The Guerbet Reaction Applied to Diodone

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In 1920 Guerbet\(^1\) introduced a general test for the aromatic nucleus. The reaction scheme is given in the following 3 steps. An aromatic compound, represented here by benzene, is treated with fuming nitric acid. The nitronium ion present in the fuming nitric acid attacks the nucleus in an electrophilic displacement reaction (step 1). In step 2 the nitro-product is reduced with zinc in hydrochloric acid medium. In the third and final step the aromatic amine is diazotized and immediately coupled with 2-naphthol to give a deep orange-red diazo-compound.

\[\text{Scheme 1. Scheme of the Guerbet reaction}\]

1. \(\text{C}_6\text{H}_5 + \text{NO}_2^+ \rightarrow \text{C}_6\text{H}_4\text{NO}_2 + \text{H}^+\)
2. \(\text{C}_6\text{H}_4\text{NO}_2 \xrightarrow{\text{Zn/HCl}} \text{C}_6\text{H}_4\text{NH}_2\)
3. \(\text{C}_6\text{H}_4\text{NH}_2 \xrightarrow{\text{NaNO}_2/\text{HCl}} \text{C}_6\text{H}_4\text{N}=\text{N}\)

reddish orange
The Guerbet reaction can be blocked by deactivation of the aromatic nucleus, for instance by electron-withdrawing substituents, or by occupation of all the substitution sites by inactive groups or by groups causing steric hindrance.

When the nitration is successful, the subsequent reaction steps proceed smoothly, and a positive test is obtained.

We have applied the Guerbet reaction to diodone acid (3,5-diodo-4-oxo-1,4-dihydro-1-pyridyl-acetic acid) and found the test positive. The ring in diodone acid can be considered to be aromatic, but less aromatic than benzene. This prompted us to study the Guerbet reaction in more detail. Diodone (also called iodopyracet) is the diethanolamine salt of diodone acid. Diodone is used as an X-ray contrast substance. It dissolves readily in water and its solutions are used in angiography, pyelography and urography. Diodone and diodone acid were found to give the same colour in the Guerbet reaction. We chose diodone acid for this study.

**Experimental**

**Apparatus**

The mass spectra of compounds A1 and B1 were obtained with an AEI MS-902 mass spectrometer. Accurate mass measurements were made on the ions mentioned in the text. The mass spectra of all other compounds were obtained with an LKB 2091-2130 gas chromatography-mass spectrometer-computer system. All samples were introduced through a heated direct insertion probe. Spectra were recorded at 70 eV, source temperature 180° C.

**Reagents and Materials**

Diodone, obtained from Diodrast® ampoules.
Diodone acid, May & Baker.
TLC-plates, Merck, silica gel 60, F254, thickness 0.25 mm.
Chromatography column 3 cm in diameter, 25 cm long, packed with Merck silica gel GF-254 (type 60).