

Supplementary Information

Novel high yielding route for the synthesis of Melphalan dimer impurity G

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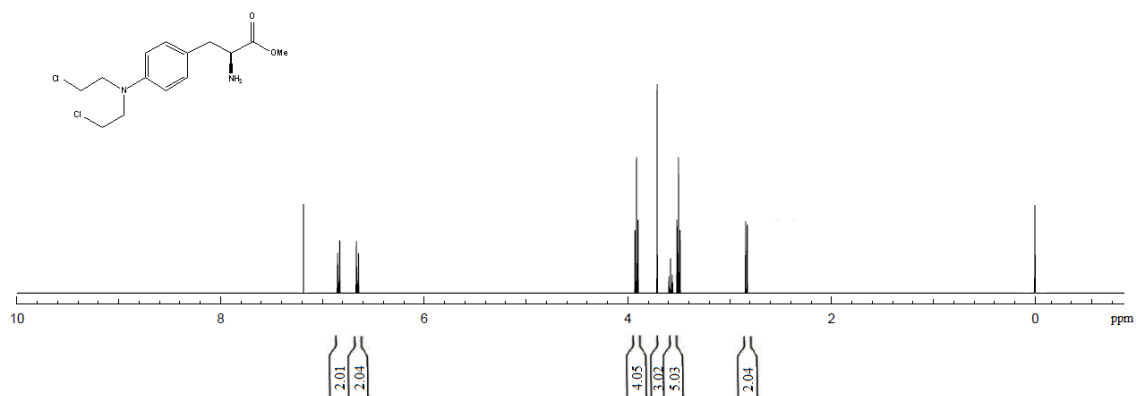


Fig. S1 — ^1H NMR spectrum of methyl-(S)-2-amino-3-(4-(di(2-chloroethyl)amino)phenyl)propanoate (10)

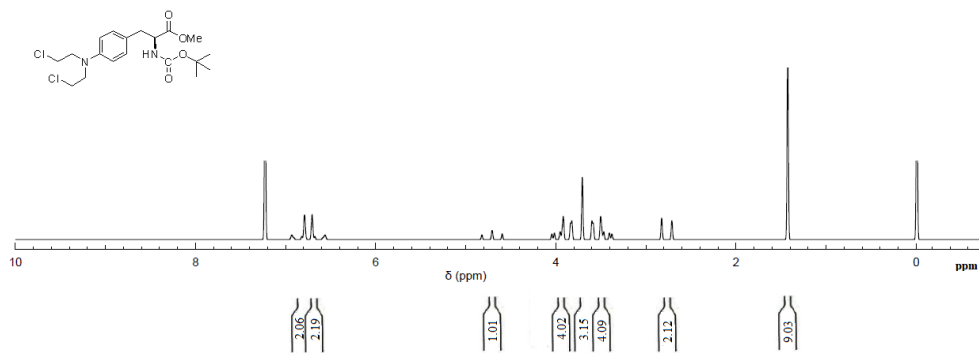


Fig. S2 — ^1H NMR spectrum of Methyl-(S)-3-(4-(di(2-chloroethyl)amino)phenyl)-2-((tert-butoxycarbonyl)amino)propanoate (11)

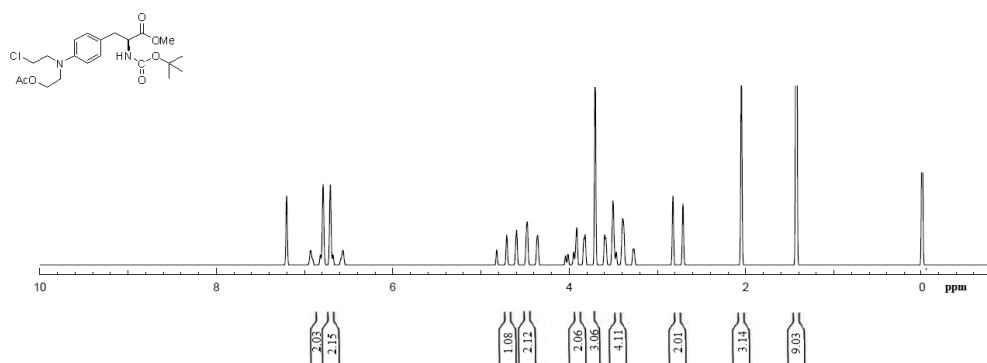


Fig. S3 — ^1H NMR spectrum of methyl-(S)-3-(4-((2-acetoxyethyl)(2-chloroethyl)amino)phenyl)-2-((tert-butoxycarbonyl)amino)propanoate (12)

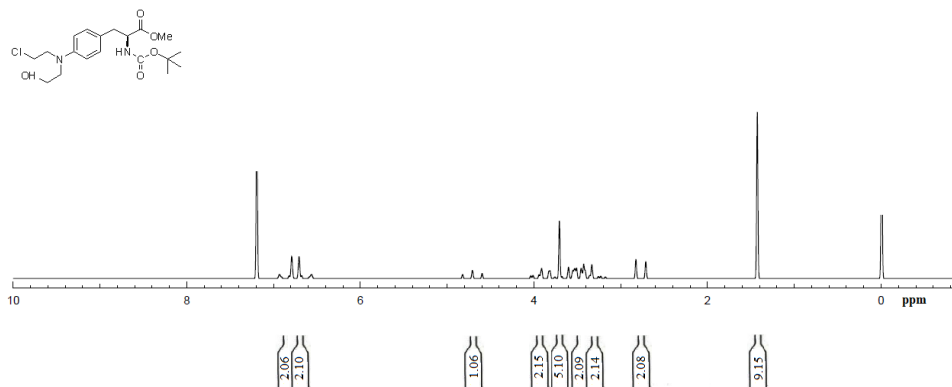


Fig. S4 — ^1H NMR spectrum of methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((2-chloroethyl)(2-hydroxyethyl)amino)phenyl)propanoate (13)

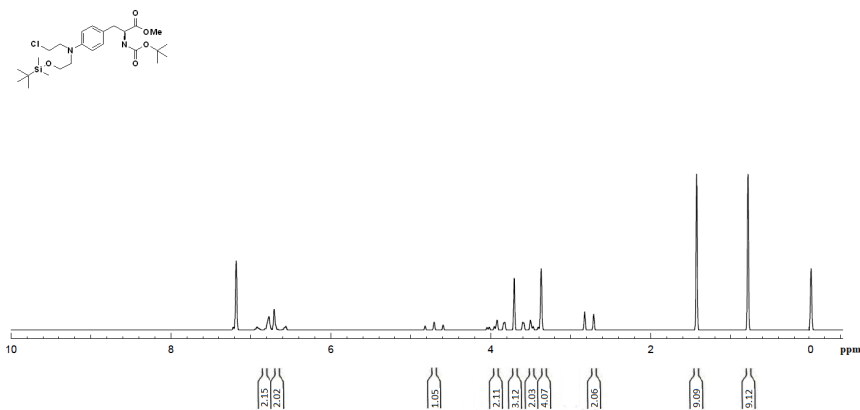


Fig. S5 — ^1H NMR spectrum of methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((2-((tert-butyl)dimethylsilyloxy)ethyl)(2-chloroethyl)amino)phenyl)propanoate (14)

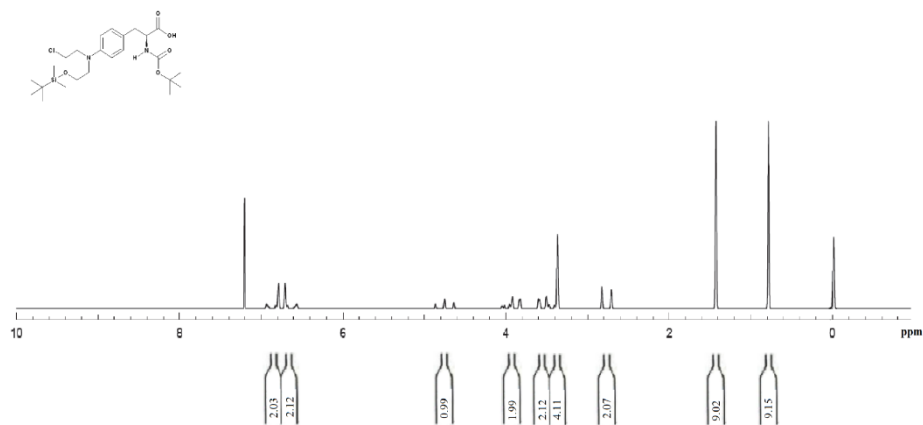


Fig. S6 — ¹H NMR spectrum of (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((2-((tert-butyl dimethylsilyl)oxy)ethyl)(2-chloroethyl)amino)phenyl)propanoic acid (15)

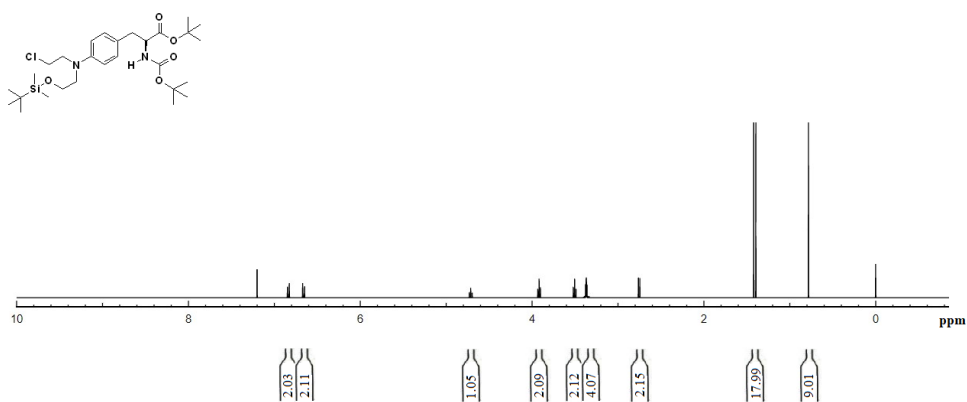


Fig. S7 — ¹H NMR spectrum of isopropyl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((2-((tert-butyl dimethylsilyl)oxy)ethyl)(2-chloroethyl)amino)phenyl)propanoate (16)

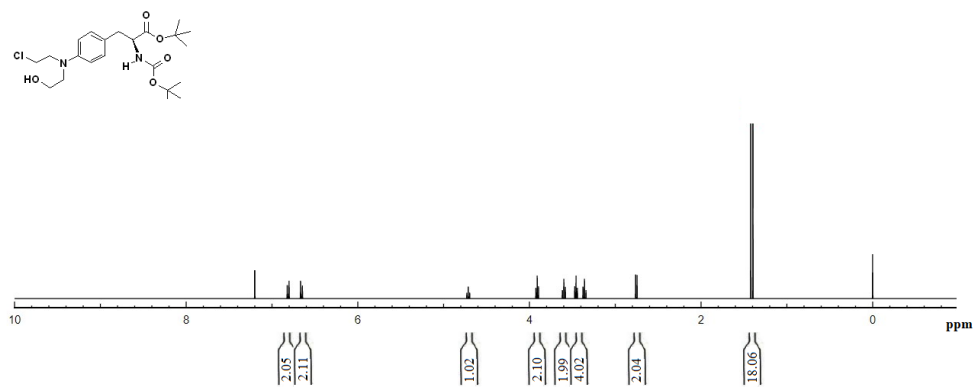


Fig. S8 — ¹H NMR spectrum of isopropyl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((2-chloroethyl)(2-hydroxyethyl)amino)phenyl)propanoate (17)

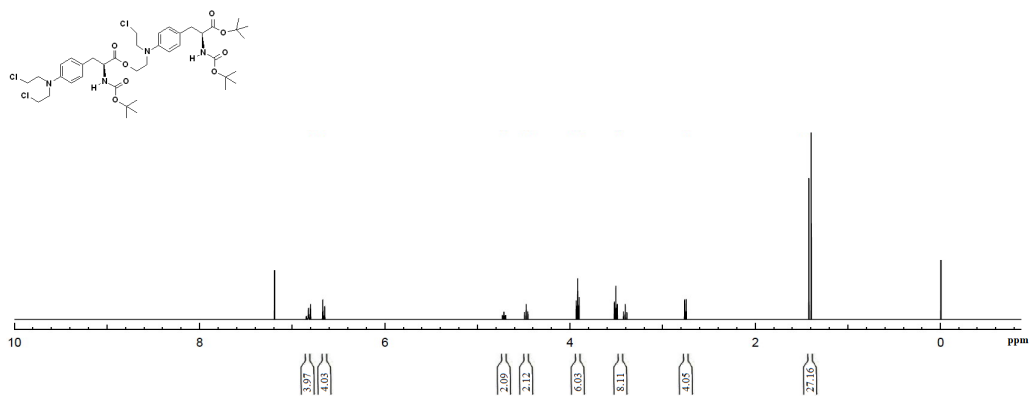


Fig. S9 — ¹H NMR spectrum of 2-((4-((S)-2-((tert-butoxycarbonyl)amino)-3-isopropoxy-3-oxopropyl)phenyl)(2-chloroethyl)amino)ethyl (S)-3-(4-(bis(2-chloroethyl)amino)phenyl)-2-((tert-butoxycarbonyl)amino)propanoate (19)

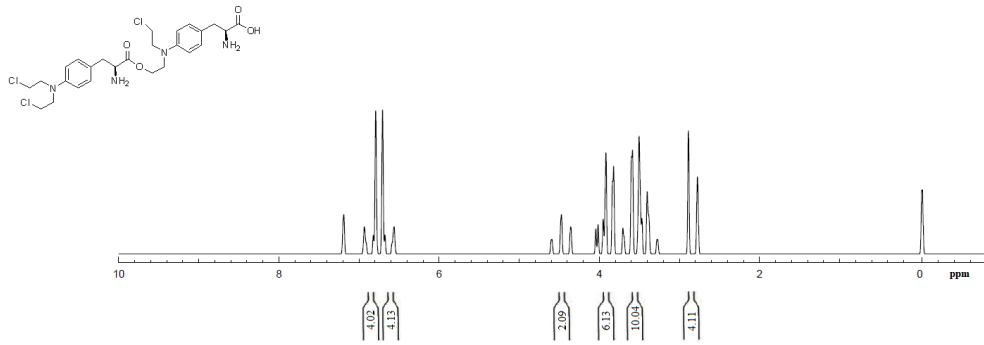
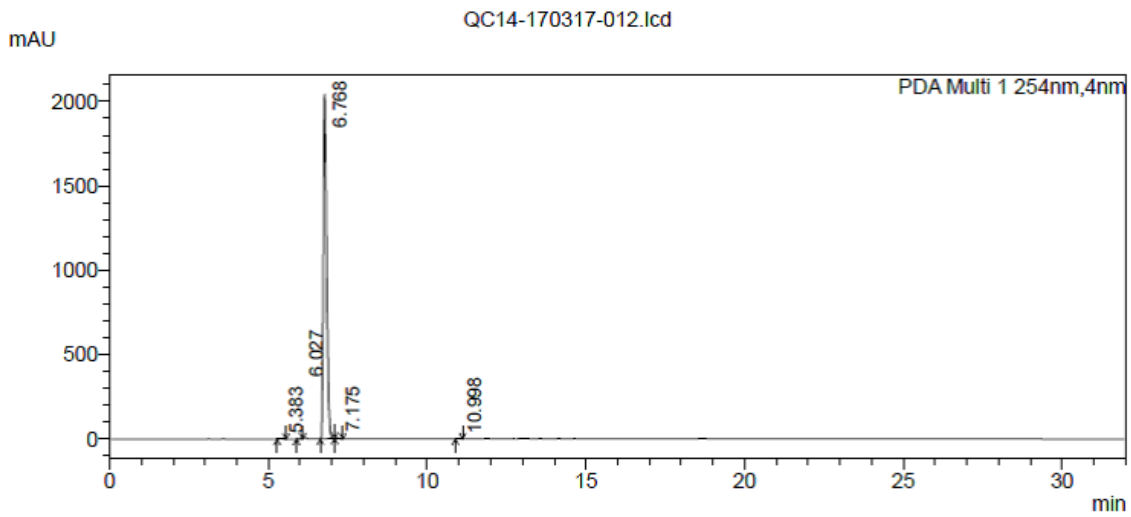


Fig. S10 — ¹H NMR spectrum of (S)-2-amino-3-(4-((2-(((S)-2-amino-3-(4-(bis(2-chloroethyl)amino)phenyl)propanoyl)oxy)ethyl)(2-chloroethyl)amino)phenyl)propanoic acid. 2,2,2-trifluoroacetic acid (20)

<Chromatogram>



<Peak Table>

QC14-170317-012.lcd

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	5.383	13859	0.096	2433
2	6.027	6973	0.048	1030
3	6.768	14369275	99.593	2038261
4	7.175	34141	0.237	6212
5	10.998	3689	0.026	563
Total		14427937	100.000	2048499

Fig. S11 — HPLC data of Melphalan dimer impurity G

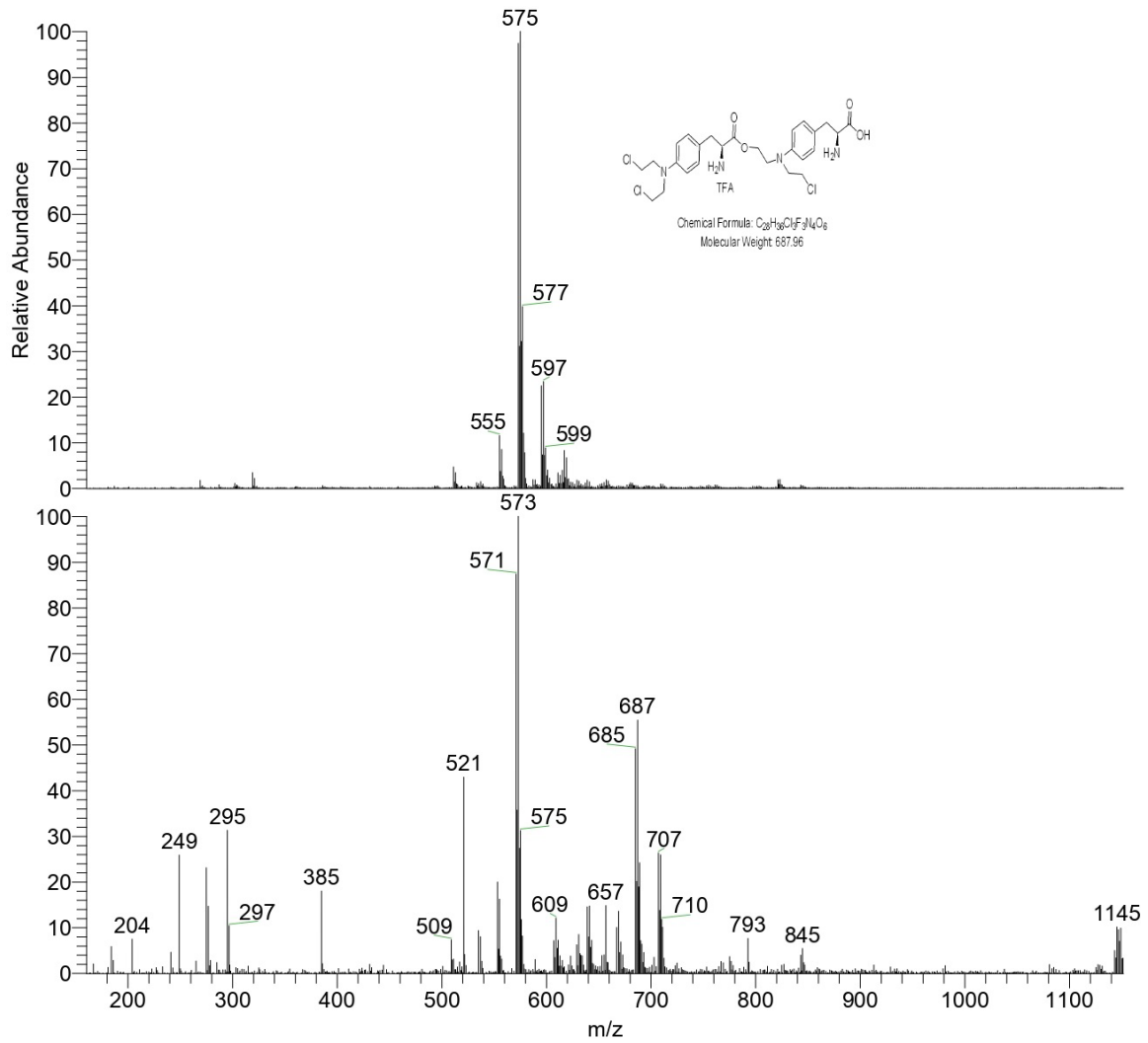


Fig. S12 — Mass spectra of Melphalan dimer impurity G

Bruker NMR 400MHz

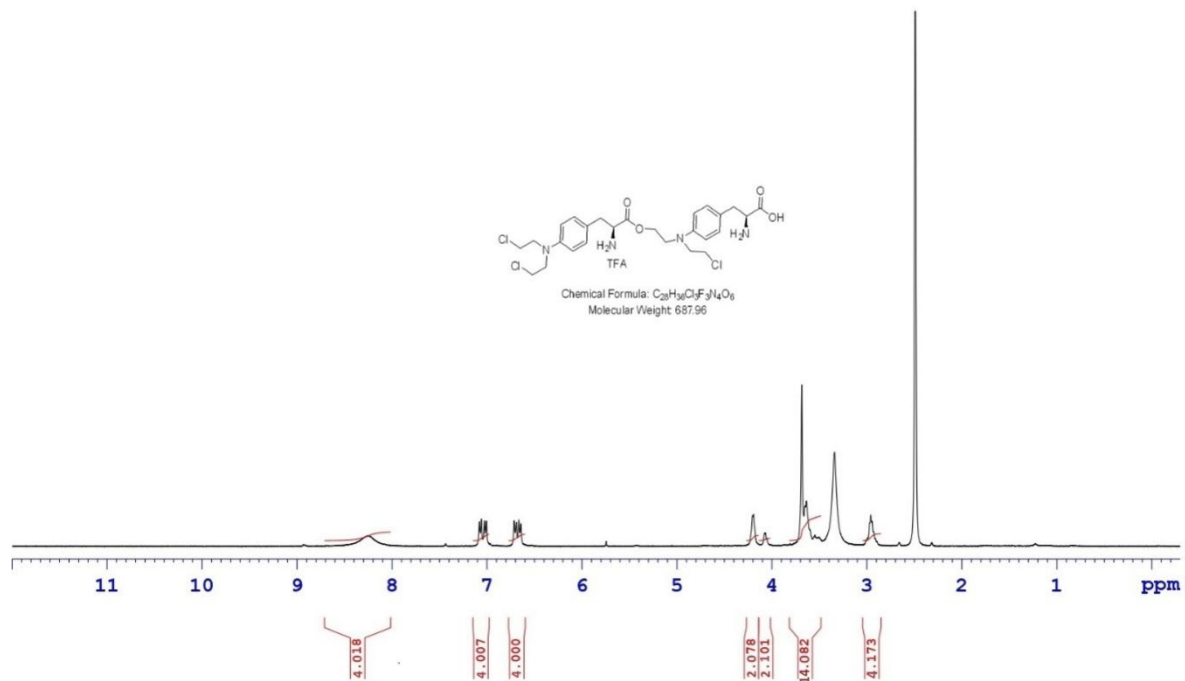


Fig. S13 — ¹H NMR spectrum of Melphalan dimer impurity G

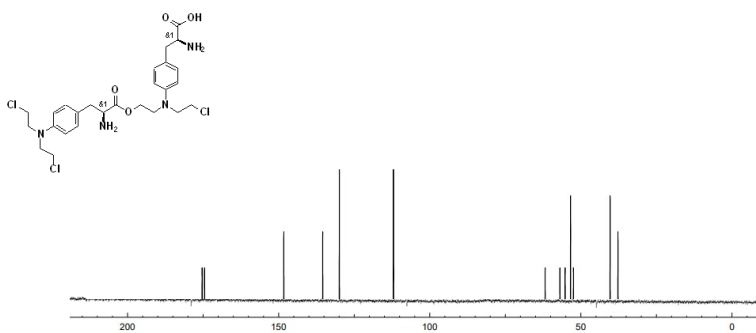


Fig. S14 — ¹³C NMR spectrum of Melphalan dimer impurity G