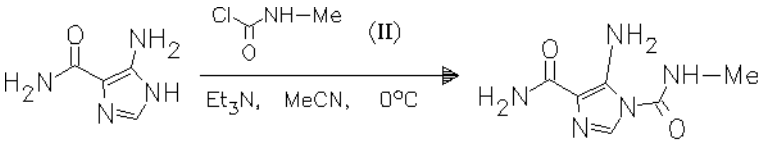
other 6-membered heterocycles (with 3 or more heteroatoms)

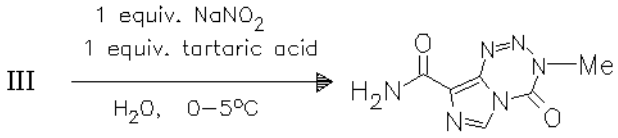
R 0670

09 - 161

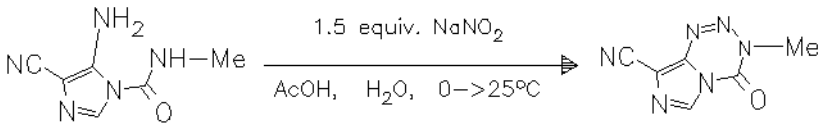
Antitumor Imidazotetrazines. Part 35. New Synthetic Routes to the Antitumor Drug Temozolomide. — Some new synthetic strategies to the title drug (IV) are developed, avoiding the use of methyl isocyanate (MIC) and employing optimized conditions for the cyclization of appropriately substituted imidazoles (III) and (V). Compounds (III) and (VI) are prepared from imidazole (I) and chloride (II) or from imidazole (V) and $NaNO_2$, resp., with lower yields (71%, 23%) than those obtained by methods using MIC (92%, 52%). Selective hydrolysis of the nitrile function of imidazotetrazine (VI) gives the salt (VII), which dissoziates in H_2O or DMSO to pure target compound (IV). — (STEVENS, M F. G.; ET AL.; J. Org. Chem. 62 (1997) 21, 7288-7294; Dep. Pharm. Sci., Univ. Nottingham, Nottingham NG7 2RD, UK; EN)



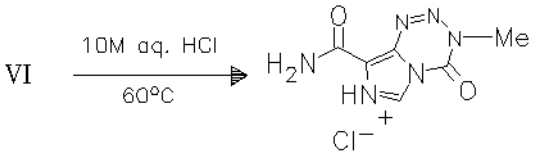
I III 71%



IV 45%



V VI 23%



VII 65%