鎝氧六甲基丙烯胺肟非鏡像立體異構物酸分解之動力學研究

蔡長書

慈濟技術學院放射技術系

摘要

Ceretec（U.K. Amersham Intl plc 製乾粉藥劑）雖已廣泛的使用於局部腦血流造影之診斷，但在臨床上的使用仍有很大的缺點，配劑後套組水溶液主成分 99mTcO-d,1-HMPAO 極不穩定,其濃度會隨時間變化而減少。不少文獻亦會針對此一不穩定性原因做深入研究和探討，然而至今尚無決定性之結論。

本文嘗試採用酸分解之動力研究方法。首先合成大量的 99TcO-HMPAO 非鏡像立體解異構物錯鹽，並在 25±0.1℃下以不同強度的酸，測定該錯鹽在溶液中的分解速率，並以所得動力學數據來判斷 99TcO-d,1-HMPAO 的體外穩定特性。根據本文所得結果，99TcO-d,1-HMPAO 及其另一光學異構物 99TcO-meso-HMPAO 兩者在鹼性（1.0M NaOH）溶液中吸收度變化很小極為穩定，在６小時內鎝物種濃度並不隨時間的變化而減小。但在不同濃度之 HC1O4 酸性條件下，99TcO-d, 1-HMPAO 與 99TcO-meso-HMPAO 的酸分解速率遵循一級反應。其酸分解速率反應式可以下式表示 ln〔99TcO-HMPAO〕t ＝ｋ obsd〔99TcO-HMPAO〕0＝ｋ1〔H+〕〔99TcO-HMPAO〕0,ｋ1 代表ｋd,1 及ｋmeso,且其直分別為 8.95 與 1.39。如果在極性較高溶媒中進行反應，於紫外光－可見光光譜中，可發現在 349 毫微米處迅速出現一新的吸收波峰，此一發現可能有助於解釋 99TcO-d,1-HMPAO 在不穩定分解過程中產生一新的鎝物種之反應模式，但其本質仍待進一步研究與確認。此外，溫度效應的測試結果，在 25±1℃，30±1℃，35±1℃及 40±1℃等不同條件下，10-4 M 99TcO－HMPAO 非鏡像立體異構物之氯仿溶液（5×10-2 M），可獲得 99TcO-d,1-HMPAO 與 99TcO-meso-HMPAO 之活性能分別為 64.5 kj / mole 與 72.6 kj / mole。

關鍵字：動力學研究，酸分解，鎝氧六甲基丙烯胺肟非鏡像立體異構物

Kinetic Studies on the Acid Decomposition of 99TcO-HMPAO Diastereoisomers

Chang-Shu Tsai

Department of Radiological Technology Tzu Chi College of Technology

Abstract

The Ceretec（kit production of Amersham International plc Buckinghamshire, U.K.）has been widely employed for the diagnosis of regional cerebral blood flow（rCBF）in the patient with neurological disorders. However, this agent also showed vital drawback, i. e. the concentration of 99mTcO-d,1-HMPAO in the reconstituted solution decreases with time. A number of workers have devoted their efforts to explore the causes of the instability of the reconstituted solution. So far not much convincing answer has been obtained.

In an attempt to kinetic studies on the subject large amount of d,1-isomer of HMPAO were prepared and large quantity of 99TcO-d,1-HMPAO complex were synthesized. The decomposition rate of the complexes were measured under various conditions at 25±1℃. With all kinetic data collected one get a better understanding about the in vitro stability of 99mTcO-d,1-HMPAO. It is clearly shown that no reaction has taken place between 99TcO-HMPAO and strong base solution within 6 hours. Kinetic studies on the acid decomposition conditions showed that the first order reaction were obeyed for the decomposition rate of both 99TcO-HMPAO diastereoisomers. Observed decomposition rate constant（k obsd）is dependent on〔H+〕for 99TcO-HMPAO diasteroisomers. It can be expressed ln〔99TcO-HMPAO〕t＝k obsd〔99TcO-HMPAO〕o＝k 1〔H+〕〔99TcO-HMPAO〕0, and k 1may be defined and termed k d,1 for d,1-isomer and k meso for meso-isomer,

respectively. It was found that the decomposition rate constant（ｋd,1）under the acid concetration were 8.95 for 99TcO-d,1-HMPAO and 1.39 for 99TcO-meso-HMPAO, respectively. In homogeneous system, it was observed that a new peak（at 394 nm）of unknown Tc-species has appeared in UV-vis spectra in more polar solvent system, which may be helpful in understanding the pattern of the instability reaction. Effect of temperature of decompose rate of ，10-4 M 99TcO－HMPAO diastereoisomers in CHC13 with 5×10-2 M of HC1O3 solution. The activation energy（Ea）were 64.5 KJ / mole for 99TcO-d,1-HMPAO and 72.6 KJ / mole for 99TcO-meso-HMPAO, respectively.

Keywords：kinetic study, acid decomposition, 99TcO-HMPAO diastereoisomers