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Synthesis of Novel Spin Labeled Daunomycin Derivatives

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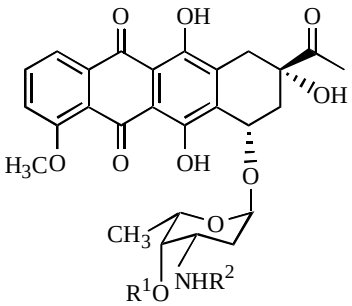
Abstract: Three spin labeled daunomycin derivatives **2-4** were synthesized and their biological activities were tested against mouse leukemia L1210 and human liver cancer BEL-7402 cells *in vitro*.

Keywords: Spin labeled daunomycin derivatives, antitumor activity, synthesis.

The anthracycline antibiotics daunomycin **1** is clinically useful antineoplastic agents, with a broad spectrum of activity. However, it is hampered by a number of undesirable side effects, especially serious cardiotoxicity and this stimulated the search for new anthracyclines with improved pharmacological profiles[1-3]. In our group, nitroxy radicals were first introduced to daunomycin and two spin labeled daunomycin derivatives have been reported recently[4]. Now we reported other three new spin labeled daunomycin derivatives **2-4**. Their antitumor activity against mouse leukemia L1210 and human liver cancer BEL-7402 cells were evaluated *in vitro*.

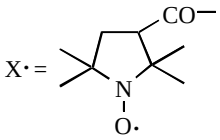


1. $R^1=R^2=H$

2. $R^1=H$, $R^2=X\cdot$

3. $R^1=R^2=X\cdot$

4. $R^1=X\cdot$, $R^2=COCF_3$



5. $\dot{X}OH$

6. $\dot{X}OCOOC_2H_5$

Compounds **2** and **3** were synthesized by condensing daunomycin **1** with **5** (molar ratio **1**:**5**=1:1.2) in the solvent of dichloromethane with DCC and DMAP as catalysts at room temperature for 18 h in the yields of 64.1% and 10.1%, respectively. Compound **4** was obtained by reaction of N-trifluoroacetyldaunomycin with **6** in 40.9% overall yield. Their structures were confirmed by IR, Elemental analysis, ESR and MS. Main spectra data of **2-4** are listed in **Table 1**.

The anticancer activities of compounds **2-4** against mouse leukemia L1210 and human liver cancer BEL-7402 cells *in vitro* were evaluated. The biological activity data

are listed in **Table 2**. As the results shown, they all possessed antitumor activity and compound **4** exhibited comparable activity to **1** in human liver cancer BEL-7402. Further experiments and biological evaluations of these compounds are in progress.

Table 1 m.p. and spectra data of **2-4***

Compd.	m.p.(°C)	IR(KBr,cm^{-1})	MS(APCI, negative)
2	137-139	3422,1716,1654,1617,	694(M+), 380, 347
3	157(dec.)	3348,1715,1652,1617,	836(M+), 380, 365, 347
4	153-155	3450,1725,1717,1630,	790(M+), 410, 380

*ESR (solid, one line), g_o = 1.997

Table 2 IC_{50} (μg/mL) of compounds **2-4** and daunomycin **1**

Compd.	**2**	**3**	**4**	**1**
L1210	>100	78.1	—	23.1
BEL-7402	>100	>100	2.9	1.8

References

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