

Application
 Data Sheet

No. 18B

GCMS

Gas Chromatograph Mass Spectrometer

 Analysis of Potential Genotoxic
 Impurities in Active Pharmaceutical
 Ingredients

Chemicals such as methanesulfonic acid (mesylate), benzenesulfonic acid (besilate), and *p*-toluenesulfonic acid (tosylate) are used in the process of synthesizing active pharmaceutical ingredients. These compounds are likely to generate sulfonic acid ester (Fig. 1) as a reaction byproduct. These compounds are known as potential genotoxic impurities (PGI) and are a significant cause for concern among pharmaceutical manufacturers. This article introduces the analysis of sulfonic acid esters utilizing the GCMS-QP2010 Ultra.

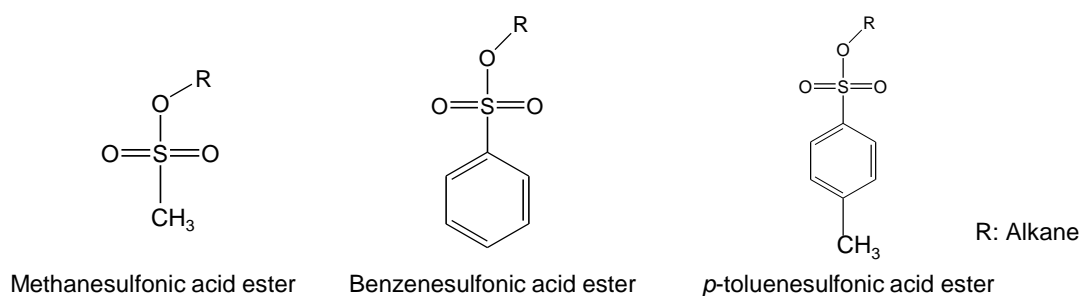


Fig. 1: Structural Formulas for Sulfonic Acid Esters

Analysis Conditions

FASST (Fast Automated Scan/SIM Type), which is capable of simultaneous Scan and SIM measurements, was used as the measurement mode. The analysis conditions are shown in Table 1, while the SIM measurement monitoring *m/z* values are shown in Table 2.

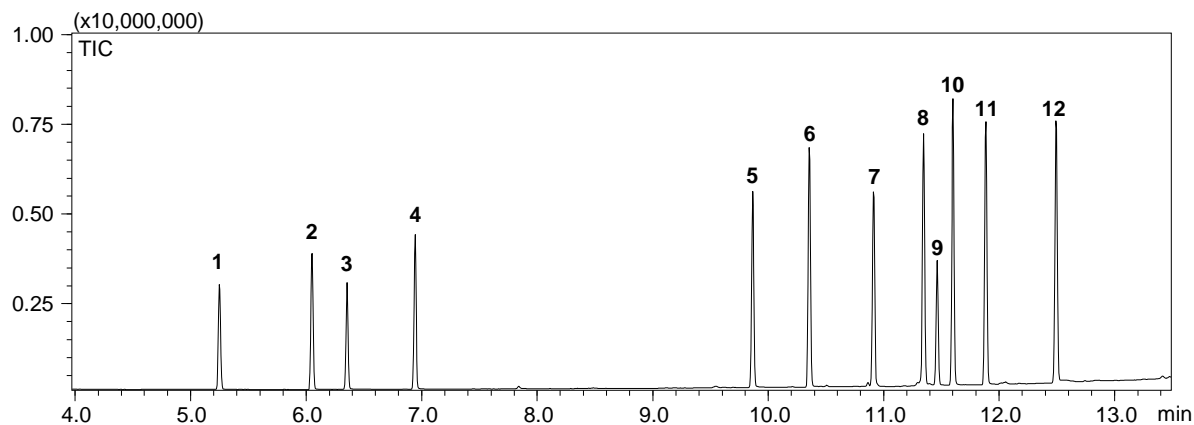
Table 1: Analysis Conditions

GC-MS	: GCMS-QP2010 Ultra		
Column	: Rtx-200 (30 mL X 0.25 mm I.D., df=0.25 μm, Restek P/N: 15023)		
Glass insert	: Deactivated split liner with wool (P/N: 225-20803-01)		
[GC]		[MS]	
Injection temp.	: 280°C	Interface temp.	: 280°C
Column oven temp.	: 70°C (2 min) → (15°C/min) → 320°C (3min)	Ion source temp.	: 230°C
Injection mode	: Split	Solvent cut time	: 1.5 min
Carrier gas	: He	Tuning mode	: High sensitivity
Flow control mode	: Linear velocity (40 cm/sec)	Acquisition mode	: FASST(Scan/SIM measurements)
Purge flow rate	: 3.0 mL/min	Scan mass range	: <i>m/z</i> 40 - 330
Split ratio	: 10	Scan event time	: 0.1 sec
Injection volume	: 1.0 μL	SIM monitoring <i>m/z</i>	: See Table 2
		SIM event time	: 0.3 sec

 Table 2: Monitoring *m/z* for Target Compounds

	Monitoring <i>m/z</i>		Monitoring <i>m/z</i>
Methyl methanesulfonate	80, 95	Methyl <i>p</i> -toluenesulfonate	155, 186
Ethyl methanesulfonate	109, 97	Ethyl <i>p</i> -toluenesulfonate	155, 200
Isopropyl methanesulfonate	123, 79	Isopropyl <i>p</i> -toluenesulfonate	172, 155
<i>n</i> -propyl methanesulfonate	109, 97	<i>n</i> -propyl <i>p</i> -toluenesulfonate	155, 172
Methyl benzenesulfonate	172, 141	Butyl <i>p</i> -toluenesulfonate	173, 91
Ethyl benzenesulfonate	141, 186		
Butyl benzenesulfonate	141, 159		

Analysis Results



ID	Compound Name	Retention Time	ID	Compound Name	Retention Time
1	Methyl methanesulfonate	5.252	7	Methyl <i>p</i> -toluenesulfonate	10.911
2	Ethyl methanesulfonate	6.052	8	Ethyl <i>p</i> -toluenesulfonate	11.345
3	Isopropyl methanesulfonate	6.355	9	Isopropyl <i>p</i> -toluenesulfonate	11.462
4	<i>n</i> -propyl methanesulfonate	6.944	10	Butyl benzenesulfonate	11.598
5	Methyl benzenesulfonate	9.865	11	<i>n</i> -propyl <i>p</i> -toluenesulfonate	11.883
6	Ethyl benzenesulfonate	10.356	12	Butyl <i>p</i> -toluenesulfonate	12.491

Fig. 2: Total Ion Current Chromatogram

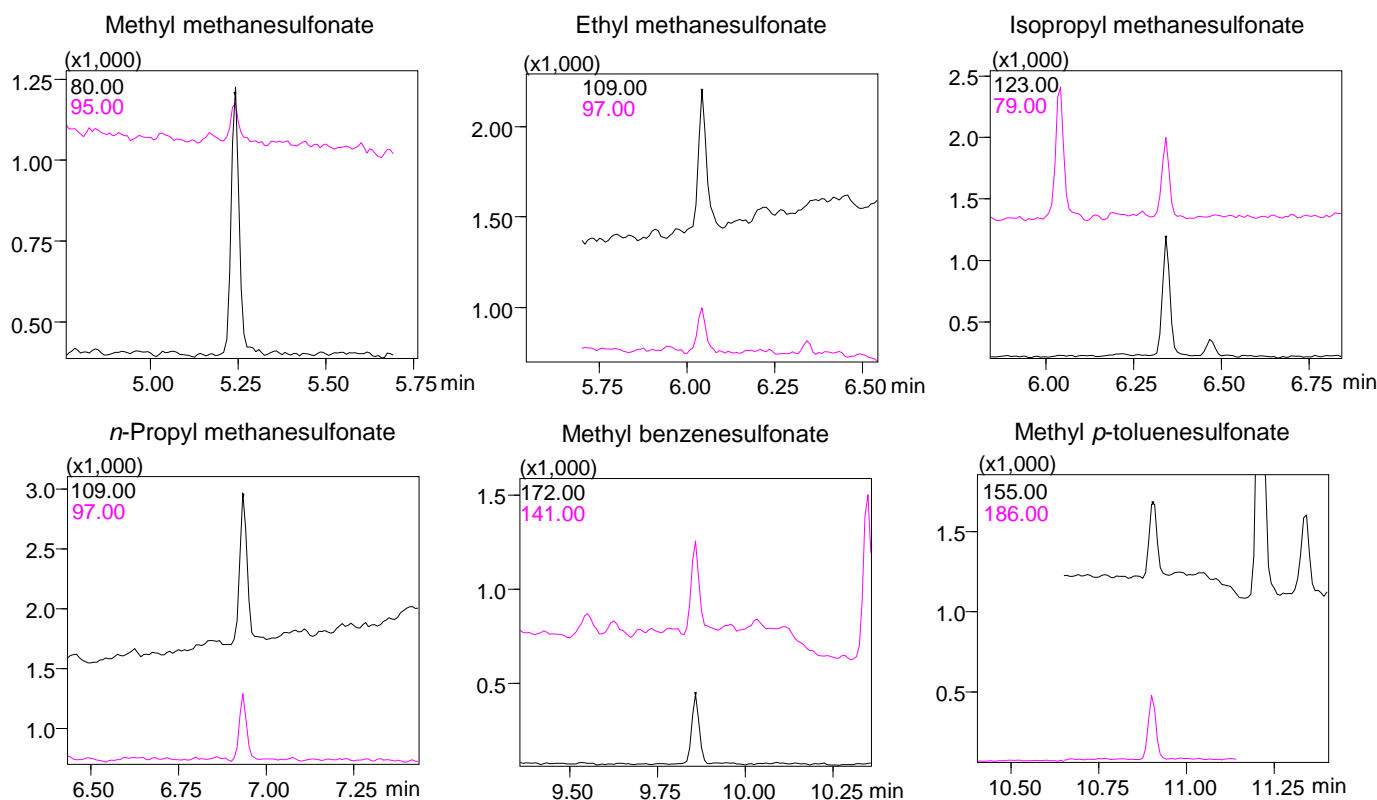


Fig. 3: Mass Chromatograms for Sulfonic Acid Esters

The standard concentration is 10 ng/mL. It is equivalent to 1 ng/mg in active pharmaceutical ingredients when diluted 100 times in pretreatment with a recovery ratio of 100 %.

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