A portion of our tetra-*p*-tolylethylene was reduced to the corresponding ethane by treating a boiling solution of 0.35 g. of the ethylene in 10 cc. of amyl alcohol with 0.5 g. of sodium cut in small pieces. After ten minutes water was added and the product was taken up in benzene; concentration of the solution deposited the *s*-tetra-*p*-tolylethane in colorless prisms; m. p. 278–279°; yield, 95%. The ethane is little soluble in hot alcohol or in cold benzene; it is soluble in hot benzene.

Anal. Calcd. for $C_{30}H_{30}$: C, 92.3; H, 7.7. Found: C, 92.1; H, 7.8.

s-Tetra-*p*-tolylethane was synthesized by heating a mixture of 1.1 g. of di-*p*-tolylbromomethane and 0.05 g. of magnesium ribbon in 5 cc. of ether and 5 cc. of benzene for twenty hours; yield, 50%; m. p. 278–279°; the product so obtained was identical in all respects with the product produced by reduction of the ethylene.

Tetraphenylethyl Acetate, $(C_6H_5)_3CCH(OCOCH_3)C_6H_5$.—A mixture of 1.0 g. of *as*-tetraphenylethyl alcohol, 10 cc. of acetyl chloride and 5 cc. of benzene was refluxed for ten hours. The product obtained by evaporation of the solvents was recrystallized from a mixture of benzene and alcohol; colorless needles; m. p. 151°; yield, 1.11 g. (99%); Delacre[1] reported a m. p. of 131°. Tetraphenylethyl acetate is little soluble in cold alcohol or acetic acid; it is readily soluble in hot benzene and in hot acetic acid.

Anal. Calcd. for $C_{28}H_{24}O_2$: C, 85.7; H, 6.1. Found: C, 85.7; H, 6.3.

A 0.1-g. portion of tetraphenylethyl acetate was warmed for a few minutes with a mixture of 1 cc. of 40% potassium hydroxide and 2 cc. of alcohol; this treatment hydrolyzed the ester to acetic acid and tetraphenylethyl alcohol; the latter was then cleaved into triphenylmethane[1] and benzaldehyde. When the ester was heated with acetic acid and iodine for a few minutes, rearrangement to tetraphenylethylene took place.

Summary

as-Tetraphenylethyl alcohol is dehydrated and rearranged to tetraphenylethylene when it is heated with a solution of iodine in acetic acid. Five new tetraarylethanols have been synthesized and subjected to the retropinacolone rearrangement.

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The Alkyl Derivatives of the Mono Substituted Thiazolidones. I

BY F. B. DAINS AND FLOYD EBERLY

Some years ago Beckurts and Frerich[1] published a paper on the ethylation of the monoarylthiazolidones which were prepared by the action of potassium thiocyanate upon the chloracet derivatives of various monoarylamines. Several intermediate products were described, but the ones used in their investigation were regarded as $\overset{1}{S}\overset{2}{C}(\overset{3}{NH})\overset{4}{N}R\overset{5}{C}OCH_2$ 2-imino-3-aryl-4-thiazolidones. The reason given for this structure was that on hydrolysis 3-aryl-2,4-thiazolediones were formed.

Wheeler and Johnson[2] have shown in an exhaustive study that this

(1) Beckurts and Frerich, *Arch. Pharm.*, **253**, 233–65 (1915).
(2) Wheeler and Johnson, *Am. Chem. J.*, **28**, 121–128 (1902).

formula of Beckurts and Frerich represented a labile form which rearranged to the stable 2-arylamino(or imino)-thiazolidone. This on hydrolysis gave both the unsubstituted 2,4-thiazoledione and the 3-aryl diketo product obtained by Beckurts and Frerich. They assumed[3] that the two compounds resulted from the hydrolysis of an intermediate aryl thiohydantoic acid, the ring again closing after the loss of aniline or ammonia.

We have found that a benzal group at 5 stabilized the ring and that on hydrolysis a 5-benzal-2,4-thiazoledione resulted and not a 3-aryl diketo compound which would be necessitated by the formula of Beckurts and Frerich.

These authors by the ethylation of the sodium salts of the thiazolidones obtained mono ethyl derivatives which were assumed to be 2-ethylimino-3-aryl-4-thiazolidones, $\underline{SC(NC_2H_5)NRCOCH_2}$. Wheeler and Johnson[4] had made the observation that the stable phenylthiazolidone in alkaline solution with benzyl chloride gave 2-phenyl-2-benzylaminothiazolidone, a fact not in harmony with the above assumption. The following experimental work has confirmed the Wheeler–Johnson formula for the stable hydantoins (as 2-aryl derivatives). It has also been shown that alkylation of the monoarylthiazolidones gave two isomers: one the 2-aryl-2-alkyl compound and the other a 2-aryl-3-alkylthiazolidone which corresponded to the Beckurts–Frerich idea but with the aryl and alkyl groups reversed in position.

Experimental

2-*p*-Bromophenylaminothiazolidone.—*p*-Bromoaniline (1 mole) was dissolved in acetone (300 cc.) and pyridine (96 g.) in a flask fitted with an air condenser and cooled in ice water. To this mixture was added slowly chloroacetyl chloride (135 g.) with constant agitation. After standing for an hour, water was added and the ω-chloro-*p*-bromoacetanilide was filtered, washed and dried. Crystallization from alcohol gave a pure product (m. p. 178°).[5] The chloroacetyl compound (135 g.) and potassium thiocyanate (60 g.) were dissolved in alcohol (300 cc.) and refluxed for twenty hours. The yield of crude thiazolidone was nearly the theoretical. From glacial acetic acid, the pale yellow needles melted at 224°.

Anal. Calcd. for $C_9H_7BrN_2OS$: N, 10.35. Found: N, 9.96.

The 5-benzal derivative did not melt at 310° (N, 7.80. Found: N, 7.57). The thiazolidone (m. p. 224°) was soluble in hot 5% sodium hydroxide and on cooling the yellow sodium salt crystallized out.

Ethylation of the Sodium Salt.—The dry salt was dissolved in alcohol with a slight molar excess of ethyl iodide and refluxed for ten hours. After removal of the alcohol and excess of ethyl iodide with steam, the residue was dissolved in ether. The ethereal solution was extracted repeatedly with hydrochloric acid (10%). On neutralizing the acid solution there was obtained 2-ethyl-2-*p*-bromophenylamino-4-thiazolidone; the white needles from ligroin melted at 121°.

Anal. Calcd. for $C_{11}H_{11}BrN_2OS$: N, 9.36. Found: N, 9.42.

(3) Ref. 2, p. 124.

(4) Ref. 2, p. 146.

(5) Beckurts and Frerich, *Arch. Pharm.*, **241**, 212 (1903). The above seems to give better yields than the methods recorded in the literature for the preparation of these chloroacet derivatives.

Proof of Constitution.—The compound (m. p. 121°) was hydrolyzed by boiling with sulfuric acid (50%) for several hours. The mixture was made alkaline with sodium hydroxide and distilled with steam. Ammonia was evolved and an oil, ethyl-*p*-bromoaniline, appeared in the distillate. This oil with phenyl isocyanate gave α-ethyl-α-*p*-bromophenyl-β-phenyl urea; the rhombic crystals from alcohol melted at 108°.

Anal. Calcd. for $C_{15}H_{15}BrN_2O$: N, 8.77. Found: N, 8.62.

For comparison ethyl-*p*-bromophenylamine was made by the action of diethyl sulfate on powdered *p*-bromoaniline at 50°. The fraction of b. p. 146–152° (25 mm.) gave with phenyl isocyanate the same urea (m. p. 108°). Also the same benzoyl-*p*-bromoanilide, m. p. 88°, was obtained from both amines.

Anal. Calcd. for $C_{15}H_{14}BrNO$: N, 4.60. Found: N, 4.66.

***p*-Bromophenyl Ethyl Cyanamide,** $BrC_6H_4N(CN)C_2H_5$.—The residue in the steam distillation flask contained a small amount of the above compound; colorless plates from alcohol which melted at 78°.

Anal. Calcd. for $C_9H_9BrN_2$: N, 12.44. Found: N, 12.42.

It was identical with a synthetic preparation made from ethyl-*p*-bromophenylamine, bromine and potassium cyanide. This cyanamide was also obtained easily by the action of sodium hydroxide (20%) upon the ethyl thiazolidone.

The ethyl thiazolidone (m. p. 121°) condensed with benzaldehyde in hot alcohol solution using piperidine or a few drops of sodium hydroxide and gave a 5-benzal derivative (m. p. 225°).

Anal. Calcd. for $C_{18}H_{15}BrN_2OS$: N, 7.23. Found: N, 7.21.

5-Benzal-2,4-thiazoledione (m. p. 243°).[6]—This was obtained in small amounts by the direct hydrolysis of the 5-benzal-2-aryl-2-alkyl compounds, but was also prepared in an interesting way by the action of an excess of sodium hydroxide (40%) on a mixture in hot alcohol of the ethyl *p*-bromophenylthiazolidone and benzaldehyde and precipitating the product with dilute acid.

2-*p*-Bromophenylimino-3-ethyl-4-thiazolidone, $\overline{SC(NC_6H_4Br)NC_2H_5COCH_2}$.—This was isolated from the original ether solution of the ethylation product, remaining in solution after extraction with dilute acid. It formed about one-sixth of the total product, the needles from alcohol melting at 91°.

Anal. Calcd. for $C_{11}H_{11}BrN_2OS$: N, 9.36. Found: N, 9.44.

The same thiazolidone (m. p. 91°) was made by the action of chloroacetyl chloride upon α-ethyl-β-*p*-bromophenyl thiourea in acetone and pyridine solution,[7] thus showing the separate attachment of the ethyl and phenyl groups (N, found, 9.22).

Hydrolysis of this thiazolidone with sulfuric acid gave *p*-bromoaniline and ethylamine, identified by the carbylamine reaction and analysis of its hydrochloride.

2-*p*-Bromophenyl-3-ethyl-5-benzal-4-thiazolidone was made from benzaldehyde and the 91° product from both sources.

Anal. Calcd. for $C_{18}H_{15}BrN_2OS$: N, 7.23. Found: N, 7.21.

On hydrolysis in acid solution it gave *p*-bromoaniline and 3-ethyl-5-benzal-2,4-thiazoledione, melting at 95.5°.

Anal. Calcd. for $C_{12}H_{11}NO_2S$: N, 6.00. Found: N, 5.97.

The formation of the 3-ethyl derivative gives added proof of the structure of the isomeric thiazolidone. Its synthesis from α-ethyl-β-aryl thiourea shows that these thioureas tend to react with the acid chloride in the enol form $C_2H_5NHC(SH)NR$, thus yielding a 3-alkyl-2-aryl-thiazolidone, a fact that has been noted in other cases.

(6) Andreasch, *Monatsh.*, **10**, 75 (1889).

(7) Hunter, *J. Chem. Soc.*, **129**, 2955 (1926); Dains, Brewster and Olander, "Organic Syntheses," Vol. VI, p. 72.

The Methylation of the Sodium Salt of *p*-Bromophenylaminothiazolidone.—The same results were obtained both from the use of methyl iodide and of methyl sulfate. The reaction product on extraction with ether left a residue which was soluble in dilute hydrochloric acid and proved to be the 2-methyl-2-*p*-bromophenylaminothiazolidone, prisms from alcohol (m. p. 197°).

Hydrolysis with sulfuric acid (50%) gave ammonia and methyl-*p*-bromophenylamine. This was identified by its reaction with phenyl isocyanate, yielding α-methyl-α-bromophenyl-β-phenyl urea (m. p. 137°) and by the formation of a benzoyl derivative (m. p. 77°). When the 5-benzal compound (m. p. 256° was hydrolyzed it gave the 5-benzal-2,4-thiazoledione (m. p. 242°).

The ether extract from the original methylation product insoluble in dilute acid consisted of the isomeric 2-*p*-bromophenylimino-3-methyl-thiazolidone (m. p. 111°). On hydrolysis methylamine and *p*-bromoaniline were isolated, this proving its constitution. The relative position of the groups was indicated by the hydrolysis of the 5-benzal compound (m. p. 166°) which yielded *p*-bromoaniline and 3-methyl-5-benzal-2,4-thiazoledione (m. p. 133°).

2-Benzyl-2-*p*-bromophenylaminothiazolidone.—This was the only product isolated from the action of benzyl chloride on the sodium salt. It is only slightly soluble in dilute acid. Acid hydrolysis gave ammonia and benzyl-*p*-bromoaniline (m. p. 55°). This was confirmed by a synthetic specimen made from benzyl chloride and *p*-bromoaniline.[8] The fraction of b. p. 237–242° (33 mm.) solidified and melted at 55°.

2-Dibromo-*p*-tolylthiazolidone from 2,6-Dibromo-*p*-toluidine.—This was made by the usual method of refluxing the chloracet derivative with potassium thiocyanate. Methylation of the sodium salt gave nearly equal amounts of the two isomers. The acid soluble 2-methyl-2-dibromo-tolylaminothiazolidone melted at 194°, while the 3-methyl isomer (m. p. 132°) gave a benzal derivative which on hydrolysis yielded the dibromotoluidine, thus proving the structure.

PROPERTIES AND ANALYSES

Thiazolidones	Formula	M. p., °C.	Nitrogen, % Calcd.	Found
2-Methyl-2-*p*-bromophenyl	$C_{10}H_9BrN_2OS$	197	9.82	9.98
5-Benzal-2-methyl-2-*p*-bromophenyl	$C_{17}H_{13}BrN_2OS$	256	7.50	7.52
2-*p*-Bromophenyl-3-methyl	$C_{10}H_9BrN_2OS$	111	9.82	9.88
5-Benzal-2-*p*-bromophenyl-3-methyl	$C_{17}H_{13}BrN_2OS$	166	7.50	7.59
2-Benzyl-2-*p*-bromophenyl	$C_{16}H_{13}BrN_2OS$	153	7.75	7.88
2-Benzyl-2-*p*-chlorophenyl[a]	$C_{16}H_{13}ClN_2OS$	129	8.84	8.77
5-Benzal-2-benzyl-2-*p*-bromophenyl	$C_{23}H_{17}BrN_2OS$	192	6.23	6.38
2-Dibromo-*p*-tolyl	$C_{10}H_8Br_2N_2OS$	250	7.69	7.30
2-Methyl-2-dibromotolyl	$C_{11}H_{10}Br_2N_2OS$	194	7.40	7.68
3-Methyl-2-dibromotolyl	$C_{11}H_{10}Br_2N_2OS$	132	7.40	7.02
2-Ethyl-2-*p*-bromophenyl-5-*o*-chlorobenzal	$C_{18}H_{14}ClBrN_2OS$	192	6.64	6.98
3-Methyl-2,4-diketo-5-benzal	$C_{11}H_9NO_2S$	133	6.39	6.42
5-*o*-Chlorobenzal-diketo[b]	$C_{10}H_6ClNO_2S$	172	5.84	5.86
Other Derivatives				
α-Methyl-α-*p*-bromophenyl-β-phenyl urea	$C_{14}H_{12}BrNO$	77	4.96	4.54
Benzyl-*p*-bromoaniline	$C_{13}H_{12}BrN$	55	5.34	5.21
ω-Chloracet-dibromo-*p*-toluide	$C_9H_8Br_2ClNO$	184	4.09	4.06

[a] This *p*-chlorophenyl thiazolidone gave only the 2-benzyl isomer. [b] From the hydrolysis of *o*-chlorobenzal derivative of the 2-ethyl-2-*p*-bromophenyl thiazolidone.

(8) "Organic Syntheses," Vol. VIII, p. 38.

Summary

The aryl thiazolidones studied correspond to the 2-arylamino or stable forms of Wheeler and Johnson.

Their sodium salts with methyl or ethyl iodide yield a mixture of 2-alkyl-2-aryl and of 3-alkyl-2-aryl thiazolidones. With benzyl chloride only the 2-benzyl derivative has been found.

These results have failed to confirm the formulation of Beckurts and Frerich, who assumed that the products they obtained were 2-alkylimino-3-aryl thiazolidones. Further unpublished investigations in this Laboratory support our experimental results.

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The Catalytic Hydrogenation of the Halogenomorphides: Dihydrodesoxymorphine-D[1]

BY LYNDON F. SMALL, KECHEE C. YUEN AND LOUIS K. EILERS

In a previous paper from this Laboratory[2] it was shown that catalytic hydrogenation of the halogenocodides yielded, according to the conditions, varying amounts of three hydrogenated desoxycodeine derivatives. By empirical selection of the proper catalyst and solvent, it was possible to direct the hydrogenation in such a way that the non-phenolic dihydrodesoxycodeine-D (IV) was the principal product obtained from any of the four known halogenocodides. Dihydrodesoxycodeine-D,[3] and its unsaturated analog, desoxycodeine-C (II),[4] in both of which the 4,5-ether bridge is still intact, are of particular interest pharmacologically, since they differ structurally from certain codeine derivatives (dihydrocodeine and pseudocodeine, respectively) only in having a hydrogen atom in place of the alcoholic hydroxyl of the codeine series. The demethylated analog of desoxycodeine-C, namely, desoxymorphine-C (I), which may be regarded as a derivative of γ-isomorphine, has already been described,[5] and has been found extraordinarily active in the animal body. With the view of preparing a dihydrodesoxymorphine of the dihydrodesoxycodeine-D type, corresponding in fundamental structure to dihydromorphine (Paramorfan), the catalytic hydrogenation of the halogenomorphides has been investigated.

(1) This investigation was supported by a grant from the Committee on Drug Addiction of the National Research Council from funds provided by the Bureau of Social Hygiene, Inc., and the Rockefeller Foundation.

(2) Mosettig, Cohen and Small, THIS JOURNAL, **54**, 793 (1932).

(3) Small and Cohen, *ibid.*, **53**, 2227 (1931).

(4) Small and Cohen, *ibid.*, **53**, 2214 (1931).

(5) Small and Morris, *ibid.*, **55**, 2874 (1933).