BRIEF COMMUNICATIONS

STUDY OF THE ELECTROPHILIC SUBSTITUTION OF ALKYL-, ARYL-, AND ARALKYL-5(6)-HYDROXYBENZIMIDAZOLES

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A series of new 4-sulfo-5(6)-hydroxybenzimidazoles was obtained including mono-, di-, and trinitro derivatives of 2-phenyl- and 2-benzyl-5-hydroxybenzimidazoles. Aromatic groups at C^2, in contrast to alkyl groups, enhance the reactivity of the benzimidazole system in electrophilic substitution.

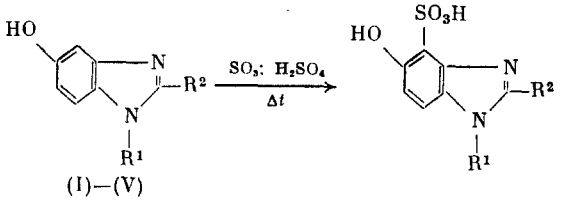
In a study of the electrophilic substitution of 5(6)-hydroxybenzimidazole (I) and its derivatives, namely, 2-methyl- (II), 1-ethyl-2-methyl- (III), 2-phenyl- (IV), and 2-benzyl-5(6)-hydroxybenzimidazoles (V), we obtained a series of new 4-sulfonic acid derivatives of (I)-(V) as well as mono-, di-, and trinitro derivatives of (IV) and (V).

Aromatic substituents at C^2, in contrast to alkyl groups, enhance the reactivity of the benzimidazole system in electrophilic substitution although the presence of a methylene bridge somewhat reduces this reactivity.

In a further study of 5(6)-hydroxybenzimidazole (I) and its derivatives [1-4], we investigated the effect of aromatic substituents at C^2 on the reactivity in electrophilic substitution.

In a previous work [5], we showed that the sulfonation of 2-phenyl- and 2-benzyl-3-hydroxypyridines is directed exclusively to the para position of the phenyl and benzyl rings. In this regard, a comparison was carried out on the reactivity of the benzimidazole system and aromatic ring in electrophilic substitution reactions in the case of the sulfonation of (IV) and (V).

In a study of the sulfonation of (I)-(V), we used various methods for the introduction of the sulfonic acid group into aromatic compounds. Thus, the oxidative sulfonation using Na_2SO_3 and MnO_2 [6] did not prove successful and the starting reagent was recovered. The direct introduction of a sulfonic acid group using the sulfite reaction of phenolic compounds with sodium sulfite or bisulfite also was unsuccessful [7]. The sulfonation of (I)-(V) could be carried out only at 170-190°C in sulfuric acid with oleum.



(I)—(V)

$R^1 = R^2 = H$ (I); $R^1 = H$, $R^2 = Me$ (II); $R^1 = Et$, $R^2 = Me$ (III); $R^1 = H$, $R^2 = Ph$ (IV); $R^1 = H$, $R^2 = CH_2Ph$ (V).

The substitution proceeds exclusively only at C^4. The formation of products of the disulfonation of (I)-(V) or substitution in the phenyl or benzyl ring were not observed. These results differ significantly from previous data on the sulfonation of 2-phenyl- and 2-benzyl-3-hydroxypyridines, which is accompanied by the exclusive formation of 2-(4′-sulfophenyl)- and 2-(4′-sulfobenzyl)-3-hydroxypyridines [5]. This indicates greater reactivity of the hydroxybenzimidazole ring in comparison with hydroxypyridine ring in the sulfonation reaction.

Thus, the scope of sulfonation as a method for studying the reactivity of 5(6)-hydroxybenzimidazoles proves rather limited and we turned to the well studied nitration reaction, which gives rather high yields of both mono- and dinitro derivatives of (I)-(III) [3].

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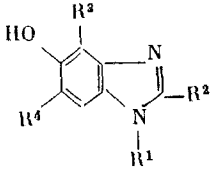
TABLE 1. Physicochemical Indices of Sulfonic Acid and Nitro Derivatives of 5(6)-Hydroxybenzimidazoles

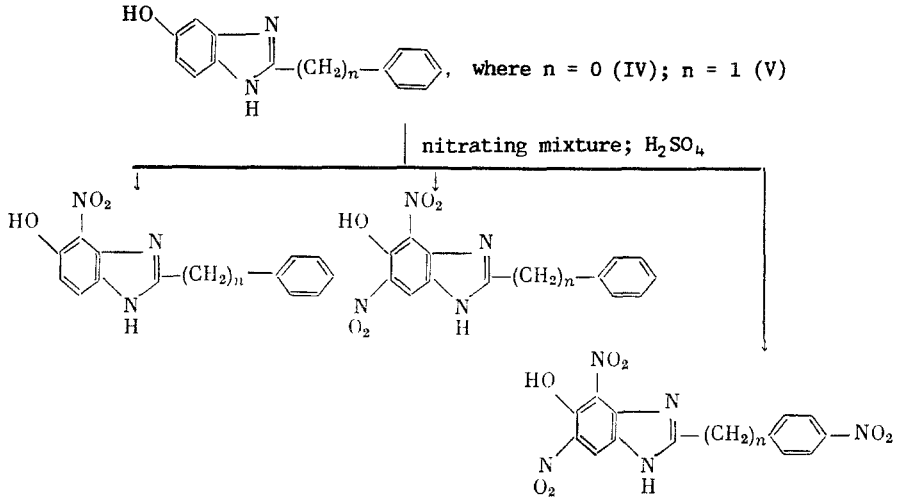


R^1	R^2	R^3	R^4	Yield, %	mp, °C	Found / Calculated, % C	Found / Calculated, % H	Chemical formula	Solvent
H	H	SO_3H	H	78,8	315–318	38,74 / 39,26	2,67 / 2,83	$C_7H_6N_2O_4S$	NaOD/D_2O
H	Me	SO_3H	H	63,1	300–302	41,55 / 42,11	3,26 / 3,54	$C_8H_8N_2O_4S$	NaOD/D_2O
Et	Me	SO_3H	H	83,6	347–350	46,15 / 46,87	4,55 / 4,73	$C_{10}H_{12}N_2O_4S$	NaOD/D_2O
H	Ph	SO_3H	H	86,2	355–360	53,28 / 53,79	3,72 / 3,48	$C_{13}H_{10}N_2O_4S$	NaOD/D_2O
H	Bzl	SO_3H	H	65,8	330–333	55,68 / 55,26	3,54 / 3,98	$C_{14}H_{12}N_2O_4S$	NaOD/D_2O
H	Ph	NO_2	H	72,2	230–231	60,88 / 61,17	3,26 / 3,56	$C_{13}H_9N_3O_3$	DMSO-d_6
H	Ph	NO_2	NO_2	42,2	256–258	52,16 / 52,00	2,77 / 2,69	$C_{13}H_8N_4O_5$	DMSO-d_6
H	(p-NO_2–) Ph	NO_2	NO_2	74,0	220–222	45,44 / 45,22	2,24 / 2,05	$C_{13}H_7N_5O_7$	DMSO-d_6
H	Bzl	NO_2	H	58,3	203–205	62,82 / 62,44	4,33 / 4,13	$C_{14}H_{11}N_3O_3$	DMSO-d_6
H	Bzl	NO_2	NO_2	39,0	213–215	53,79 / 53,50	3,41 / 3,21	$C_{14}H_{10}N_4O_5$	DMSO-d_6
H	(p-NO_2–) Bzl	NO_2	NO_2	60,5	191–193	46,26 / 46,80	2,83 / 2,53	$C_{14}H_9N_5O_7$	DMSO-d_6

TABLE 1 (continued)

R^1	R^2	R^3	R^4	δ, ppm							
				2-CH_3	2-C_6H_5	2-CH_2-C_6H_5	1-CH_2-CH_3	H^6	H^7	H^2	$J_{H^6H^7}$, Hz
H	H	SO_3H	H	–	–	–		7,83 d (1H)	7,89 d (1H)	6,74 s (1H)	9,0
H	Me	SO_3H	H	2,49 s (3H)	–	–		7,95 d (1H)	7,98 d (1H)	–	9,0
Et	Me	SO_3H	H	2,57 s (3H)	–	–	1,32 t (3H) 4,07 q (2H)	7,85 d (1H)	7,89 d (1H)	–	9,0
H	Ph	SO_3H	H	–	7,3–8,4 m (7H)	–	–	7,3–8,4 m (7H)		–	–
H	Bzl	SO_3H	H	–	–	3,37 s (2H) 7,3–8,0 m (7H)	–	7,3–8,0 m (7H)		–	–
H	Ph	NO_2	H	–	7,40 m (3H) 8,07 m (2H)	–	–	6,90 d (1H)	7,67 d (1H)	–	9,0
H	Ph	NO_2	NO_2	–	7,50 m (3H) 8,20 m (2H)	–	–	–	8,30 s (1H)	–	–
H	(p-NO_2–) Ph	NO_2	NO_2	–	7,5–8,7 m (4H)	–	–	–	8,20 s (1H)	–	–
H	Bzl	NO_2	H	–	–	4,12 s (2H) 7,10 m (5H)	–	6,68 d (1H)	7,50 d (1H)	–	9,0
H	Bzl	NO_2	NO_2	–	–	4,24 s (2H) 7,20 m (5H)	–	–	8,32 s (1H)	–	–
H	(p-NO_2–) Bzl	NO_2	NO_2	–	–	4,12 s (2H) 7,55 m (2H) 8,10 m (2H)	–	–	8,43 s (1H)	–	–

The use of equivalent amounts of a nitrating mixture in concentrated sulfuric acid with cooling gave mono- and disubstitution in the ring system in (IV) and (V). Trisubstitution in the ring system could not be carried out even by the action of a 10-fold excess of the nitrating mixture on (IV) and (V); the third nitro group substitutes only into the para position of the phenyl and benzyl groups of these substrates.



The use of more vigorous conditions, namely a 10-20-fold excess of the nitrating mixture at 90°C for 4-5 h, leads to the formation of a mixture of oxidative cleavage products. Presumably, the benzene ring of the benzimidazole system dissociates with the formation of carboxylic acids since these mixtures are highly soluble in water and ethanol but insoluble in acetone.

Comparison of the data on the nitration of 2-aryl-3-hydroxypyridines [8] with the corresponding data for (IV) and (V) again indicates the greater reactivity of the hydroxybenzimidazole system in comparison with the hydroxypyridine and analogs having aromatic substituents at C^2 in electrophilic substitution reactions.

Comparison of the conditions and reaction times for the sulfonation and nitration of 5(6)-hydroxybenzimidazole and its derivatives, and the yields and purity of the final products indicates that an aromatic substituent at C^2, in contrast to an alkyl group, enhances the reactivity of the benzimidazole system in electrophilic substitution although the presence of a methylene bridge somewhat diminishes this property.

The structures of the sulfonic acid derivatives obtained from (I)-(V) and the nitro derivatives obtained from (IV) and (V) were confirmed by PMR spectroscopy. The downfield region lacks a signal from H^4, while the signals for H^6 and H^7 are doublets with $J_{6,7} = 9.0$ Hz (Table 1).

EXPERIMENTAL

The PMR spectra of the sulfonic acid and nitro derivatives of (I)-(V) were taken on a Varian T-60 spectrometer with $NaOD/D_2O$ or $(CD_3)_2SO$ as the solvents with tert-butyl alcohol as the internal standard. The chemical shifts are given relative to TMS.

Sulfonation of (I)-(V). A sample of 5 ml 20% oleum was added to a solution of 0.005 mole (I)-(V) in 10 ml concentrated sulfuric acid and heated for 3.0-4.5 h at 170-190°C. The sulfonic acid derivative of the specific 5(6)-hydroxybenzimidazole was separated by pouring the cooled reaction mass into ice or by the addition of sodium bicarbonate to bring the solution pH to 3.0-3.5. The products were recrystallized from aqueous ethanol.

Nitration of (IV) and (V). An equimolar amount of a nitrating mixture was added to a solution of 0.003 mole (IV) or (V) in 10 ml concentrated sulfuric acid. After 0.5-1.5 h, the reaction mass was poured into ice water. The precipitate was separated, washed with water, and recrystallized from aqueous ethanol.

The physicochemical properties and PMR spectral data of the products obtained are given in Table 1.

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IMPROVED METHOD FOR THE PREPARATION OF A RUTHENIUM CARBONYLCARBIDE CLUSTER, $Ru_6C(CO)_{17}$

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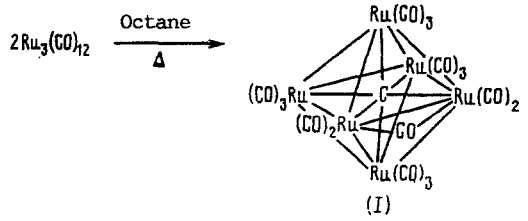
An improved method has been developed for the synthesis of the ruthenium carbonylcarbide cluster $Ru_6C(CO)_{17}$ by heating $Ru_3(CO)_{12}$ in octane at reflux.

$Ru_6C(CO)_{17}$ (I), which is an octahedral ruthenium carbonylcarbide cluster, is one of the first reported transition metal carbonylcarbide clusters. This cluster holds great interest in light of its variegated reactivity [1] and potential catalytic activity [2]. The extensive study of cluster (I) has been hindered due to the lack of a convenient method for its preparation. Heating $Ru_3(CO)_{12}$ in dibutyl ether at reflux gives (I) in 22-30% yield [2, 3], but isolation of the pure product requires chromatography to eliminate ruthenium hydrides formed as reaction by-products. The synthetic method based on the reaction of $Ru_3(CO)_{12}$ with ethylene at 150°C and 30 atm, although providing (I) in yields up to 70% [4], leads to a mixture of products. Repetition of this method [2] gave (I) in a yield of only 43%.

We have markedly simplified the synthesis of cluster (I). The yield of (I) upon heating $Ru_3(CO)_{12}$ in thoroughly deoxygenated octane at reflux is increased to 55% and the product is formed without impurities, thereby eliminating the need for chromatographic purification.



(I)

We studied the possibility of substituting three CO ligands by arenes in order to obtain π-complexes of the type (arene)$Ru_6C(CO)_{14}$ obtained previously in only about 15% yield upon heating $Ru_3(CO)_{12}$ at reflux in aromatic hydrocarbons [5] or by using not readily available starting reagents [6]. We should note that unsubstituted cluster (I) also always separates out in significant yield upon heating $Ru_3(CO)_{12}$ in mesitylene at reflux along with the arene cluster. Thus, we may propose that (I) is an intermediate in the formation of (II).

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