

REACTION OF o-AMINOBENZAMIDE DERIVATIVES WITH ETHYL 3-ETHOXY-
METHYLENE-2,4-DIOXOVALERATE. SYNTHESIS OF PYRROLO[1,2-a]-
QUINAZOLINE-1,5-DIONES

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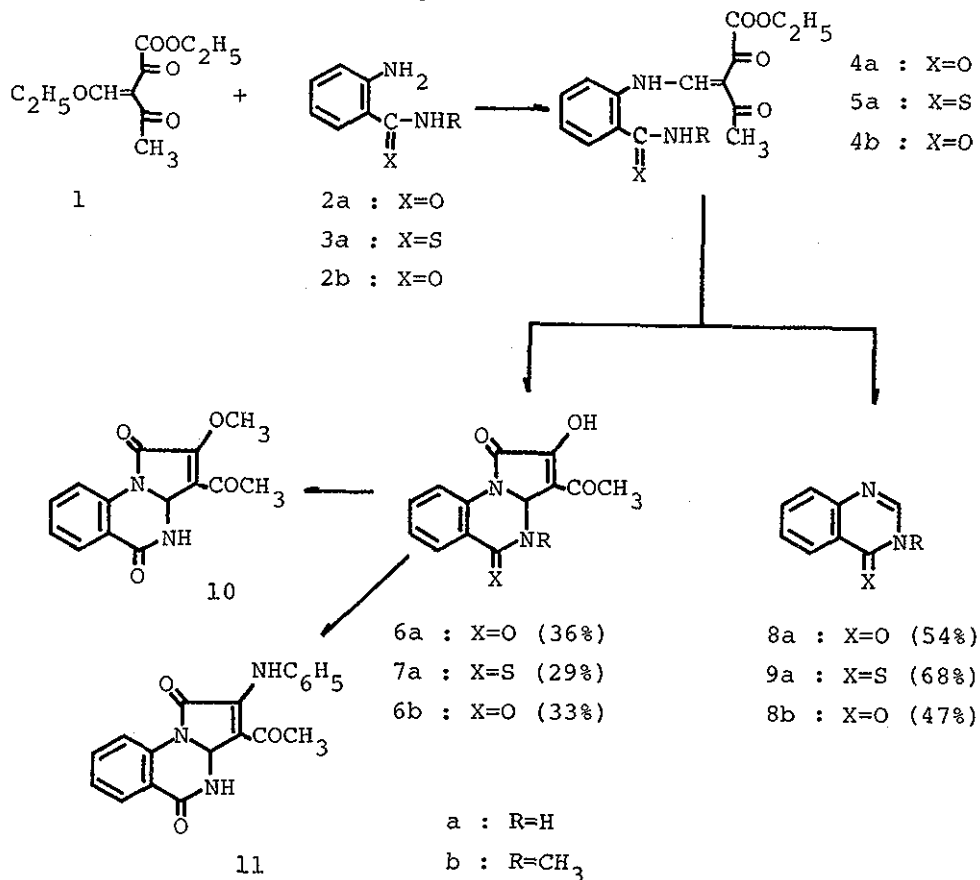
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Reaction of ethyl 3-ethoxymethylene-2,4-dioxo-
valerate (1) with o-aminobenzamide derivatives
gave 3-aminomethylene derivatives (4a,b and 5a),
which were subsequently refluxed in ethanol to
give rise to a mixture of pyrrolo[1,2-a]quinazo-
line-1,5-diones (6a,b and 7a) and 3,4-dihydro-4-
oxoquinazoline analogue (8a,b and 9a) in moderate
yields, respectively.

The synthesis of derivatives of pyrrolo[1,2-a]quinazoline-
1,5-diones, some of which showed the anti-edema activity¹, have
hitherto been reported by some workers². In connection of our
studies on the reactivity of ethyl 3-ethoxymethylene-2,4-dioxo-
valerate (1)³ (EMDV) to various type of amines⁴, we wish to report
here the synthesis of pyrrolo[1,2-a]quinazoline-1,5-diones (6a,b
and 7a) by the reaction of EMDV with o-aminobenzamide derivatives.

Refluxing a solution of 2a with an equimolar of EMDV in ethanol for 3 hr gave a mixture of 3,4-dihydro-4-oxoquinazoline (8a)⁵ in 70% yield and 3-acetyl-3a,4-dihydro-2-hydroxypyrrolo[1,2-a]quinazoline-1,5-dione (6a) in 12% yield. Compound 6a is soluble in NaHCO₃ solution and showed wine-red color when treated with FeCl₃. Structural elucidation of 6a was fully achieved on the bases of elemental analysis, spectral data [6a : $\nu_{\max}$ (KBr) 3400, 3280, 1710, and 1630 ; $\lambda_{\max}$ (EtOH) 247 (4.22), 308 (3.99), and 333 (3.87); δ (DMSO-d₆) 2.45 (3H, s, COCH₃), 6.10 (1H, s, CH), 7.30-8.10 (4H, s,



aromatic-H), and 8.30 (1H, s, NH)], and the following chemical reactions. Methylation of 6a with CH_3N_2 gave the methyl ether (10). The enol structure was further confirmed by conversion of 6a to 3-acetyl-2-anilino-3a,4-dihydropyrrolo[1,2-a]quinazoline-1,5-dione (11) on reaction with aniline⁶. When EMDV was treated with 2a in ether at room temperature or below ethyl 3-(*o*-carbamoylphenyl)-aminomethylene-2,4-dioxovalerate (4a) was isolated in 97% yield. This intermediate was then refluxed in ethanol for 3 hr to give 6a in 36% and 8a in 54% yield as a mixture. Compounds 7a and 6b mixed with 9a⁷ and 8b⁸ were prepared similarly in moderate yield, respectively. Physical data of these pyrrolo[1,2-a]quinazoline-1,5-diones are summarized in the Table.

Table Physical properties of pyrrolo[1,2-a]quinazoline-1,5-diones

Product No.	mp (°C) (solvent)	ir ν KBr (cm^{-1})	uv λ EtOH [nm (log ϵ)]	pmr (DMSO- d_6) δ $\text{C}_{3a}\text{-H}$
6a	268-270 (DMF)	3400, 3280 1710, 1630	247 (4.22) 308 (3.99) 333 (3.87)	6.10
7a	227-228 (MeOH)	3400, 3280 1715, 1650	265 (4.20) 321 (4.09)	5.93
6b	231-232 (EtOH)	3400, 1710 1650, 1620	246 (4.25) 304 (3.95) 327 (3.81)	6.13
10	188-190 (EtOH)	3280, 1720 1680, 1650 1620	305 (3.95) 317 (3.97) 330 (3.95)	6.13
11	292-294 (EtOH)	3280, 1720 1670, 1640	312 (3.96) 368 (4.23)	6.30

Consequently, this reaction provides a convenient route for the preparation of 4-substituted 3-acetyl-3a,4-dihydro-2-hydroxy-pyrrolo[1,2-a]quinazoline-1,5-dione analogue.

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