[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF TEXAS.]

THE 5,5-DIMETHYL-3-R-2-THIOHYDANTOINS.[1]

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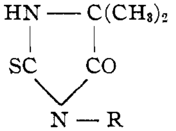
In the year 1908, Bailey and Randolph published in the *Berichte* of the German Chemical Society an article entitled "Kritische Bemerkungen zu einer Abhandlung von W. Marckwald, M. Neumark and R. Stelzner: Ueber Thiohydantoine und von diesen derivierende Basen."[2] In working out methods for the desulfurization of thiohydantoins,[3] Bailey and Randolph had occasion to prepare certain 5,5-dimethyl-3-R-2-thiohydantoins of the general formula



where R represents an alkyl or an aryl.

In the table below is given a list of the substances described in the article of Marckwald, Neumark and Stelzner, "Ueber Thiohydantoine und von diesen derivirende Basen,"[4] which were later prepared by Bailey and Randolph. The compounds in the article of the German investigators, which were under criticism by Bailey and Randolph, as well as the additional substances which are discussed in the present paper, were contributed to the article of Marckwald, Neumark and Stelzner by Dr. Stelzner, at the time a co-worker of Prof. Marckwald. A comparison of the melting points of the substances, obtained by Stelzner on the one hand and by Bailey and Randolph on the other hand, indicates beyond any doubt that the compounds, obtained in these two investigations and to which are ascribed the same constitution, are not identical.

	Melting points.	
	By Stelzner.	By Bailey and Randolph.
(*a*) 3,5,5-Trimethyl-2-thiohydantoin..........	53°	145°
(*b*) 5,5-Dimethyl-3-phenyl-2-thiohydantoin....	67°	174°
(*c*) Methyl ether of "*b*".....................	Zähflüssiges helles Liquidum	96°
(*d*) Platinum salt of "*c*".....................	132°	240°
(*e*) Picrate of "*c*".........................	174°	194°
(*f*) 5,5-Dimethyl-3-*p*-tolyl-2-thiohydantoin....	85°	223°

In regard to the results tabulated above, Bailey and Randolph made the following statement:

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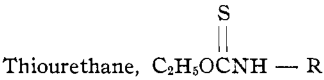
[1] This paper was sent to Dr. Stelzner in May for his criticism but no reply has been received. Because of the uncertainty of mails to Germany at the present time it does not seem best to wait longer before publication.—EDITOR.

[2] *Ber.*, **41**, 2505 (1908).

[3] *Ibid.*, **41**, 2494 (1908).

[4] *Ber.*, **24**, 3278 (1891).

"Da nun aus den Ergebnissen unserer Mitteilung über die Entschwefelung von Thiohydantoinen mit grösster Wahrscheinlichkeit zu folgern ist, dass wir die wirklichen Thiohydantoine erhalten haben, so kann die von Stelzner den betreffenden Verbindungen zugesprochene Konstitutionsformel nicht zutreffend sein. Welche formel die in Rede stehenden Substanzen in Wirklichkeit besitzen, haben wir nicht ermitteln können. Da bei den betreffenden Versuchen stets eine alkoholische Lösung der Senföle benutzt wurde, so drängte sich uns der Gedanke auf, dass die von Stelzner beschriebenen Derivate vielleicht Thiourethane, $C_2H_5O\overset{\overset{\displaystyle S}{\|}}{C}NH — R$, waren, die irrtümlicherweise für Thiohydantoine gehalten worden sind. Dieser Annahme steht jedoch die Thatsache entgegen, dass die Analysenresultate Stelzners die in den meisten Fällen die Bestimmung von Kohlenstoff, Wasserstoff, Stickstoff und Schwefel umfassen, gut auf die Thiohydantoin-Formel stimmen. Da die in unseren beiderseitigen Beobachtungen zutage getretenen Differenzen kaum auf Tautomerie zurückgeführt werden können, so muss es sich um eine Isomerie handeln, deren Aufklärung noch aussteht."



The substances obtained by Stelzner are now given in Richter's "Lexikon der Kohlenstoffverbindungen" as *isomers* of the Bailey and Randolph compounds. However, Dr. Stelzner has, since the publication of the Bailey and Randolph article, worked over the ground and writes:

"Wie Sie bereits richtig vermuteten, beziehen sich die von mir herrührenden Schmelzpunktsangaben auf die bei der Kondensation von Aminosäuren mit Senfölen bei Gegenwart von alkolholischen Kali gleichzeitigoder vielleicht richtiger zunächst entstehenden Thiourethane............meine Analysenzahlen aber sich auf die Thiohydantoine." In justice to Dr. Stelzner his explanation should be quoted of "der ganz merkwürdige Zufall dass die in der Bruttoformel so gänzlich verschiedenen Thiourethane und Thiohydantoine in der prozentualen Zusammensetzung sich einander recht nahe stehen, und dementsprechend auch die teils von mir, teils von anderer Seite ausgeführten Analysen keinen Hinweis auf die in meinen Thiohydantoinen zweifellos noch vorhandenen Verunreinigungen gaben."

In whatever way the errors in Stelzner's work may be accounted for, it is simply our aim in the present article to direct attention to the fact that none of the supposed 5,5-dimethyl-3-R-2-thiohydantoins or their derivatives, described in the article referred to above, were obtained by Stelzner—at least in a form approximating purity.

As *o*-tolyldimethylthiohydantoin and some derivatives of this are also described by Stelzner in the article referred to above, it seemed desirable that this work also be investigated. Here again products have been obtained that do not correspond in their melting points with the results obtained by Stelzner, as is evident from the following tabulated comparison:

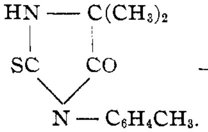
	Melting points.	
	By Stelzner.	By Bailey and McPherson.
(*a*) 5,5-Dimethyl-3-*o*-tolyl-2-thiohydantoin.	175°	195.5°
(*b*) Methyl ether of "*a*"..................	Schmilzt bei Zimmertemperatur	75°
(*c*) Platinum salt of "*b*"................	No data	220°
(*d*) Sulfate of "*b*"......................	208°	196°
(*e*) Picrate of "*b*"......................	212°	152°

There is no possibility that Stelzner was confused in the work on the *o*-tolyl derivatives by the presence of *o*-tolylthiourethane, because the latter substance is described in the literature as a liquid. It is true that, as shown in the experimental part of this article, this thiourethane, when pure, is a crystalline solid at room temperature, but in its preparation a liquid is always obtained and considerable care must be exercised in its preparation to effect crystallization.

In justice to Dr. Stelzner, attention should be directed to the fact that at the time he carried out his work α-aminoisobutyric acid was a substance difficult to prepare and the sulfate with which he worked might have been contaminated with ammonium sulfate. There is some probability of this, in view of the fact that he assigned to this salt the formula $(CH_3)_2C(NH_2)COOH.H_2SO_4$. Bailey and Randolph showed the formula of the normal salt to be $[(CH_3)_2C(NH_2)COOH]_2.H_2SO_4$. Experiments have convinced us that Stelzner's acid salt can be prepared, but it will not stand recrystallization from water as stated by Stelzner.

Experimental Part.

The α-aminoisobutyric acid used in this work was prepared according to the method of Gulewitsch.[1] The *o*-tolyl mustard oil, made from *o*-toluidine, boiled at 238° at 744 mm. The boiling point given by Mainzer[2] is 237°. As a further confirmation of the purity of the mustard oil, the following derivatives were made: $o\text{-}CH_3C_6H_4NHCSNH_2$, $o\text{-}CH_3C_6H_4\text{-}NHCSNHC_6H_5$, and $(o\text{-}CH_3C_6H_4NH)_2CS$. These preparations melted at 159°, 139.5°, and 158.5°, respectively, which data stand in accord with the melting points given in Beilstein for these substances.



5,5-Dimethyl-3-*o*-tolyl-2-thiohydantoin, —The thiohydantoin is readily prepared according to the method of Marckwald, Neumark and Stelzner,[3] as follows: An alcoholic solution of equimolecular amounts of *o*-tolyl mustard oil and potassium aminoisobutyrate is boiled one hour, the alcohol distilled off, the residue taken up with water, and then the thiohydantoin precipitated by the addition of hydrochloric acid. Our preparation, purified by recrystallization from dilute alcohol and then from benzene, melted at 195.5° without decomposition. From benzene the thiohydantoin crystallizes in short, thick, microscopic prisms without end faces.

Calc. for $C_{12}H_{14}ON_2S$: C, 61.54%; H, 5.98%; N, 11.97%; S, 13.67%.
Found: C, 61.69; H, 6.19; N, 12.03; S, 13.92.

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[1] *Ber.*, **39,** 1184 (1906).

[2] *Ibid.*, **15,** 1413 (1882).

[3] *Ibid.*, **24,** 3280 (1891).

5,5-Dimethyl-3-*o*-tolylhydantoin.—As a proof of the constitution of the above thiohydantoin, it was desulfurized with bromine by the method of Bailey and Randolph.[1] The new substance thus obtained crystallizes from a benzene-petrolic ether mixture in the form of characteristic, thin, prismatic plates, melting at 172° undecomposed.

Calc. for $C_{12}H_{14}O_2N_2$: C, 66.06%; H, 6.42%; N, 12.84%.
Found: C, 66.16; H, 6.61; N, 12.62.

Methyl Ether of 5,5-Dimethyl-3-*o*-tolyl-2-thiohydantoin.—The methyl ether was prepared according to the method of Marckwald, Neumark and Stelzner by boiling an alcoholic solution of the thiohydantoin with a slight excess of methyl iodide in the presence of one mol of potassium hydroxide until the solution was neutral to litmus. On recrystallization from petrolic ether, it is obtained in the form of short prisms, which melt undecomposed at 75°.

Calc. for $C_{13}H_{16}ON_2S$: C, 62.90%; H, 6.45%; N, 11.29%; S, 12.91%.
Found: C, 63.05; H, 6.56; N, 11.47; S, 12.87.

Picrate of the Methyl Ether.—The picrate separates in thin, yellow plates on the addition of picric acid to an alcoholic solution of the methyl ether. After recrystallization from alcohol, it melts with decomposition at 152°.

Calc. for $C_{19}H_{19}O_8N_5S$: N, 14.68%. Found: N, 14.75.

Platinum Salt of the Methyl Ether.—On the addition of platinic chloride to a solution of the methyl ether in dilute hydrochloric acid, an oil separates which, on standing a short time, changes to an orange-red, crystalline solid. Purification is effected by washing with water and with petrolic ether. On rapid heating this substance melts with complete decomposition at 220°.

Calc. for $C_{26}H_{34}O_2N_4S_2PtCl_6$: Pt, 21.57%. Found: Pt, 21.50.

Sulfate of the Methyl Ether.—The methyl ether is dissolved in the calculated amount of sulfuric acid in alcohol and the sulfate then precipitated with dry ether. The substance purified by several precipitations from alcoholic solution with ether, is obtained in the form of slender, microscopic prisms and melts at 196°.

Calc. for $C_{13}H_{18}O_5N_2S_2$: S, 18.51%. Found: S, 18.35.

***o*-Tolylthiourethane,** $CH_3C_6H_4NHCSOC_2H_5$.—*o*-Tolylthiourethane prepared by Schiff's method[2] is obtained as an oil, which does not solidify in a freezing mixture, and is so described by Liebermann and Natanson.[3] However, either on being dried over fused chloride of calcium, or after long standing, it changes to a crystalline solid. Furthermore, if the oil be dissolved in petrolic ether, the solution strongly cooled, and then

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[1] *Ber.*, **41**, 2497 (1908).
[2] *Ibid.*, **9**, 1316 (1876).
[3] *Ann.*, **207**, 161 (1881).

a crystal of the substance added, the thiourethane separates in thin prismatic plates. It melts at 37° apparently undecomposed.

Calc. for $C_{10}H_{13}ONS$: C, 61.52%; H, 6.66%; N, 7.18%; S, 16.43%.
Found: C, 61.37; H. 6.84; N, 7.31; S, 16.42.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE MICHIGAN AGRICULTURAL COLLEGE.]

ACTION OF AROMATIC ALCOHOLS ON AROMATIC COMPOUNDS IN THE PRESENCE OF ALUMINUM CHLORIDE. I.

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The condensation of aromatic alcohols with aromatic compounds to form derivatives of di- or triphenylmethane is commonly brought about by the following dehydrating agents: sulfuric acid,[1] phosphorus pentoxide,[2] zinc chloride,[3] dilute or concentrated hydrochloric acid,[4] sulfuric and acetic acids,[5] absolute alcohol,[6] stannic chloride,[7] and acetic acid.[8]

Aluminum chloride has been used as a dehydrating agent in organic chemistry by Merz and Weith,[9] Sholl and Seer,[10] Wass,[11] Graebe,[12] Jaubert,[13] Frankforter and Kritchevsky,[14] Frankforter and Kokatnur,[15] and others.[16]

We do not find, however, a record of the dehydrating action of aluminum chloride on aromatic alcohols and aromatic compounds. This preliminary

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[1] Myer and Wurster, *Ber.*, **6**, 964 (1873); Becker, *Ibid.*, **15**, 2091 (1882); Noelting, *Ibid.*, **24**, 3127, 3136 (1891); Gatterman and Koppert, *Ibid.*, **26**, 2811 (1893); Bistrzycki and Flateau, *Ibid.*, **28**, 989 (1895); Fritsch, *Ibid.*, **29**, 2300 (1896); Bistrzycki and Simonis, *Ibid.*, **31**, 2812 (1898), etc.

[2] Hemilian, *Ber.*, **7**, 1203 (1874); Michael and Jeanpretre, *Ibid.*, **25**, 1615 (1892), etc.

[3] Fischer and Roser, *Ber.*, **13**, 674 (1879); *Ann.*, **206**, 113, 155 (1880); Liebmann, *Ber.*, **15**, 152 (1882); Kippenberg, *Ibid.*, **30**, 1140 (1897), etc.

[4] Suais, *Bull.*, [3] **17**, 517 (1897); D. R. P. 27032; Noelting, *Ber.*, **24**, 3127 (1891); Noelting, *Ibid.*, 24, 553 (1891), etc.

[5] Paterno and Fileti, *Gazz.*, **5**, 381 (1875); Mohlau and Klöpfer, *Ber.*, **32**, 2147, 2149 (1899).

[6] Möhlau and Klöpfer, *Ber.*, **32**, 2150, 2153 (1899).

[7] Bistrzycki, *Ibid.*, **37**, 659 (1904).

[8] Khotinski and Potzewitch, *Ibid.*, **42**, 3104 (1909).

[9] *Ber.*, **14**, 189 (1881).

[10] *Ann.*, **394**, 119 (1912).

[11] *Ber.*, **15**, 1128 (1882).

[12] *Chem. Ztg.*, **25**, 268 (1901); *Ber.*, **34**, 1778 (1901).

[13] *Compt. rend.*, **132**, 841 (1901).

[14] THIS JOURNAL, **36**, 1511 (1914); **37**, 385 (1915).

[15] *Ibid.*, **36**, 1529 (1914).

[16] *Ber.*, 40, 1694 (1907); D. R. P. 136,015, etc.