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Research paper

## Design, synthesis and biological evaluation of novel isoindolinone derivatives as potent histone deacetylase inhibitors

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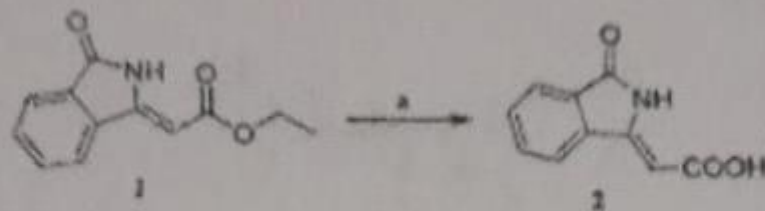
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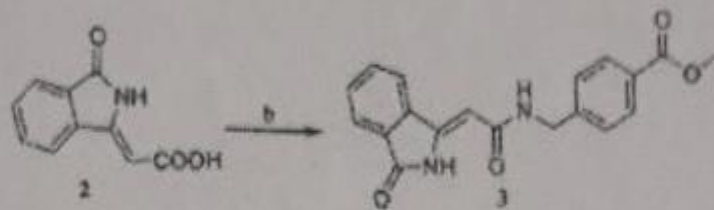
## STEP 1. Sintesi di (Z)-2-(3-oxoisindolin-1-ylidene)acetic acid (2)



Reagenti e condizioni: (a) LiOH, MeOH, 50 C, 2 h

- considerare **10g** di **1**
- calcolare il PM di **1** e le moli corrispondenti a 10 g
- reazione di idrolisi con LiOH: **4 equivalenti di LiOH**
- Resa = **90%**
- ottenuti grammi.....del composto **2**

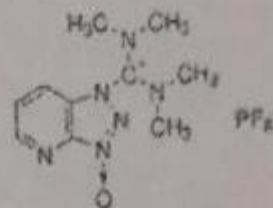
**Step. 2 Sintesi del Methyl (Z)-4-((2-(3-oxoisindolin-1-ylidene)acetamido) methyl)benzoate (3).**



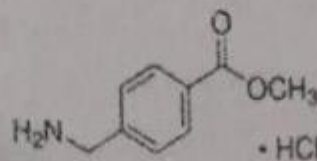
*Reagenti e condizioni:* (b) HATU, N, N-diisopropylethyl amine (DIPEA), N, N-dimethylformamide (DMF), methyl 4-(aminomethyl)benzoate hydrochloride, r. t., 6 h;

HATU

1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate

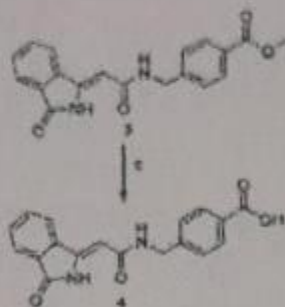


- Considerare la quantità effettiva ottenuta nello step 1 del composto 2 e quindi le moli.....
- Reazione con **methyl 4-(aminomethyl)benzoate hydrochloride (1.5 equivalenti)**
- **Corrispondenti a grammi..... e a moli.....**
- **Resa 75%**
- **Ottenuti grammi.....di 3**



PM = 201.65

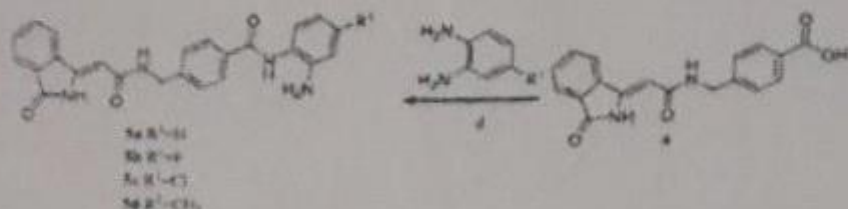
**Step. 3 Sintesi del (Z)-4-((2-(3-oxoisindolin-1-ylidene)acetamido) methyl)benzoic acid (4).**



*Reagenti e condizioni:* (c) LiOH, MeOH, 50 C, 2 h

- considerare la quantità effettiva di 3
- LiOH 4 equivalenti
- Resa 98%
- Ottenuti grammi ..... di 4

Step. 4 Sintesi del (Z)-N-(2-aminophenyl)-4-((Z-(3-oxoisindolin-1-ylidene) acetamido)methyl)benzamide (5a).



Reagenti e condizioni: (d) HATU, DIPEA, DMF, r. t., 6 h

- considerare la quantità di 4 ottenuta nello step 3
- reazione con 1,2-diaminobenzene (PM = 108.14 g/mol), 1.5 equivalenti
- Resa 35%
- ottenuti grammi .....di 5a
- Calcolare la resa totale della reazione