103–104 | 11 | (13) | 1.5390 | 1.5420 | (9) |
| | | | | II | 22 | 7 | 113–114 | 10 | 247–250 | Atm. | (11) | 1.5628 | | |
| Br | 127–129 | 128–129 | (8) | I | 49 | 35 | 118–119 | 11 | 116 | 10 | (9) | 1.5629 | 1.5691 | (9) |
| | | | | II | 12 | 5 | 131–132 | 10 | 143–147 | 20 | (14) | 1.5891 | | |
| I | 156–158 | [d] | | I[e] | | 14[e] | 75–76 | 14[e] | 77–78 | 16[e] | (12) | 1.5231[e] | | |
| | | | | II[e] | | 7[e] | 85–86 | 14[e] | 84 | 10[e] | (8) | 1.5500[e] | 1.5559[e] | (9)[f] |

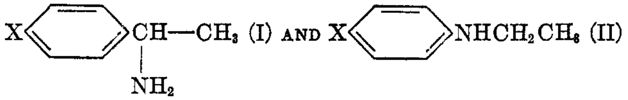
[a] *Anal.* Calc'd for $C_8H_8FNO$: N, 9.15. Found: N, 9.48. [b] Analyzed in the form of the carbonate, m.p. 93–94° (d). *Anal.* Calc'd for $C_9H_{10}FNO_2$: N, 7.65. Found: N, 8.36, 7.42. [c] *Anal.* Calc'd for $C_8H_{10}FN$: N, 10.06. Found: N, 9.73, 9.95. [d] *Anal.* Calc'd for $C_8H_8INO$: N, 5.37. Found: N, 5.66. [e] The only products isolated were (I) 1-phenyl-1-ethylamine, and (II) N-ethylaniline. The constants reported are for these compounds. [f] The refractive index of this compound was reported at 20°C.

the aromatic group in the pinacol rearrangement (7) indicates that the electron—releasing groups in the *para*-position of the acetophenone oxime facilitate the rearrangement. Thus this rearrangement appears to be comparable to the Beckmann or pinacol rearrangements. This similarity is noteworthy since both the Beckmann and pinacol rearrangements are usually accomplished by electrophilic reagents, whereas reactions with lithium aluminum hydride normally occur by attack of the nucleophilic hydride ion. It is apparent that some entity such as $AlH_3$, a weak acid, is important for the initiation of this rearrangement (2). See Table III.

The amines isolated from the reduction of *p*-iodoacetophenone oxime were the unsubstituted 1-phenyl-1-ethylamine and N-ethylaniline. Apparently, the reductive dehalogenation occurred before the reduction or rearrangement of the

TABLE II

DERIVATIVES OF AMINES



$X{-}C_6H_4{-}CH(NH_2){-}CH_3$ (I) AND $X{-}C_6H_4{-}NHCH_2CH_3$ (II)

| X | Amine | M.P., °C. | HCl Lit. M.P. °C. | Ref. | *p*-Toluenesulfonamide M.P., °C. | Lit. M.P., °C. | Ref. |
|---|---|---|---|---|---|---|---|
| $CH_3O$ | I | 158–160[a] | 159 | 15 | | | |
| | II | 150–152[a] | 153 | 16 | | | |
| $CH_3$ | I | 163–165[b] | 167–168 | 15 | 117–119 | | |
| | II | 158–160[b] | 162 | 16 | 69–70 | 71 | (11) |
| H[c] | I | 155–157 | 158 | 8 | | | |
| | II | 174–176 | 176 | 8 | | | |
| F | I | 192–193 | [d] | | 118–119 | [f] | |
| | II | 151–153 | [e] | | | | |
| Cl | I | 188–190 | 192–193 | 9 | 128–129 | [h] | |
| | II | 133–136 | [g] | | 100–102 | 102–104 | (11) |
| Br | I | 212–214 | 213–214 | 9 | | | |
| | II | 168–171 | [i] | | | | |

[a] A mixture of these two salts melted at 114–145°. [b] A mixture of these two salts melted at 112–140°. [c] These derivatives were also isolated from the amines from *p*-iodoacetophenone oxime. [d] *Anal.* Calc'd for $C_8H_{11}ClFN$: Cl, 20.19. Found: Cl, 20.26, 20.12. [e] *Anal.* Calc'd for $C_8H_{11}ClFN$: Cl, 20.19. Found: Cl, 20.01, 20.63. [f] *Anal.* Calc'd for $C_{15}H_{16}FNO_2S$: N, 4.78. Found: N, 4.61, 4.71. [g] *Anal.* Calc'd for $C_8H_{11}Cl_2N$: Cl, 18.46. Found: Cl, 18.15. [h] *Anal.* Calc'd for $C_{15}H_{16}ClNO_2S$: N, 4.53. Found: N, 4.62, 4.41. [i] *Anal.* Calc'd for $C_8H_{11}BrClN$: Cl, 14.98. Found: Cl, 14.93.

TABLE III

COMPARISON OF PERCENTAGE REARRANGEMENT WITH HAMMETT'S *sigma* CONSTANT AND WITH AROMATIC MIGRATORY APTITUDES

| *Para* Substituent | Percentage Rearrangement Crude | Distilled | Hammett's *Sigma* Constant (6) | Migratory Aptitude (7) |
|---|---|---|---|---|
| $CH_3O$ | 83 | 94 | −0.268 | 400 |
| $CH_3$ | 64 | 64 | −0.17 | 15.7 |
| H | 33 | 23 | 0.00 | 1 |
| F | 31 | 19 | .062 | |
| Cl | 26 | 12 | .227 | 0.7 |
| Br | 20 | 12.5 | .232 | .7 |

oximino group, for the yield of the secondary amine is much greater than would be expected by comparison with the other *p*-haloacetophenones (see Table I).

Thus the reduction of oximes of phenyl ketones with lithium aluminum hydride may be expected to occur with partial rearrangement to form a secondary amine.

Furthermore, the greater the electron release at the aromatic carbon to which the oximino group is attached the greater is the extent of the rearrangement.

## EXPERIMENTAL

*Reduction of the oximes.* A suspension of 4.2 g. (0.11 mole) of lithium aluminum hydride in 150 ml. of anhydrous ether was prepared by heating and stirring the mixture. After the lithium aluminum hydride was uniformly distributed, 0.02 mole of the oxime was added. The mixture was heated under reflux for 3 hours, cooled, and decomposed by addition of water. The insoluble precipitate was removed and washed well with ether. The ethereal filtrate and washings were extracted with 250 ml. of 10% hydrochloric acid, and any unreacted oxime was recovered from the ether. The hydrochloric acid solution was neutralized with a saturated sodium hydroxide solution and was extracted with 300 ml. of ether. The amines remaining after removal of the ether were separated by the procedure of Smith (4a). The amines were dissolved in 70 ml. of 0.5 *N* hydrochloric acid. The solution was neutralized to the end-point of Methyl Red with 20% sodium hydroxide solution and was extracted with 150 ml. of ether. The basicity of the solution was checked after each extraction. The ether extracts were dried, and the ether was removed to give the secondary amine (II).

The aqueous layer was neutralized with sodium hydroxide solution and was extracted with 150 ml. of ether. From this ether solution was obtained the primary amine (I).

## SUMMARY

Acetophenone oxime and six *para*-substituted-acetophenone oximes were reduced with lithium aluminum hydride. The products from normal reduction, 1-(*p*-substituted-phenyl)-1-ethylamine (I), and from reduction with rearrangement, *p*-substituted-N-ethylaniline (II), were isolated from every reaction. The yield of the product of reductive-rearrangement, II, was shown to increase with an increase in electron-releasing capacity of the *para*-substituent.

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