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Synthesis of some oxopyrano-oxazine compounds from the reactions of malonyl chloride with organonitriles.

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ABSTRACT

The reaction of malonyl chloride with RCN (R= Cyclopentyl , $CHPh_2$, C_6H_3BrF) at 100 C° and room temperature yielded pyrimidine derivatives , 2(R= Cyclopentyl) and oxopyrano oxazine derivatives 4(R,cyclopentyl ; $CHph_2$, C_6H_3BrF) respectively ,

The structures of these products have been determined by elemental analysis and spectroscopic methods .

INTRODUCTION

The reaction of malonyl chloride and substituted malonyl chloride with thiocyanates[1,2,3,4] , isothiocyanates[5] and nitriles at different conditions gave generally three main types of products , namelly ; pyridine(1) ,pyrimidine(2) and oxopyranooxazine (4,5) derivatives , depending upon the structures of the reactants . The nitrile having α - methylene group (-CH_2CN) produced pyridine derivatives[6,7] , while the nitriles without α - methylene group gave either a pyremidine or oxopyranooxazine products[8] . Other nitriles produced mixtures of two main products , such as : pyridine with pyrimidine[9] or pryrimidine with oxazine derivatives[10] , and the reaction of malonyl chloride with

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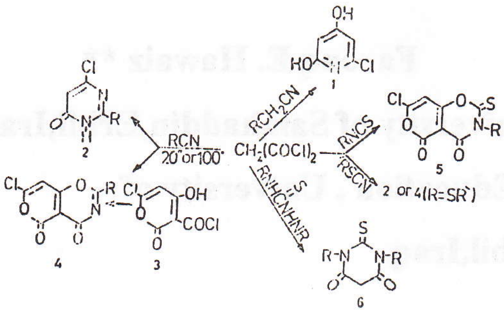
**Cited from his M.Sc. Thesis

thiosemicarbazides also yielded pyrimidine (6) derivatives[11].

Here, we report the reaction of some carbocyclic and aromatic nitriles with malonyl chloride. The reactions produced some expected new heterocyclic compounds of pyrimidine and oxopyranooxazine derivatives(scheme I).



(scheme I)

RESULTS AND DISCUSSION

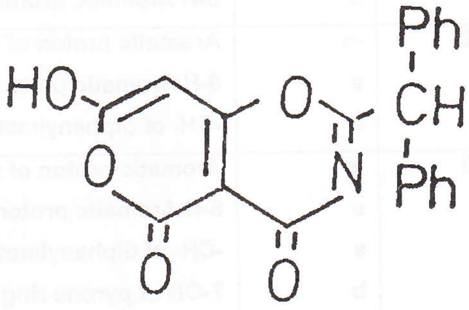
Reaction of malonyl chloride with nitriles :

A mixture of malonyl chloride and cyclopentanecarbonitrile interacted briskly at 100 C° with evoluation of hydrogen chloride . They also reacted slowly at room temperature with evoluation of hydrogen chloride and afforded same solid product . Thin layer chromatography, showed the product to be a mixture of two components , which were purified and separated by flash chromatography technique. One of these was soluble in benzene and the other was insoluble in benzene completely . Techniques of : Kjeldahl's nitrogen estimation , elemental analysis , i,r, and ^{1}H.n.m.r spectroscopy indicated that the benzene insoluble component to be 4-chloro-2-cyclopentyl-6-hydroxy pyrimidine 2 (R= cyclopentyl) , I.R spectrum (tab.1), it showed a strong band at $1685cm^{-1}$ as related 2-substituted-4-chloro-6-hydroxy pyrimidines[9].

The absorption at such a high frequency can hardly be attributed to ring vibration because the derivatives of pyrimidine without amino or hydroxy groups do not show bands in this region[12]. the benzene soluble compound showed a strong band at $1748cm^{-1}$ corresponding to carbonyl group of pyrone ring as found in the related 2-pyrones[13], and a second band at $1680cm^{-1}$ could be attributed to the 4-carbonyl group at the 1,3-oxazine ring, these bands agree with reported spectroscopic data [8,10]. Further evidence for the new product's being 7-chloro-4,5-dioxo-2-cyclopentyl pyrano [3,4-e]-[1,3]-oxazine, 4(R=cyclopentyl) was provided by ^{1}H-n.m.r. epectrum (tab.2) and elemental analysis. Which was obtained by the reaction of one mole of the nitrite with two moles of malonyl chloride. It was suggested that this reaction probably proceeded in to two main stages. The first appeared to be a self-condensation of malonyl chloride to the pyrone acid chloride (3) , induced by the weakly basic nitrile , and the second stage proceeded through acylation of the nitrogen atom of the nitrile to give compound 4 (R= cyclopentyl) . The mechanism of the reaction is analogous to that reported by Elvidge[13] .

Diphenylacetonitrile and 3-bromo-4-fluoro benzonitrile , behaved similarly to the benzene soluble compound and afforded with malonyl chloride the chloro – oxopyrano – oxazine 4(R= $CH(Ph)_2$) and (R= C_6H_3BrF) respectively .

The new heterocyclic compound 4 (R= -$CH(Ph)_2$) were treated with aqueous acetone , the 7-chloro was displaced by hydroxyl group and the new compound (7) was abtained . Support for this formulation came from its i.r and ^{1}H.n.m.r data (tab.1,2) .



(7)

Table (1): Characteristic frequencies (cm^{-1}) in i.r data of the prepared pyrimidine and oxazine compounds .

Compound	5- C=O	4- C=O	C=N	C=C	OH or NH	Other bands
2;R-Cyclopentyl			1580	1530 ,1470	3210 ,2120	1685 6-C=O
4;R-Cyclopentyl	1748	1680	1575	1500,1405		
4; R-$CHPh_2$	1754	1695	1580	1630, 1510 1490 ,1450		3060-Ph
4; R-C_6H_3BrF	1770	1680	1580	1625,1568 1535,1480		3060-Ph
7	1746	1690	1585	1640,1510 1460,1495	3200-2300	

to 60 C° for about six hours . Finally , the palle yellow malonyl chloride was distilled at reduced pressure (40 g. , 56.7%) boiling point 65 C° /30 mm.

2-Reaction of malonyl chloride with cyclopentanecarbonitrile :

Malonyl chloride (4.1 ml. , 0.04 mole) and cyclopentanecarbonitrile (2 ml. , 0.02 mole) , were warmed together on a water bath , under anhydrous condition , for 5 min. , and then heated under reflux at 100 C° for 30 min. until solidification occurred and evoluation of hydrogen chloride gas ceased. The brown stickey mass was treated with dry ether .

Two compounds were obtained , one soluble in benzene and the other insoluble in benzene completely . The benzene soluble compound was recrystallized from ethyl alcohol to give coluorless crystalline 4-chloro-2-cyclopentyl-6-hydroxy pyrimidine 2 (R= cyclopentyl) (0.4g. , 20.2%) .,m.p 220 C° (decomp.) ; R_f = 0.76 (ethanol) . Anal calc. For $C_9H_{11}ClN_2O$:C, 54.5 ; H,5,55 : N,14.14 % : found : C,53.98 ; H,5.69;N, 13.96 %.

The benzene soluble compound was recrystallized from a mixture of benzene and n-heptain to give a coluorless crystalline 7-chloro-4,5-dioxopyrano-2-cyclopentyl –[3,4-e]-[1,3]-oxazine 4(R – cyclopentyl (2.4g. , 44.85%) , m.p. 132-134 °C ; R_f=0.69 (ethanol) . Anal. Calc. For $C_{12}H_{18}ClNO_4$: C,53.9 ; H,3.74 ; N,5.24 : found : C,54.8 ; H,3.86 ; N,5.31%.

The same reaction was repeated at room temperature , after four days a brown sticky mass was obtained and treated as above and was shown to be the above compound 10% of 2(R-cyclopentyl) and 41.13% of the compound 4 (R= Cyclopentyl) .

3-Reaction of malonyl chloride with diphenylacetonitrile :

Malonyl chloride (2ml , 0.02 mole) and diphenylacetonitrile (1.93 g. ,0.01 mole), were warmed together on a water bath , under anhydrous conditions , to dissolve the nitrile , and then heated at 100 C° for (2 hours) until the mixture solidified completely and the evolution of hydrogen chloride gas ceased . The red sticky mass was triturated with dry ether the product recrystallized from a mixture of acetone and dry ether to yellowish – white crystalline product , 7-chloro-4,5-dioxopyrano-2(diphenylmethyl)-[3,4-e]-[1,3]oxazine 4(R=CHPh2) , (2.2 g. , 61.79 %) m.p.(170-172) °C ; R_f = 0.74 (ethanol) . Anal. Calc. for $C_{20}H_{12}ClNO_4$: C,65.7 ; H,3.28 ; N,3.83 ; Found ; C,64.9 ; H,3.8;N,3.65 % .

4-Preparation of 7- hydroxy-4,5-dioxopyrano-2(diphenylmethyl)-[3,4-e]-[1,3]-oxazine(7):

Finely powdered compound 4(R= -$CHPh_2$) , (1g.,0.0027 mole) was dissolved in a mixture of acetone and water (15:1) by heating under reflux for 10 min. , during which the solid compound was dissolved and hydrogen chloride gas was evolved . The solution was evaporated to small bulk , and dry ether was added . The 7-hydroxy-4,5-dioxopyrano-2-(diphenyl methyl)-[3,4-e]-[1,3] oxazine (7) 0.62 g. , 65.95%) was obtained and recrystallized from a mixture of ether – acetone as yellow product , m.p.(191-192) °C , R_f= 0.78 (ethanol) . Anal. Calc. For $C_{20}H_{13}ClNO_4$: C,69.16 ; H,3.74 ; N,4.03 : Found : C,68.3 ; H,3.71 ; N,4.23 %.

5-Reaction of malonyl chloride with 3-bromo-4-fluoro benzonitrile :

The procedure of the reaction of 3-bromo-4-fluoro-benzonitrile (2g,0.01 mole) with malonyl chloride (2g. ,0.02 mole) was the same as described for diphenylacetonitrile , the reaction needed about (30 min.) to solidify completely . the product was treated with a mixture of dry dioxane and ether (1:1) and washed with ether and acetone to give yellowish crystalline product 7-chloro-4,5-dioxopyrano-2-(3-bromo-4-fluorophenyl)-[3,4-e]-[1,3]-oxazine 4(R= C_6H_3BrF) (1.9 g. ,51.07%) , m.p. 210 C° (decomp.) ; R_f=0.75(ethanol). Anal. Calc. For $C_{13}H_4BrClFNO_4$;C,41.93;H,1.09 ; N,3.76 : Found : C,40.95 ; H,1.55 ; N,3.34%. The same reaction was repeated at room temperature and after seven days the same product was obtained in 29.56 % yield .

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پەسەند کرا لە ۲۰۰۰/۵/۲۸ دا

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ئامادەکردنی هەندێك ئاوێتەی ئۆکسۆ پایرانۆ - ئۆکزازین لەکارلێکردنی کلۆریدی مالۆنیل لەگەڵ نتریلە ئەندامیەکان

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پوختە

ئەم لێکۆڵینەوە یە کارلێکەکانی کلۆریدی مالۆنیل لەگەڵ هەندێ لە ئاوێتەکانی نیتریلە پارافینی و نیتریلە ئەرۆماتیەکان دەگرێتە خۆ لەوانە (RCN , R= Cyclopentyl ,C_6H_3BrF, $CHPh_2$) کلرلێکەکان لە پلەی گەرمی ژوورو 100°C دا ئەمجام دران و بوونە هۆی پێکهێنانی ئاوێتەکانی پایریمدین 2 (R= Cyclopentyl) و ئۆگزازین 4 (R= Cyclopentyl ,C_6H_3BrF, $CHPh_2$) شێووگی کیمیاوی مادده بەرهەم هاتووەکان بە بەکارهێنانی ڕێگای کیمیاوی و ڕێگای فیزیکی وەك شەبەنگی ژێر سوور (IR) و شەبەنگی لەرینەوەی ناووکی ^1H- NMR و شیکردنەوەی توخمی دیاری کران.

تحضير بعض مركبات أوكسوبايرانو - أوكزازين من تفاعل كلوريد المالونيل مع النتريلات العضوية

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الخلاصة

يتضمن البحث دراسة تفاعلات كلوريد المالونيل مع بعض مشتقات النتريلات الاروماتية والنتريلات الاليفاتية مثل (RCN , R= Cyclopentyl ,C_6H_3BrF, $CHPh_2$) وذلك في درجة حرارة الغرفة و درجة 100°C وتم الحصول على مشتقات البريميدين 2 (R= Cyclopentyl) ومشتقات الاوكزازين 4 (R= Cyclopentyl ,C_6H_3BrF, $CHPh_2$) وقد تم تشخيص هذه المركبات بوساطة الطرق الكيميائية والطرق الطيفية مثل طيف اشعة تحت الحمراء (IR) وطيف الرنين النووي المغناطيسي ^1H- NMR والتحليل الكمي للعناصر .