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PHENYLIODONIUM DERIVATIVES OF N-HETEROCYCLES AND CH-ACIDS, THEIR SYNTHESIS, AND THEIR USE IN THE CHEMISTRY OF HETEROCYCLES. (REVIEW)

O. Neilands

The reactions of iodosylbenzene with CH-acids, including β-dicarbonyl and N-heterocyclic compounds in the presence of alkali, which lead to the aryliodonium ylides (betaines) used in the synthesis of new derivatives of heterocycles, are examined. Both β-dicarbonyl compounds and the anions of various heterocyclic compounds (pyrrole, indole, pyrazolidinedione, hydroxypyrones, hydroxypyridones, oxo- and dioxopyrimidines) and β-keto sulfones, β-disulfones, cyclopentadienes, and malononitrile enter into the reaction.

Keywords: betaines, β-dicarbonyl compounds, ylides, indole, iodosylbenzene, malononitrile, pyrazolidinedione, pyrrole, sulfones, uracil, cyclopentadienes.

Iodosylarenes react with β-dicarbonyl compounds in the presence of bases and give aryliodonium betaines (ylides). This review is devoted to description of the first experiments conducted in our laboratory in 1956-1965, discussion of the reaction mechanisms of anionic C-nucleophiles with iodosylbenzene, and discussion of the applicability limits of aryliodonization in the chemistry of heterocyclic compounds. There have been other reviews on the chemistry of the aryliodonium betaines of β-dicarbonyl compounds [1-6].

THE FIRST REACTIONS OF IODOSYLBENZENES WITH β-DICARBONYL COMPOUNDS

The reaction of iodosylbenzene with the cyclic β-diketone 5,5-dimethyl-1,3-cyclohexanedione (**1**) (dimedone) in various solvents was first realized in 1956 [7]. The reaction of iodosylbenzene with the dimedone anion went more slowly (24 h) than the reaction with dimedone in an aqueous suspension (1 h). The hydrate of the 2-phenyliodoniodimedone betaine (**2**) was formed as large colorless crystals. The anhydrous substance was identical with the product formed in the reaction of dimedone with (difluoroiodo)benzene in chloroform solution. The obtained compound represents a completely new type of derivatives of phenyliodonium salts and β-diketones. We called compounds of this type iodones, and compound **2** in particular was called phenyldimedonyliodone. However, this name is not in common use, and such names as 2-phenyliodoniodimedone betaine, 2-phenyliodoniodimedonide, and 4,4-dimethyl-2,6-dioxo-1-phenyliodoniocyclohexan-1-ide have been encountered. Phenyliodonization was also observed during the reaction of iodosylbenzene with 5-phenyl-1,3-cyclohexanedione [8].

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* Dedicated to Academician Prof. J. Stradins on his 70th birthday.

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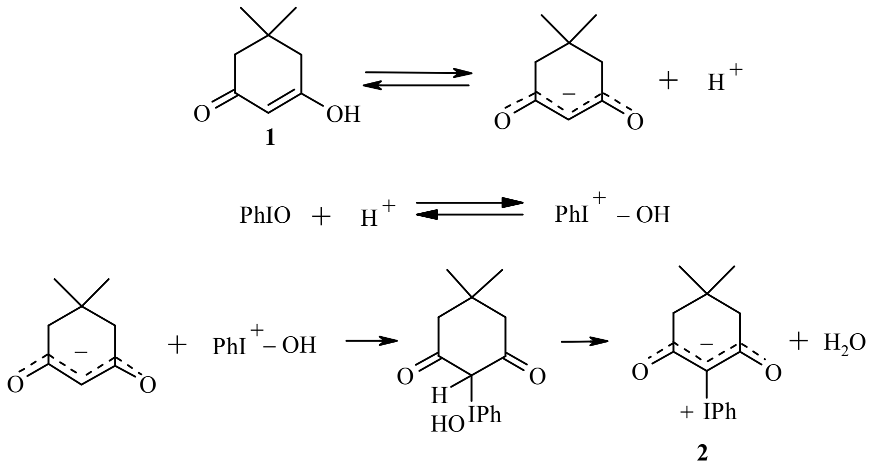
THE MECHANISM OF THE REACTION OF IODOSYLBENZENE WITH THE ANION OF A β-DICARBONYL COMPOUND. A NEW PRINCIPLE FOR THE SYNTHESIS OF PHENYLIODONIUM COMPOUNDS

Iodosylbenzene is a weak base, a weak electrophilic reagent, and a weak oxidizing agent. Its electrophilic characteristics increases during protonation.

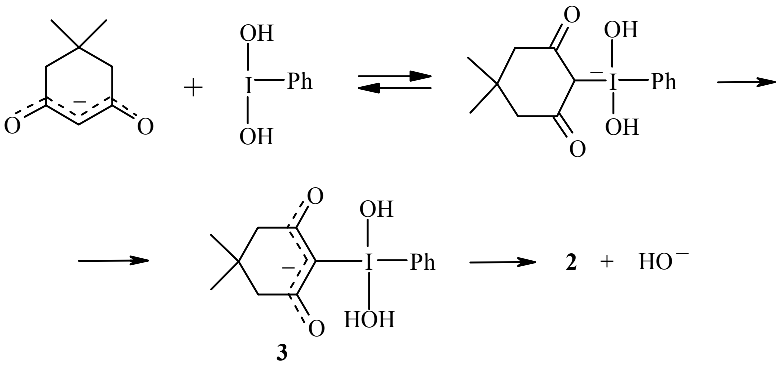
In aqueous solution dimedone (**1**) is an enolized cyclic β-diketone and a weak OH acid with p*K* 5.3. Dimedone is weakly dissociated in aqueous solution and reacts with iodosylbenzene as a weak acid, activating its electrophilic characteristics. Such protonated iodosylbenzene can react with the nucleophilic 2-carbon atom of the enolic form or the anion and form a C–I bond. After rapid ionization of the C–H and I–OH bonds the phenyliodonium betaine **2** is formed, as shown in Scheme 1.

Scheme 1



The iodosylbenzene is not activated in an alkaline medium on account of the absence of the acid. As a weak I-electrophile iodosylbenzene reacts with the C-nucleophile, extending the coordination sphere of the iodine atom. Iodosylbenzene dissolves extremely poorly in water on account of its oligomeric character. When it dissolves in water iodosylbenzene presumably forms the hydrated form $PhI(OH)_2$. Reaction of iodosylbenzene with the dimedone anion can lead to an adduct, which is transformed by rapid ionization of the C–H and I–OH bonds into the intermediate product **3** (Scheme 2), containing an I–OH bond capable of ionization. Ionization results in the production of the phenyliodonium betaine **2** an a hydroxide ion. This means that the pH of the aqueous solution is increased during the reaction of iodosylbenzene and the dimedone sodium salt. This extremely unusual fact was demonstrated experimentally.

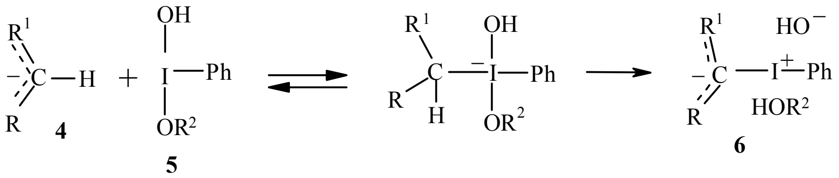
Scheme 2



In [9] we established that (diacetyliodo)benzene $PhI(OOCOCH_3)_2$ can be used in place of iodosylbenzene for the synthesis of the phenyliodonium betaine of dimedone **2**. This significantly simplifies the preparation of the betaine **2**. The phenyliodonium betaines of other derivatives of 1,3-cyclohexanediones can be synthesized in the same way. However, the corresponding phenyliodonium betaines were not obtained during the reaction of (diacetoxyiodo)benzene with open-chain β-dicarbonyl compounds (diethyl malonate, ethyl acetoacetate, acetylacetone, benzoylacetone, dibenzoylmethane). Iodosylbenzene and the products from acetoxylation of the β-dicarbonyl compounds were formed [10]. We assumed that the acidity of the open-chain β-dicarbonyl compounds is too low compared with the acidity of acetic acid, and the respective phenyliodonium betaines are unstable in the presence of acetic acid. The reactions of the open-chain β-dicarbonyl compounds were therefore conducted in the presence of alkali: The (diacetoxyiodo)benzene was added to a solution of the β-dicarbonyl compound and potassium hydroxide in methanol at -5 to +5°C. The phenyliodonium betaine crystallized out or was precipitated with water [11].

In 1961 we proposed a new method for the production of aryliodonium derivatives (betaines) [11]. The anionic CH-nucleophile **4**, which contains electron-accepting groups or other structural elements that secure delocalization of the charge in the molecule, reacts with the iodosylbenzene **5** generated from (diacetoxyiodo)benzene in a solution of potassium hydroxide in methanol (Scheme 3). In methanol solution iodosylbenzene may be hydrated (**5**, R^2 = H) or may exist in the form of a methanol adduct (**5**, R^2 = Me).

Scheme 3



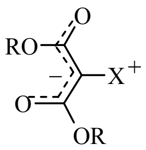
The new method of aryliodonization applies not only to β-dicarbonyl compounds but also to heterocyclic compounds that are capable of forming an anion (pyrrole, indole, pyrazolinediones, oxo- and dioxopyrimidines). β-Keto sulfones and β-disulfones, cyclopentadienes, and malononitrile may also be suitable components. In reaction with iodosylbenzene phenolates form oxidation products and iodobenzene. However, phenolates stabilized by electron-withdrawing substituents are capable of being transformed into stable phenyliodonium betaines during reaction with iodosylbenzene [12, 13].

SYNTHESIS OF PHENYLIODONIUM BETAINES OF OPEN-CHAIN β-DICARBONYL COMPOUNDS AND THEIR TRANSFORMATION INTO HETEROCYCLIC BETAINES

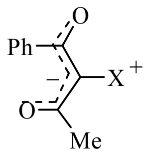
The synthesis of phenyliodonium betaines of diethyl malonate (dialkoxycarbonylphenyliodoniomethanides) (**7**) was first worked out in 1961-1963 and was described in detail in 1965 [14]. The dialkyl malonate and (diacetoxyiodo)benzene were added to a solution of potassium hydroxide (3 eq.) in methanol or ethanol at -5°C. After stirring for 1 h the betaines **7a** crystallized. Transesterification takes place during the reaction; in a methanol solution the phenyliodonium betaine of dimethyl malonate is obtained, while in ethanol the phenyliodonium betaine of diethyl malonate is obtained irrespective of the structure of the initial dialkyl malonate.

The yellow phenyliodonium betaines of benzoylacetone **8a** [15] and dibenzoylmethane **9a** [15] and the colorless phenyliodonium betaines of acetoacetates **10a** (R = Me, Et) [16] were synthesized similarly. The betaine **10a** (R = Me) was obtained in the reaction of ethyl acetoacetate in methanol, while the betaine **10a** (R = Et) was obtained in ethanol.

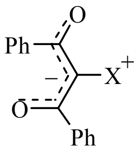
The described phenyliodonium betaines are extremely unstable compounds but can be kept at reduced temperature for a short time. On heating they readily react with pyridine, substituted pyridines, isoquinoline, and quinoline and are converted into yellow and orange azinium betaines **7b-10b** [6, 14-16].



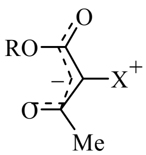
7a,b



8a,b

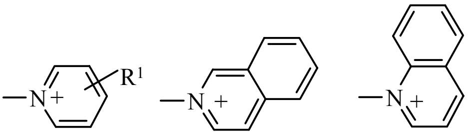


9a,b



10a,b

a X = IPh, **b** X =

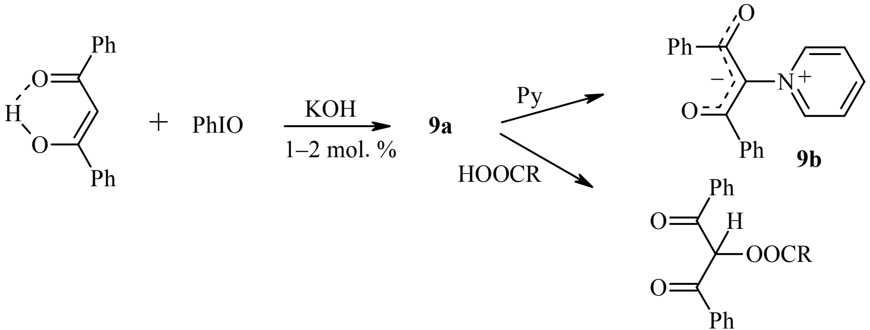


From 1970 our method of phenyliodonization of open-chain β-dicarbonyl compounds by iodosylbenzene was used by other research groups. Hayasi [17] synthesized the phenyliodonium betaine of dibenzoylmethane **9** and investigated the products of its thermal decomposition. Schank and coworkers [18] synthesized the phenyliodonium betaines of methyl acetoacetate, acetylacetone, and dibenzoylmethane by our method with small modifications; after dilution with water the reaction mixture was extracted with methylene chloride. The phenyliodonium betaines were isolated from the extract. With the exception of the phenyliodonium betaine of acetylacetone the yields of the products were lower than in our experiments. We were unable to isolate this compound in the pure form on account probably of its better solubility in water. Schank used the obtained betaines for the synthesis of tricarbonyl compounds by reaction with ozone. Lloyd and coworkers [19] used our method to synthesize the phenyliodonium betaines of dialkyl malonates, dibenzoylmethane, and benzoylacetone and used them for catalytic cleavage in the presence of triphenylarsine, sulfides, and cyclohexene. Examples of other syntheses and reactions can be found in the review [6].

Further use of the phenyliodonium betaines in syntheses required their isolation and purification. In view of the low stability of the phenyliodonium betaines of open-chain β-dicarbonyl compounds it was necessary to find methods of realizing the further transformations without isolating the compounds in the individual form. To solve this problem we used the nature of the reaction between the salt of the β-dicarbonyl compound and the iodosylbenzene. A hydroxide ion is formed in this reaction, as shown in schemes 2 and 3. If we used separately prepared iodosylbenzene, it was sufficient to add catalytic amounts of alkali to the reaction mixture with the β-dicarbonyl compound. It is not difficult to prepare iodosylbenzene from a methanol solution of (diacetoxyiodo)benzene. It is more difficult to filter the fine precipitate of the iodosylbenzene and to wash it free from alkali. It is also possible not to add the catalytic amounts of alkali in the above-mentioned reaction but simply during the preparation of the iodosylbenzene and not to wash it completely from the sorbed alkali. Through washing of course requires a large amount of time.

In the reaction with dibenzoylmethane [20] freshly prepared iodosylbenzene was added to its methanol solution with cooling. It is possible but not essential to add 1-2 mole % of alkali. The iodosylbenzene dissolves, and sometimes the phenyliodonium betaine begins to crystallize. Carboxylic acids or pyridine are added to the reaction mixture. In the first case the acyloxy-substituted dibenzoylmethanes **11** are obtained with high yields as a result of protonation of the betaine and nucleophilic substitution of the phenyliodonium group. In the reaction with pyridine the pyridinium betaine **9b** is formed (Scheme 4).

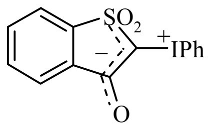
Scheme 4



R = Me, CCl_3, Ph, p-$O_2NC_6H_4$; $TosO^{-}\ {}^{+}H_3NCH_2$ **11**

THE REACTIONS OF β-OXO SULFONES AND β-DISULFONES

β-Oxo sulfones are close analogs of β-diketones. For example, 3-oxo-2H-benzo[*b*]thiophene 1,1-dioxide is an analog of 1,3-indanedione. In reaction with iodosylbenzene generated from bis(trifluoroacetoxyiodo)benzene and sodium bicarbonate in a water–ethanol medium this substance is converted into the phenyliodonium betaine **12**.



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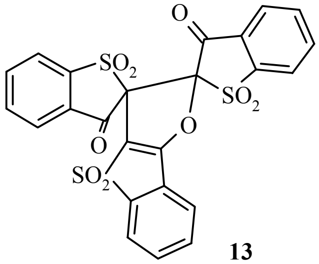

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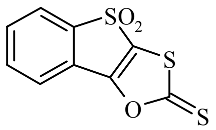

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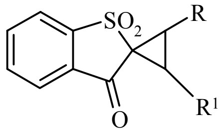

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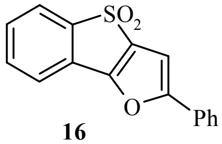

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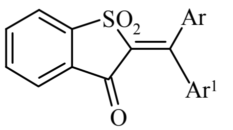
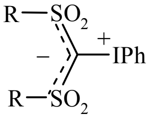


17

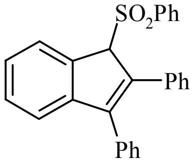
These investigations were commenced and conducted in Schank's laboratory [21-23]. The betaine **12** has high reactivity. Some important reactions of the betaine **12** characterizing its possible use in the chemistry of heterocyclic compositions are described below. In solutions the betaine **12** is soon transformed after the elimination of iodobenzene into the unusual trimer **13**. During reaction with hydrogen sulfide the condensed system **14**, containing benzothiophene dioxide and thioxolethione fragments, is formed. The thermal reaction of the betaine **12** with alkenes in the presence of copper acetylacetonate leads to the extremely interesting spiro compounds **15**. However, the analogous reaction with phenylacetylene gives a different product, i.e., the condensed system **16**, containing benzothiophene dioxide and furan fragments. The catalytic thermal reaction of the betaine **12** with thiobenzophenones leads to the diarylmethylene derivatives **17**.

The reactions of β-disulfones with iodosylbenzene were studied by Varvoglis' group. β-Disulfones react with (diacetoxyiodo)benzene in the presence of potassium hydroxide in methanol solution at -10°C and are converted into the phenyliodoniobis[aryl(alkyl)sulfonyl]methanides **18** [24, 25].



18

R = Me, Ar, RR = $(CH_2)_3$



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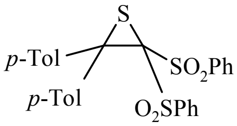

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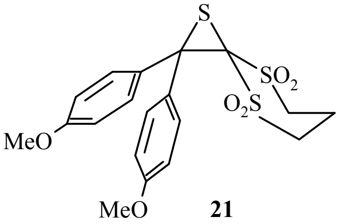

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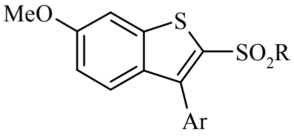
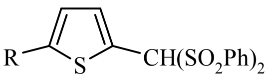


22

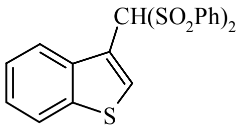
These phenyliodonium betaines (ylides) are extremely reactive. In reaction with alkenes under conditions of photolysis or catalytic thermolysis cycloaddition occurs, and cyclopropane derivatives are formed. The analogous reaction with diphenylacetylene leads to indene derivatives of type **19**. The thermal reaction of the betaines **18** in the presence of copper acetylacetonate with thiobenzophenones takes place as cycloaddition at the C=S double bond, and derivatives of thiirane **20** and **21** or products of further transformations such as benzothiophenes **22** are obtained depending on the structure of the initial compounds.

It can be supposed that carbenes are formed during photolysis or catalytic thermolysis of the betaines **18** and enter into cycloaddition, attack the atoms with unshared electron pairs, or enter at the C–H bond. During photolysis of the phenyliodonium betaine of bisphenylsulfonylmethane **18** (R = Ph) in the presence of thiophenes or benzothiophene the carbene is inserted at the C–H bond with the formation of the thiophenes **23** and **24**, or the sulfur atom is attacked. In this case compound **25**, which is a betaine (ylide), is obtained. An analogous betaine is also formed from dibenzothiophene [26].



23

R = H, Me



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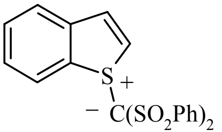

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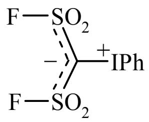
Akiyama [27] considers that a carbene may also be formed during the action of strong reducing agents on the betaine **18** (R = Ph). Unique phenyliodonium betaines (ylides) **26** and **27** were obtained from bisfluorosulfonylmethane and bistrifluoromethylsulfonylmethane [28].



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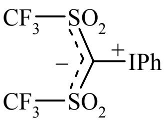

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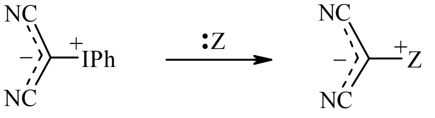
REACTIONS OF MALONONITRILE

Varvoglis and coworkers studied the reaction of malononitrile with iodosyl compounds. It was found that phenyliodoniocyanomethanide **28** is formed from malononitrile and (diacetoxyiodo)benzene in the presence of a small amount of sodium methoxide at low temperature. However, the compound was so unstable that it could not be isolated from the reaction mixture. The existence of this betaine in the solution was confirmed by further reactions with N-, S-, and As-nucleophiles. New dicyanomethanides **29** were obtained [29] (Scheme 5).

Scheme 5

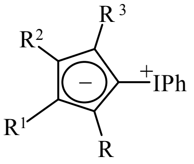


28 **29**

Z = pyridines, quinolines, isoquinolines, dibenzyl sulfide, thianthrenes, Ph_3As

REACTIONS OF SUBSTITUTED CYCLOPENTADIENES WITH IODOSYLBENZENE

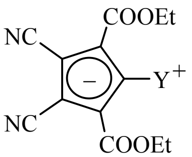
In reaction with iodosylbenzene in the presence of potassium hydroxide unsubstituted cyclopentadiene undergoes oxidation with the formation of iodobenzene and dark unidentified products [11]. Cyclopentadienes substituted with electron-withdrawing groups are not oxidized during reaction with iodosylbenzene.



30a–d

30 a $R = R^1 = R^2 = CN, R^3 = H$; **b** $R = R^1 = R^3 = CN, R^2 = H$; **c** $R = R^1 = R^3 = CHO, R^2 = H$; **d** $R = R^3 = COOEt, R^1 = R^2 = CN$

Friedrich and Amann [30-32, 34] showed that the potassium salts of substituted cyclopentadienes react with (diacetoxyiodo)benzene, resulting in the production of the phenyliodoniocyclopentadienides **30**. The crystal and molecular structures were determined for compound **30d** [33]. These compounds are extremely stable during storage but readily enter into reaction with nucleophiles (sulfides, selenides, phosphines, arsines, thioureas). In these reactions iodobenzene is eliminated, and new cyclopentadienides (betaines) are formed. A series of new betaines **31** were obtained from phenyliodonium betaine **30d**.



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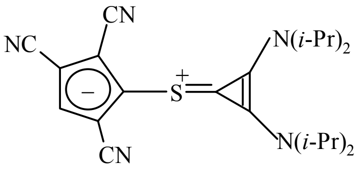

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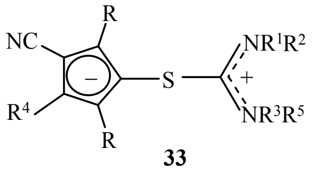
$Y = SR_2, SePh_2, PPh_3, AsPh_3$



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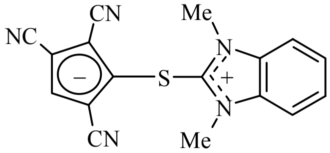


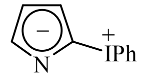
34

R = CN, COOEt; R^4 = H, CN

In the reaction of the betaine **30b** with bisdiisopropylaminocyclopentenethione the interesting betaine **32** is formed [35]. The reactions of the betaines **30** with thioureas, including cyclic thioureas, take place readily. The products of the reaction are the betaines **33** containing the cyclopentadienide anion and the isothiuronium cation, linked by a σ-bond, in the molecule [29, 34, 36, 37]. Derivatives of cyclic thioureas such as the betaine **34** are interesting from the standpoint of the chemistry of heterocyclic compounds [37].

SYNTHESIS AND PROPERTIES OF PHENYLIODONIUM BETAINES OF FIVE-MEMBERED NITROGEN HETEROCYCLES

Pyrroles, indoles, and pyrazoles are weak NH acids and are capable of forming a C-nucleophilic anion in the presence of potassium hydroxide. These heterocycles can be suitable components in reactions with iodosylbenzene. We were able to realize the phenyliodonization of pyrrole by iodosylbenzene in the presence of potassium hydroxide [11]. The yellow crystalline betaine of 2-phenyliodoniopyrrole **35** crystallized from the reaction mixture at -5 to -10°C. This betaine was extremely unstable and decomposed at 75°C with explosion. The betaine reacts with acids and is converted into the colorless salts **36**. The salts are not very stable in the crystalline state and decompose very quickly at room temperature. It was not therefore possible to obtain elemental analyses and spectra for these compounds. Nevertheless the phenyliodonium derivatives of pyrrole and particularly of pyrroles substituted by electron-withdrawing groups may be of great interest in the chemistry of pyrroles.



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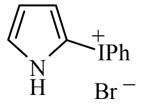

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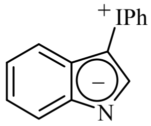

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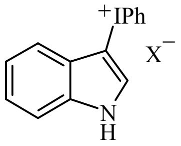


38

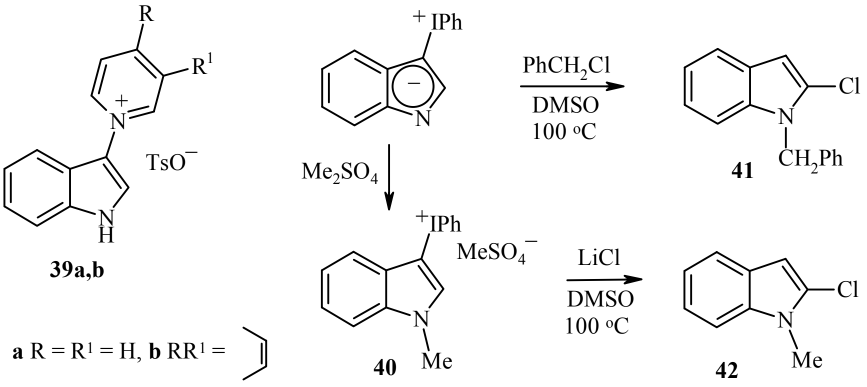
X = TsO, BF_4, CF_3COO, Cl, Br

Phenyliodonization of indole takes place readily in reaction with iodosylbenzene in the presence of potassium hydroxide in methanol solution at -5°C. The iodosylbenzene is generated in the reaction medium from (diacetoxyiodo)benzene. The yellow betaine of 3-phenyliodonioindole **37** crystallizes from the reaction mixture with a yield of 70% [11, 38]. The betaine is unstable at room temperature and decomposes explosively at 99-100°C. The colorless salts **38**, which are obtained from the betaine **37** and acids, are more stable during storage in the refrigerator. The salts also decompose explosively when heated. We investigated certain chemical transformations of the tosylate **38** (X = TsO) and demonstrated the possibility of nucleophilic substitution of the phenyliodonium group. This opens up a new path to the production of 3-substituted indoles. For example, the reaction of the tosylate **38** with pyridine or isoquinoline gives N-(3-indolyl)pyridinium tosylates **39a** and N-(3-indolyl)isoquinolinium tosylates **39b** [38].

The transformations of the betaine **37** and its salts **38** were studied in Kost's laboratory [39-42]. The investigated thermal reactions of the salts **38** with chlorides and bromides lead to substitution of the phenyliodonium group by the halogen atom. It is interesting that both 3-substituted and 2-substituted halogenoindoles are obtained depending on the initial salt and on the reaction conditions. For instance, only 75-80% of the 3-haloindoles is obtained in the reaction of the trifluoroacetate **38** in DMSO solution at 100°C in the presence of the halides LiBr, NH_4Br, and LiCl. In the presence of NH_4Cl, Bu_4NCl, or LiCl + 15-crown-5, however, the formation of up to 25% of 2-chloroindole is also observed.

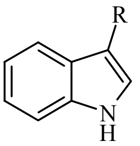
Alkylating agents attack the nitrogen atom of the betaine **37**, and subsequent cleavage of the N-alkylindolylphenyliodonium salts **40** leads to the 2-chlorine-substituted indoles **41** and **42** (Scheme 6).

Scheme 6



Moriarty's group [43] showed that the trifluoroacetate **38** reacts with organolithium compounds in THF at -78°C in the presence of $BF_3{\cdot}Et_2O$, and good yields of 3-substituted indoles **43** are obtained.

Chugtai [42] mentioned the reaction of the salts **38** with phenylmagnesium bromide. 3-Phenylindole **43c** was isolated from the mixture of products. The reaction of the salts **38** with hydrogen sulfide in DMSO leads to 3-mercaptoindole **43e**.



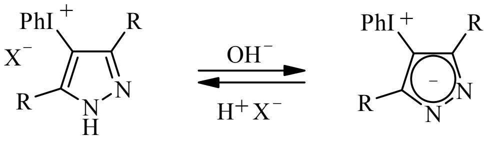
43a–e

a R = Me, **b** R = *n*-Bu, **c** R = Ph, **d** R = CH_2=$CHCH_2$, **e** R = SH

The molecular and crystal structures of the trifluoroacetate **38** were determined [44]. The molecule has the usual T-shaped configuration for iodonium compounds.

Pyrazole and 3,5-disubstituted pyrazoles react with iodosylbenzene too slowly in the presence of alkali, and it is therefore necessary to conduct the reaction with the more active phenyliodonizing agent (diacetoxyiodo)benzene in the presence of *p*-toluenesulfonic acid [44]. Pyrazol-4-ylphenyliodonium tosylates **44** (X = OTs) are obtained very readily and with high yields. In the presence of alkali the tosylates are converted into internal salts – the betaines **45** (Scheme 7). The tosylates **44** are weak NH acids; in 50% aqueous ethanol pK_a 10.00 (**44a**), 11.0 (**44b**), and 9.3 (**44c**).

Scheme 7

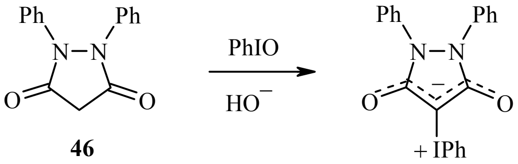


44a–c **45**

44 **a** R = H, **b** R = Me, **c** R = Ph

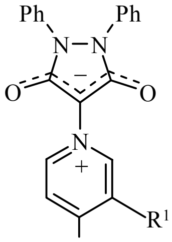
The pyrazolylphenyliodonium salts **44** and the betaines **45** are surprisingly stable. They can be stored at room temperature for an unlimited time without decomposition. It is extremely difficult to achieve nucleophilic substitution of the phenyliodonium group in compounds **44** and **45**, and this reaction has not so far been specifically studied.

Scheme 8

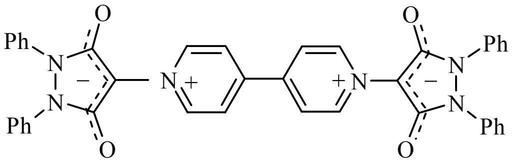


46 **47**

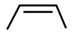
1,2-Diphenylpyrazolidine-3,5-dione (**46**) reacts readily with the iodosylbenzene generated from (diacetoxyiodo)benzene and potassium hydroxide in methanol solution. The reaction product is the 4-phenyliodonium betaine of 1,2-diphenylpyrazolidine-3,5-dione (**47**) [46] (Scheme 8). In reaction with pyridine and substituted pyridines, isoquinoline, and 4,4′-bipyridyl in ethanol solution in the presence of *p*-toluenesulfonic acid (boiling) this betaine is transformed with good yields into the new colored heterocyclic onium betaines **48** and **49**. During reaction with dimethyl sulfide and triphenylphosphine the corresponding colorless dimethylsulfonium and triphenylphosphonium betaines are formed.



48

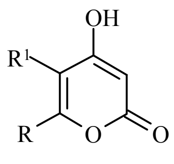


49

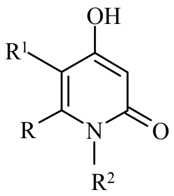
48 **a** R = R^1 = H, **b** R = CN, R^1 = H; **c** R = NH$_2$, R^1 = H; **d** RR^1 = 

SYNTHESIS AND PROPERTIES OF THE PHENYLIODONIUM BETAINES OF SIX-MEMBERED HETEROCYCLIC COMPOUNDS WITH ONE HETEROATOM

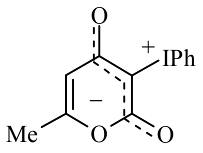
In order to realize the reactions with iodosylbenzene it is necessary to introduce functions that promote the formation of a C-nucleophilic anion into the heterocyclic compound. Such groups can be hydroxyl and carbonyl. For example, among the pyrans hydroxypyrones and, specifically, 4-hydroxy-2-pyrones **50** will be reactive. In the pyridine class 4-hydroxy-2-pyridones **51** will be reactive.



50



51



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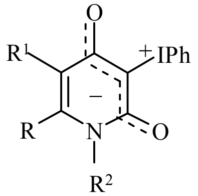
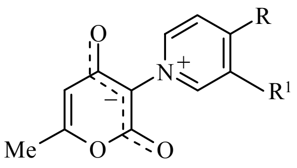


53

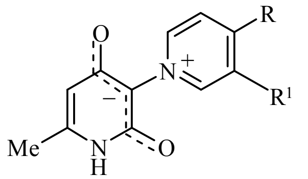
50, **51**, **53** **a** R = Me, R^1 = R^2 = H, **b** R^2 = Ph, RR^1 = $(CH_2)_4$

In the structure of compounds **50** and **51** it is easy to see the elements of a β-dicarbonyl compound in the enolic form.

4-Hydroxy-2-pyrones and 4-hydroxy-2-pyridones react very readily with the iodosylbenzene generated from (diacetoxyiodo)benzene and sodium carbonate in an aqueous medium [47], and the corresponding betaines **52** or **53** crystallize. The obtained compounds are very reactive and readily substitute the phenyliodonium group. If the betaines are boiled with pyridines, isoquinoline, or thiophane in methanol solution in the presence of *p*-toluenesulfonic acid, the new onium betaines **54** or **55** are formed. In the crystalline state the obtained yellow betaines, pyridinium derivatives **54a** and **54b** and isoquinolinium derivatives **54c** and **55c**, exhibit phosphorescence [47].



54



55

a R = R^1 = H, **b** R = H, R^1 = $CONH_2$; **c** RR^1 = 

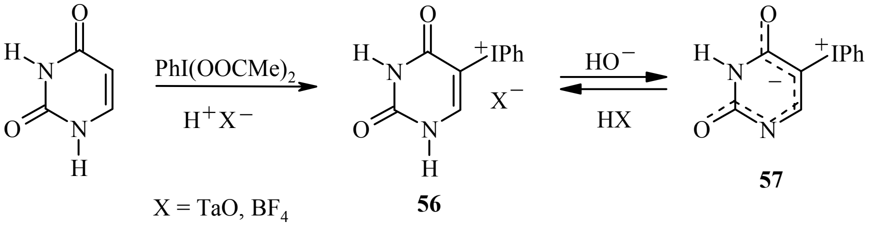
As close analogs of β-dicarbonyl compounds the phenyliodonium betaines of 4-hydroxycoumarin and 4-hydroxycarbostyril were examined in the review [6].

SYNTHESES AND PROPERTIES OF PHENYLIODONIUM BETAINES – PYRIMIDINE DERIVATIVES

Hydrogenated dioxo- and trioxopyrimidines are capable of forming C-nucleophilic anions. The phenyliodonium betaines of barbituric acid and 2-amino(1H,5H)pyrimidine-4,6-dione were examined in the review [6] as derivatives of β-dicarbonyl compounds. In this section the phenyliodonium salts and betaines of uracil and 6-substituted uracils will be examined.

In an alkaline medium uracil forms an anion, but its C-nucleophilicity is insufficient for reaction with iodosylbenzene. The phenyliodonization of uracil requires a stronger phenyliodonizing reagent, namely (diacetoxyiodo)benzene in the presence of *p*-toluenesulfonic acid. Thus, it was possible to obtain the uracil-5-ylphenyliodonium salt **56** and by the action of alkali on the salt **56** – an internal salt – the betaine **57** [48] (Scheme 9). These phenyliodonium derivatives of uracil are stable during storage. Their reactivity with nucleophilic reagents has been studied little.

Scheme 9

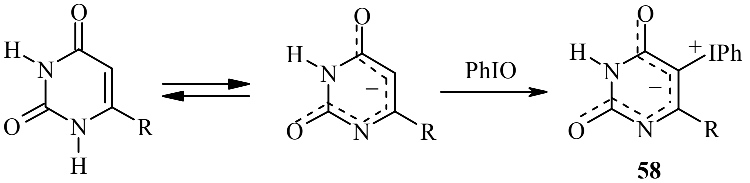


56

57

In contrast to the inertness of the uracil anion toward iodosylbenzene 6-substituted uracils react readily in an alkaline medium. The 6-amino-, 6-chloro-, and 6-methoxyuracils were studied. The substituted uracil was dissolved in water in the presence of sodium carbonate, and a solution of (diacetoxyiodo)benzene in methanol was added. Fine colorless crystals of the betaines of 6-substituted 5-phenyliodoniouracils **58** separated from the mixture ([49] and the author's unpublished data). The yield was not higher than 90%, and the betaines were unstable during prolonged storage.

Scheme 10



58

a R = NH_2, **b** R = Cl, **c** R = OMe

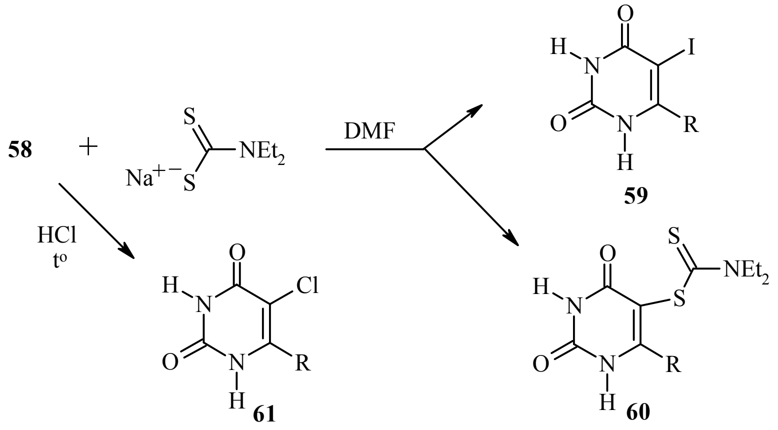
The structure of the betaines **57** and **58** is confirmed by the IR spectra. The absorption of the carbonyl groups of the uracils is observed at 1660-1760 cm^{-1} (several maxima). For the betaines absorption is observed at 1560-1660 cm^{-1}. The low wave numbers indicate formation of the anionic system of uracil. The betaines **58** are poorly soluble in water and organic solvents but dissolve in dilute solutions of strong acids (HCl, H_2SO_4, HNO_3, HBF_4) and form salts.

The reactivity of the betaines **58** with nucleophiles was found to differ depending on the substituent R. The strong S-nucleophile sodium diethyldithiocarbamate was chosen as reagent. It is known that the phenyliodonium betaine of barbituric acid reacts with sodium diethyldithiocarbamate in DMF solution, and 5-diethylaminothiocarbonylthiobarbituric acid is obtained as the product from nucleophilic substitution of the phenyliodonium group [50].

According to our data, the phenyliodonium betaine of 6-aminouracil **58b** reacted in a different direction in reaction with sodium diethyldithiocarbamate, and 6-chloro-5-iodouracil (**59**) was formed. Conversely, the phenyliodonium betaine of uracil **59a** was converted under analogous conditions into 6-amino-5-diethylaminothiocarbonylthiouracil (**60**) [49] (Scheme 11).

On heating in solutions of acids nucleophilic substitution of the phenyliodonium group by the anion of the acid can occur. For example, the author obtained 5,6-dichlorouracil (**61**) from the phenyliodonium betaine of 6-chlorouracil (Scheme 11).

Scheme 11



59, **61** R = Cl, **60** R = NH$_2$

CONCLUSION

The reaction of iodosylbenzene with the anions of C-nucleophiles begins with the formation of the C–I bond and usually ends with the formation of the phenyliodonium betaine (ylide). Oxidation and insufficient nucleophilicity in the anion are interfering factors. This aryliodonizing reaction was discovered 47 years ago in Riga at the Latvian State University and was developed further at the Chemical Faculty of Riga Polytechnical Institute. A new method for the production of phenyliodonium compounds published in 1961 involved the following reactions. An anionic CH-nucleophile containing electron-withdrawing groups or other structural elements involved in delocalization of the charge in the molecule is transformed by reaction with iodosylbenzene into a phenyliodonium betaine. Subsequent investigations, carried out both in our group and in other groups showed that this principle applies not only to β-dicarbonyl compounds but also to β-keto sulfones, β-disulfones, substituted cyclopentadienes, and a whole range of heterocyclic compounds (pyrrole, indole, pyrazolidinediones, hydroxypyrones, hydroxypyridones, oxo- and dioxopyrimidines). The phenyliodonization of anionic CH-nucleophiles is widely used at the present time on account of the high reactivity of most of the obtained phenyliodonium betaines.

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