described by the present authors.[14] The *d*-arabinose, prepared in this Laboratory by the method of Hockett and Hudson,[15] showed $[\alpha]^{20}D$ −103.4°; the *l*-arabinose, from the Difco Laboratories in Detroit, after one recrystallization, rotated +104.2° in water (*c*, 6). The other sugars were either high grade commercial products or prepared by other workers in this Laboratory. All sugar solutions were made up to contain 1.20 mg. of anhydrous substance in each 5 cc. of solution.

The Alkaline Ferricyanide Reagent.—The procedure of Hagedorn and Jensen[16] as modified by Hanes[17] was used, except that the oxidizing solution contained 6.60 g. instead of 8.25 g. of potassium ferricyanide per liter; thus 5 cc. of this solution was equivalent to 5 cc. of the alkaline copper solutions, each requiring about 20 cc. of the same 0.005 *N* thiosulfate solution in the blank determinations.

The Alkaline Copper Reagents.—According to the latest procedure of Shaffer and Somogyi,[6] four solutions were prepared, the only variation being in the use of an equivalent amount of the sodium tartrates instead of the sodium potassium tartrate (Rochelle salt) recommended. Thus, 3.32 g. of *d*-tartaric acid (or 3.32 g. of the *l*-acid, or 3.72 g. of the *meso* or racemic acid monohydrates) was dissolved in 50 cc. of water, and neutralized with *N* sodium hydroxide, with phenol red as indicator. Then were added in succession 6.25 g. of anhydrous sodium carbonate, 1.875 g. of copper sulfate pentahydrate in 20 cc. of water, 5.00 g. of sodium bicarbonate, 0.25 g. of potassium iodide and 50 cc. of standard potassium iodate solution, 0.1 *N* as to iodine. The mixture was diluted exactly to 250 cc., and allowed to stand for several days before filtering through washed and dried filter paper into a Pyrex flask. This reagent should be the exact equivalent of the "Shaffer–Somogyi Copper Iodometric Reagent 50 with 1 g. KI;" 5 cc. of it required about 20 cc. of 0.005 *N* thiosulfate in a blank determination. The preparation and standardization of the solutions, and the oxidations of the sugars, were carried out as directed, observing all the precautions noted by the original writers. The solutions were kept, and the titrations performed, in a room equipped with a white light and kept constant at 20°.

(14) Richtmyer and Hudson, ref. 2, and THIS JOURNAL, **58**, 2534 (1936).

(15) Hockett and Hudson, *ibid.*, **56**, 1632 (1934).

(16) Hagedorn and Jensen, *Biochem. Z.*, **135**, 46 (1923).

(17) Hanes, *Biochem. J.*, **23**, 99 (1929).

Summary

1. A study of the oxidation of the *d*- and *l*-forms of altrose and of arabinose by an alkaline ferricyanide reagent and by four modifications of an alkaline copper reagent containing the *d*-, *l*-, racemic and *meso* forms of tartaric acid, respectively, has been made.

2. The reagents which are optically inactive show no difference in their relative oxidizing power on the *d*- and *l*-forms of the sugars.

3. The reagents which are optically active oxidize the *d*- and *l*-forms of the sugars asymmetrically. Striking relationships have been noted in the four systems composed of the *d*- and *l*-sugars with the *d*- and *l*-reagents. The results are in full accord with the classical theories of stereochemistry.

4. The behavior of twelve other sugars toward the *d*-, *l*- and racemic copper reagents has been studied.

5. The practical adaptation of this asymmetric oxidation for the identification of sugars has been suggested.

WASHINGTON, D. C. RECEIVED OCTOBER 19, 1936

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KANSAS]

On the Formation and Reactions of the Substituted Thiazolidones. IV

BY FLOYD A. EBERLY AND F. B. DAINS

Previous papers from this Laboratory[1] have shown that the alkylation of the 2-arylthiazolidones gave both the 2-aryl-2-alkyl and the 2-aryl-3-alkyl derivatives. This paper is a study of the influence of allyl groups, of acyl groups and of phenyl and diphenylchloroacetyl chlorides in the formation and properties of such thiazolidones. Thus from mono-allylthiourea was obtained the 3-allyliminothiazolidone (the unstable form of Wheeler and Johnson) which did not rearrange; while allylphenylthiourea formed a thiazolidone in which the allyl group assumed position 2 with the phenyl at 3. Allyl iodide and the sodium salt of monophenyl thiazolidone gave the two remaining isomers of phenylallylthiazolidone.

The symmetrical benzoyl and carbethoxyphenylthiourea yielded thiazolidones with the acyl radical at 2. Dixon had erroneously assigned the reverse formula to his carbethoxyphenylthiazolidone.

Our work also indicated that the stable form of phenyl-5-phenylthiazolidone is the 2-phenyl isomer and not the 3-phenyl as was suggested by Wheeler and Johnson since it gave alkylation

(1) Eberly and Dains, THIS JOURNAL, **55**, 3859 (1933); Davis and Dains, *ibid.*, **57**, 2627 (1935); Long and Dains, *C. A.*, **28**, 2356 (1934); *Kan. Acad. Sci.*, **16**, 119 (1933).

products with the phenyl group at 2 and the alkyl radical entering at either 2 or 3.

The 2-arylthiazolidone from diphenylchloroacetyl chloride was obtained by the action of aniline upon thiocyanodiphenylchloroacetic ester, and not from the acid chloride and phenyl thiourea. The isomeric 2-thio-3-phenyl-5-diphenyl-4-imidazolone unexpectedly resulted from the action of ammonium thiocyanate upon diphenylchloroacetanilide.

Symmetrical phenylmethylthiourea and diphenylchloroacetyl chloride gave the two possible isomeric thiazolidones, the only case noted thus far.

Experimental

1. 2-Imino-3-Allyl-4-Thiazolidone HCl I, $\overline{SC(NH)NC_3H_5COCH_2}\cdot HCl$.

Allyl thiourea and chloroacetic acid on warming, either in water or in alcohol solution, gave an oil, the above labile form of Wheeler and Johnson, which is very easily hydrolyzed to the 2,4-diketo compound II with loss of ammonia. Benzaldehyde condensed with II under the influence of alkali or piperidine yielding 5-benzal-3-allyl-2,4-thiazoledione III, colorless needles melting at 88°. The constitution of III was shown as follows: 2,3-diallyl-thiazolidone, an oil at −10°, prepared from chloroacetyl chloride and diallyl thiourea in acetone and pyridine solution, gave a 5-benzal derivative V, m. p. 53°, which on hydrolysis with hot 50% sulfuric acid yielded allylamine and the diketo compound III.

N-Phenyl-N'-Allyl Thiourea and Chloroacetyl Chloride.—These compounds were refluxed in acetone solution with two moles of pyridine for thirty minutes. The 2-allyl-3-phenyl-4-thiazolidone VI melted at 151° and was soluble in dilute hydrochloric acid. In the majority of cases previously the alkyl group has been found at position 3 and the aryl group at 2. The ring was easily ruptured with alkali but heating with benzaldehyde, sodium acetate and acetic anhydride gave a 5-benzal compound VII (m. p. 141°).

Heating VII with 50% sulfuric acid at 140° gave 5-benzal-3-phenyl-2,4-thiazoledione VIII (m. p. 208°),[2] thus proving the structure.

Further evidence was obtained by the synthesis of the two possible isomers. When the sodium salt of 2-phenylthiazolidone was treated with allyl iodide in absolute alcohol solution, two compounds were isolated: (A) 2-phenyl-2-allylaminothiazolidone IX (95% yield), soluble in dilute acid and melting at 92°; and (B) 2-phenylimino-3-allyl-4-thiazolidone X (5% yield), an oil insoluble in acid which gave a 5-benzal derivative XI (m. p. 106.5°). Hydrolysis of XI with acid yielded the diketo compound III and aniline. The isomeric benzal derivative XII melted at 165°.

2. The Benzoyl and Carbethoxy Thiazolidones.—In these cases it is noteworthy that ring closure occurred with the acyl group at position 2.

(2) Andreasch, *Monatsh.*, **39**, 419 (1918).

2-Benzoylimino-3-*p*-bromophenyl-4-thiazolidone XIII, $\overline{SC(NCOC_6H_5)NC_6H_4BrCOCH_2}$, m. p. 213°, was made by heating N-benzoyl-N'-*p*-bromophenylthiourea[3] in acetone solution with chloroacetyl chloride and two moles of pyridine.

Alkaline Hydrolysis.—The compound dissolved in dilute alkali on boiling due to the formation of a thiohydantoic acid, but on continued heating there was deposited N-benzoyl-N'-*p*-bromophenyl urea XIV which melted at 233–234° with decomposition.

Acid Hydrolysis.—The benzoyl compound XIII was treated with boiling concentrated hydrochloric acid for three hours. Benzoic acid and ammonia were split off with traces of *p*-bromoaniline. The residue (m. p. 163°) gave figures on analysis corresponding to 3-*p*-bromophenyl-2,4-thiazoledione, XV. The 5-benzal derivative XVI crystallized from dioxane in needles melting at 253°. Hydrolysis with 60% sulfuric acid at 160° gave 5-benzal-3-*p*-bromophenyl-2,4-thiazoledione XVII (m. p. 247°).

2-Carbethoxy-3-phenyl-4-thiazolidone, XVIII, is best prepared by heating phenylthioallophanic ester with chloroacetyl chloride and pyridine in benzene solution.[4] The plates from dioxane decomposed slowly above 230° and melted completely at 256°. Dixon had formulated it as a 2-phenylimino-3-carbethoxy compound and stated that on hydrolysis it gave phenyl "dioxy thiazole," $\underline{SC(NC_6H_5)OCOCH_2}$.

Alkaline hydrolysis disrupted the ring completely but acid treatment gave the known 3-phenyl-2,4-thiazoledione (m. p. 146°), identical with a synthetic preparation. Additional evidence for our structure was afforded by the hydrolysis of its benzal derivative XIX (m. p. 225°), which gave the known 5-benzal-3-phenylthiazoledione, VIII.

Heating the carbethoxy compound XVIII with aniline at 150° or at 180–200° gave only diphenyl urea.

3. Derivatives of 5-Phenyl Thiazolidones

2-Phenylimino-5-phenyl-4-thiazolidone, XX.[5]—Wheeler and Johnson had prepared a diphenylthiazolidone (m. p. 185–186°), by the action of phenylchloroacetic ester on phenylthiourea, to which they assigned a 2-imino-3-phenyl structure since it gave a 3-phenyl-2,4-diketo compound (m. p. 173°) on hydrolysis. This work was repeated and the thiazolidone (m. p. 185°), XX, hydrolyzed by heating with 40% sulfuric acid at 140° for four hours. The acid solution contained both aniline and ammonia while from the solid residue were isolated two compounds; one, soluble in dilute alkali and in cold alcohol, proved to be 5-phenyl-2,4-thiazoledione XXI (m. p. 130°), obtained also by the hydrolysis of 5-phenylthiazolidone (m. p. 233–234°); the other compound was Wheeler's product (m. p. 173°), 3,5-diphenyl-2,4-thiazoledione, XXII. These results are due to the formation of the thiohydantoic acid, loss of either ammonia or aniline and subsequent ring closure. Approximately one part of XXI and two parts of XXII were found.

The original compound XX has the phenyl group at position 2. This was shown by the fact that its sodium salt

(3) Douglass, THIS JOURNAL, **56**, 719 (1934).

(4) Dixon and Kennedy, *J. Chem. Soc.*, **117**, 74 (1920).

(5) Wheeler, *Am. Chem. J.*, **26**, 353 (1901); Wheeler and Johnson THIS JOURNAL, **24**, 690 (1902).

No.	Thiazolidone	Formula	M. p., °C.	% N Calcd.	% N Found
I	2-Imino-3-allyl·HCl	$C_6H_5N_2OSHCl$	176	14.58	14.58
II	3-Allyl-2,4-diketo	$C_6H_7NO_2S$	Oil		
III	5-Benzal-3-allyl-2,4-diketo	$C_{13}H_{11}N_2OS$	88	5.71	5.76
IV	2,3-Diallyl	$C_6H_{12}ON_2S$	Oil		
V	2,3-Diallyl-5-benzal	$C_{16}H_{12}N_2OS$	53	9.86	9.80
VI	2-Allyl-3-phenyl	$C_{12}H_{12}N_2OS$	151	12.07	11.85
VII	2-Allyl-3-phenyl-5-benzal	$C_{19}H_{16}N_2OS$	141	8.75	8.71
VIII	3-Phenyl-5-benzal-2,4-diketo	$C_{16}H_{11}NO_2S$	208	4.98	4.92
IX	2-Phenyl-2-allyl	$C_{12}H_{12}N_2OS$	92	12.07	11.89
X	2-Phenyl-3-allyl	$C_{12}H_{12}N_2OS$	Oil		
XI	2-Phenyl-3-allyl-5-benzal	$C_{19}H_{16}N_2OS$	106.5	8.75	8.56
XII	2-Phenyl-2-allyl-5-benzal	$C_{19}H_{16}N_2OS$	165	8.75	8.53
XIII	2-Benzoyl-3-*p*-bromophenyl	$C_{16}H_{11}BrN_2O_2S$	213	7.47	7.40
XIV	N-Benzoyl-N′-*p*-bromophenyl urea	$C_{14}H_{11}BrN_2O_2$	233–234	8.78	8.78
XV	3-*p*-Bromophenyl-2,4-diketo	$C_9H_6BrN_2O_2S$	163	5.15	5.28
XVI	2-Benzoyl-3-*p*-bromophenyl-5-benzal	$C_{23}H_{15}BrN_2O_2S$	253	6.05	6.01
XVII	3-*p*-Bromophenyl-5-benzal-2,4-diketo	$C_{16}H_{10}BrNO_2S$	247	3.89	3.84
XVIII	2-Carbethoxy-3-phenyl-	$C_{12}H_{12}N_2OS$	256	10.61	10.83
XIX	2-Carbethoxy-3-phenyl-5-benzal	$C_{19}H_{16}N_2O_3S$	225	7.95	7.95
XX	2-5-Diphenyl	$C_{15}H_{12}N_2OS$	185	See Wheeler and Johnson	
XXI	5-Phenyl-2,4-diketo	$C_9H_7NO_2S$	130	7.25	7.34
XXII	3,5-Diphenyl-2,4-diketo	$C_{15}H_{11}N_2OS$	173	5.17	5.19
XXIII	2-Phenyl methyl-5-phenyl	$C_{16}H_{14}N_2OS$	144	9.93	9.71
XXIV	2-Thio-3-phenyl-5-diphenyl-4-imidazolone	$C_{21}H_{16}N_2OS$	254	8.14	8.02
XXV	3-Phenyl-5-diphenyl-2,4-imidazoledione	$C_{21}H_{16}N_2O_2$	203.5	8.54	8.26
XXVI	2-Methyl mercapto-3-phenyl-5-diphenyl-4-imidazolone	$C_{22}H_{18}N_2OS$	143	7.82	7.57
XXVII	2-Phenyl-5-diphenyl-4-thiazolidone	$C_{21}H_{16}N_2OS$	253	8.14	8.09
XXVIII	2-Methyl-phenyl-5-diphenyl	$C_{22}H_{18}N_2OS$	191	7.82	7.87
XXIX	2-Phenyl-3-methyl-5-diphenyl	$C_{22}H_{18}N_2OS$	134	7.82	7.88
XXX	3-Methyl-5-diphenyl-2,4-diketo	$C_{16}H_{13}NO_2S$	102	4.95	4.80
XXXI	2-Methyl-3-phenyl-5-diphenyl	$C_{22}H_{18}N_2OS$	119	7.82	7.77
XXXII	3-Phenyl-5-diphenyl-2,4-diketo	$C_{21}H_{16}N_2OS$	150	9.27	9.25

on methylation gave a 2-phenyl-2-methylaminothiazolidone XXIII (m. p. 144°), soluble in dilute acid and identical with the product from phenylbromoacetic ester and unsymmetrical phenylmethylthiourea.

4. Derivatives of Diphenyl Chloroacetyl Chloride[6]

The acid chloride failed to give a thiazolidone with phenylthiourea by the usual methods. However, 2-thio-3-phenyl-5-diphenyl-4-imidazolone, $HNCSN(C_6H_5)COC(C_6H_5)_2$, XXIV, was the unexpected product resulting when diphenylchloroacetanilide[7] was refluxed one hour in dry acetone solution with ammonium thiocyanate, and its formation would seem to be due to the rearrangement of the —SCN grouping in the initial product to —NCS and subsequent ring closure. It was soluble in dilute alkali and crystallized from alcohol in thick needles melting at 254°. It was desulfurized by heating with concentrated nitric acid for thirty minutes, yielding 3-phenyl-5-diphenyl-2,4-imidazoledione, XXV, prisms from alcohol (m. p. 203.5°).

The structure of the 2,4-imidazoledione was proved by its synthesis from monophenyl urea and benzilic acid[8] which were fused together one hour at 180–190°.

2-Methylmercapto-3-phenyl-5-diphenyl-4-imidazolone, XXVI.—Methylation of the 2-thioimidazolone, either alone or with the aid of potassium hydroxide, gave the thio ether, soluble in acid and melting at 143°. Hydrolysis with 50% sulfuric acid at 150° yielded XXV.

2-Phenylimino-5-diphenyl-4-thiazolidone, XXVII (m. p. 253°).—This compound, prepared according to the method of Wheeler and Johnson,[9] is an isomer of XXIV but mixed melting point and properties showed that they are not identical. This compound behaved as a normal thiazolidone, the sodium salt yielding: (a) 2-methylphenylamino-5-diphenyl-4-thiazolidone XXVIII (m. p. 191°) and (b) 2-phenylimino-3-methyl-5-diphenyl-4-thiazolidone XXIX (m. p. 134°).

The constitution of XXVIII was shown by its synthesis from unsymmetrical methylphenylthiourea and that of XXIX proved by its synthesis from symmetrical methylphenylthiourea and to the fact that it hydrolyzes to give 3-methyl-5-diphenyl-2-4-thiazoledione, XXX (m. p. 102°). The synthesis of XXIX from methylphenylthiourea and diphenylchloroacetyl chloride in benzene solution with two moles of pyridine resulted in the formation in 25% yield of the 2-phenyl-3-methyl compound, insoluble in dilute acid, while the isomeric 2-methyl-3-phenyl derivative, XXXI (m. p. 119°), soluble in dilute acid, was formed in 75% yield. XXXI on hydrolysis gave methylamine and 3-phenyl-5-diphenyl-2,4-thiazoledione, XXXII (m. p. 150°).[10] The isolation of the two isomers is of

(6) Bickel, *Ber.*, **38**, 1735 (1905); Staudinger, *Ann.*, **356**, 73 (1907).

(7) Klinger, *Ann.*, **389**, 253 (1912).

(8) Method of Biltz, *Ber.*, **41**, 1379 (1908).

(9) Wheeler and Johnson, THIS JOURNAL, **24**, 690 (1902).

(10) Becker and Bistrzyki, *Helv. Chim. Acta*, **2**, 114 (1919).

special interest since in the previous cases, doubtless due to the selective action, only one compound has been isolated from such reactions.

Summary

A study has been made of allyl and acyl substituted thiazolidones and of the use of mono- and diphenyl halogen acetyl chlorides and esters in the synthesis of thiazolidones and in one case of an imidazolone.

The diphenylchloroacetyl chloride gave with methylphenyl thiourea the two possible thiazolidones. It was noted also that the two phenyl groups at position 5 stabilize the thiazolidone ring toward hydrolysis as does the benzal group at the same position.

LAWRENCE, KAN. RECEIVED SEPTEMBER 30, 1936

[CONTRIBUTION FROM THE WALKER CHEMICAL LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE]

Ethyl Imidocyclopropanecarboxylate Hydrochlorides[1]

BY JOHN B. CLOKE, EDWIN C. KNOWLES AND RAYMOND J. ANDERSON

Preparation.—The imido ester salts were prepared by the general method of Pinner.[2] Thus, the ethyl imidocyclopropanecarboxylate hydrochloride (I) was obtained by the action of dry hydrogen chloride on an ether solution of ethanol and cyclopropyl cyanide as follows

$$\underset{\llcorner\!\!\lrcorner}{CH_2CH_2CHCN} + HOC_2H_5 + HCl \longrightarrow \underset{\llcorner\!\!\lrcorner}{CH_2CH_2CH}\text{—}C(=NH_2Cl)OC_2H_5 \quad (I)$$

Similarly, the ethyl imido-1-phenylcyclopropanecarboxylate hydrochloride

$$\underset{\llcorner\!\!\lrcorner}{CH_2CH_2C(C_6H_5)}\text{—}C(=NH_2Cl)OC_2H_5 \quad (II)$$

was obtained from 1-phenyl-1-cyanocyclopropane.[3]

Decomposition by Heat.—Pinner[4] many years ago found that the ordinary alkyl imido ester hydrochlorides are decomposed by the action of heat to give an amide and an alkyl chloride. His equation for the pyrolysis was

$$R\text{—}C(=NH_2Cl)OR' + \text{heat} \longrightarrow R\text{—}CO\text{—}NH_2 + R'Cl$$

Several years later, however, Stieglitz[5] in a much more critical study of this reaction pointed out that certain facts are more in harmony with the carbonium, $(R)(NH_2)(OR')CCl$, than with the enammonium structure for the pyrolyzing imido-ester salt. His present view, which differs from this one, will be considered in a subsequent communication on this problem.

Following the observation[6] that a cyclopropyl ketimmonium chloride $\underset{\llcorner\!\!\lrcorner}{CH_2CH_2CH}\text{—}C(=NH_2Cl)\text{—}R$, rearranges when heated to give the isomeric pyrrolinium chloride, $\underset{\llcorner\!\!\lrcorner}{CH_2CH_2CH}=C(R)NH_2Cl$, it appeared to be quite possible that the analogous imido ester derivatives such as (I) and (II) might likewise undergo a ring rupture in addition to the Pinner–Stieglitz reaction. However, the work reported in this paper, which was undertaken largely to provide an answer to this question, has demonstrated that (I) and (II) decompose normally according to the Pinner–Stieglitz reaction to give cyclopropanecarbonamide, $\underset{\llcorner\!\!\lrcorner}{CH_2CH_2CH}\text{—}CONH_2$, and 1-phenylcyclopropanecarbonamide

$$\underset{\llcorner\!\!\lrcorner}{CH_2CH_2C(C_6H_5)}\text{—}CONH_2,$$

respectively. No ethoxypyrrolinium salts were detected in the cases thus far investigated. In future work an effort will be made to obtain a definite explanation of this notable ring stability.

Decomposition by Water.—In aqueous solution the imido esters undergo two concurrent reactions. In the first place, they decompose into a nitrile and an alcohol or phenol; and, in the second, they react with water to give the ordinary ester and ammonia, $R\text{—}C(=NH)\text{–}OR' + H_2O = RCOOR' + NH_3$. The first of these reactions is accelerated by bases, whereas the second is favored by acids. The imido ester hydrochlorides, therefore, are normally decomposed by water to give the ordinary ester and ammonium chloride in accordance with the monomolecular law, although some of them undergo a significant decomposition into nitrile, hydrochloric acid and an alcohol or phenol. Many years ago Stieglitz

(1) The data reported herein have been taken from theses presented to the Rensselaer Polytechnic Institute by Edwin Chandler Knowles and Raymond J. Anderson. The work on the unsubstituted cyclopropane derivatives was done by R. J. A. and that on the phenylated compounds by E. C. K.

(2) Pinner, "Die Imidoäther und ihre Derivate," Berlin, 1892.

(3) Knowles and Cloke, THIS JOURNAL, **54**, 2028 (1932).

(4) Pinner, *Ber.*, **16**, 355, 1654 (1883).

(5) Stieglitz, *Am. Chem. J.*, **21**, 101 (1899); Lengfeld and Stieglitz, *ibid.*, **16**, 76 (1894).

(6) Cloke, THIS JOURNAL, **51**, 1174 (1929).