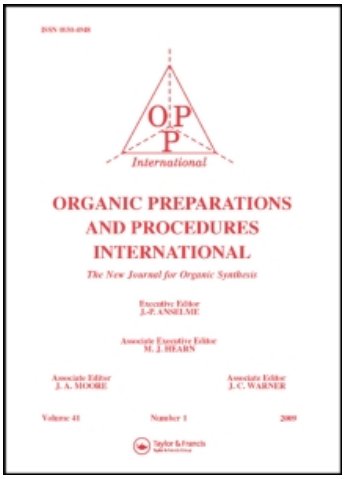


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A NEW SYNTHESIS OF 3-AMINO-1-IMIDAZOLIN-4-ONES BY THE HYDRAZINOLYSIS OF 5-OXAZOLONES

Vinod K. Ahluwalia[ab]; Mukesh K. Sharma[a]; Rashmi Sharma[a]
[a] Department of Chemistry, University of Delhi, Delhi, INDIA [b] Manipur University, Imphal, Manipur, India

To cite this Article Ahluwalia, Vinod K. , Sharma, Mukesh K. and Sharma, Rashmi(1992) 'A NEW SYNTHESIS OF 3-AMINO-1-IMIDAZOLIN-4-ONES BY THE HYDRAZINOLYSIS OF 5-OXAZOLONES', Organic Preparations and Procedures International, 24: 6, 698 — 701
To link to this Article: DOI: 10.1080/00304949209356253
URL: http://dx.doi.org/10.1080/00304949209356253

Osipov and E. G. Treshchova, *Zh. Obshch. Khim.*, **30**, 3874, (1960); *J. Gen. Chem. USSR*, **30**, 3830, (1960).

3. J. R. Boissier, R. Ratouis, C. Dumont, P. H. Derible and J.-P. Lavaux, *J. Med. Chem.*, **13**, 971, (1970).

4. a) H. Hart and G. Levitt, *J. Org. Chem.*, **24**, 1261, (1959). b) H. Hart, R. H. Schlosberg and R. K. Murray, *ibid*, **33**, 3800, (1968). c) R. Ya. Levina and P. A. Gembitskii, *Zh. Org. Khim.*, **31**, 3480, (1961). d) R. Ya. Levina, P. A. Gembitskii, V. N. Kostin, E. G. Treshchova and S. M. Shostakovskii, *J. Gen. Chem. USSR*, **30**, 358, (1960).

****

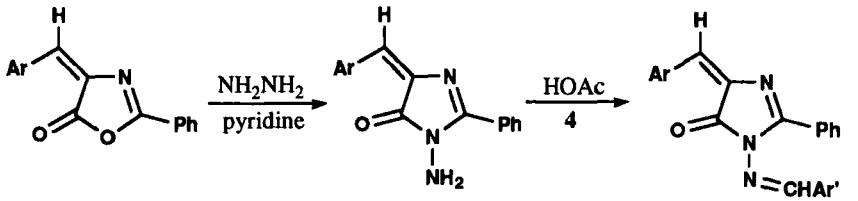
A NEW SYNTHESIS OF 3-AMINO-1-IMIDAZOLIN-4-ONES BY THE HYDRAZINOLYSIS OF 5-OXAZOLONES

Submitted by (04/24/92)

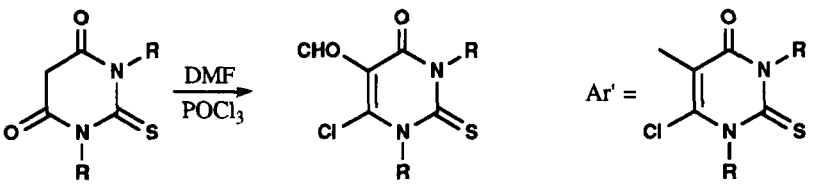
Vinod K. Ahluwalia*†, Mukesh K. Sharma and Rashmi Sharma

Department of Chemistry
University of Delhi, Delhi-110007, INDIA

The reaction of hydrazine has been reported to give triazinones by heating with 5-phenyl-4-oxazolin-2-ones in dilute alkali,[1,2] isomeric pyrazolidin-3-ones,[3] with benzylidene oxazolones in



1 2 3



4 5

a) R = 2-$MeOC_6H_4$, Ar = 4-$MeOC_6H_4$ b) R = C_6H_5, Ar = 4-$MeOC_6H_4$
c) R = 3-MeC_6H_4, Ar = 4-$MeOC_6H_4$ d) R = 4-ClC_6H_4, Ar = 4-$MeOC_6H_4$
e) R = 2-$MeOC_6H_4$, Ar = 4-MeC_6H_4 f) R = 3-$MeOC_6H_4$, Ar = 4-MeC_6H_4

boiling ethanol, and pyrazolo oxazolones with arylidene oxazolones in dioxane in the presence of acetic acid.[4] Treatment of 4-(4-methoxybenzylidene)-2-phenyl-5(4H)-oxazolone (1) with hydrazine hydrate in pyridine proceeded immediately and exothermally to give a white crystalline product mp. 220°; MS (*m/z*): 311 (M^+), presumed to be 2-benzoylamino cinnamoyl hydrazine (analogous compounds[5] have been reported earlier with anilines). On further refluxing, this compound underwent dehydrative cyclization to give a bright yellow compound; its ^1H NMR spectrum showed, along with the usual signals, a broad singlet at δ 4.43 for 2 protons exchangeable with D_2O. The IR spectrum showed a peak at 3300 cm^{-1} which confirmed the presence of an amino group. The M^+ peak in the mass spectrum at 293 (M^+) and the results of elemental analysis confirmed the structure of the compound to be 3-amino-5-(4-methoxybenzylidene)-2-phenyl-4H-1-imidazolin-4-one (2). Earlier workers had reported[6,7] tedious multi-step syntheses of similar compounds. In the present work the title compounds have been synthesized by a new and easy one-step method. Treatment of 3-amino-4H-1-imidazolin-4-ones with 1,3-diaryl-6-chloro-5-formyl-2-thiouracil (4) gave the hydrazones. The thiouracils (4) were prepared by the Vilsmeier reaction[8] of 1,3-diaryl-2-thiobarbituric acids. All structures were confirmed by spectral data and elemental analysis. The formation of the hydrazones which are important from the biological point of view,[9,10] confirmed the presence of an amino group.

TABLE: Characteristic Data for **2b** and **5a-e**

Compd. No.	mp. (°C)	Calcd. (Found) C	H	N	^1H NMR ($CDCl_3$ TMS) (δ-scale)
2b	243-244	73.64 (73.61)	5.41 (5.54)	15.16 (15.30)	8.61-7.0 (m, 10H, Ar-H), 4.43 (s, 2H, $-NH_2$), 2.5 (s, 3H, $-CH_3$)
5a	235-236	63.81 (63.71)	4.13 (4.24)	10.33 (10.16)	9.82 (s, 1H, N=CH) 8.44-6.8 (m, 18H, Ar-H), 3.93 (s, 9H, 3x-OCH_3)
5b	247-248	66.12 (66.24)	3.88 (3.97)	11.34 (11.12)	9.82 (s, 1H, N=CH), 8.61-7.20 (m, 20H, Ar-H) 4.00 (s, 3H, -OCH_3)
5c	241-242	66.97 (66.74)	4.34 (4.28)	10.85 (10.91)	9.74 (s, 1H, N=CH), 8.45-7.20 (m, 18H, Ar-H), 3.93 (s, 3H, -OCH_3), 2.51 (6H, s, 2x-CH_3)
5d	257-258	59.56 (59.32)	3.21 (3.04)	10.21 (10.35)	9.82 (s, 1H, N-CH), 8.36-6.82 (m, 18H, Ar-H), 3.98 (s, 3H, -OCH_3)
5e	249-250	65.35 (65.41)	4.23 (4.36)	10.59 (10.54)	9.62 (s, 1H, N=CH), 8.45-6.94 (m, 18H,Ar-H), 8.92 (s, 6H, 2x-OCH_3), 2.53 (s,3H, -CH_3)
5f	214-215	65.35 (65.46)	4.23 (4.32)	10.59 (10.65)	9.84 (s, 1H, N=CH), 8.42 -6.81 (m, 18H, Ar-H) 3.98 (s, 6H, 2x-OCH_3), 2.55 (s, 3H, -CH_3)

EXPERIMENTAL SECTION

Melting points are uncorrected. Infrared spectra were recorded on a Shimadzu Infrared Spectrophotometer IR-435. ^{1}H NMR spectra were recorded on a Perkin Elmer R-32 (90 MHz) spectromter, using TMS as the internal standard. The elemental analysis was determined on CHN analyser (Heraus), at University Scientific Instrumentation Centre, Delhi University, Delhi. The starting compounds **1a-b** and **3a-f** were synthesized by conventional methods.[11,12] All the reagents were freshly distilled.

3-Amino-5-(4-methoxybenzylidene)-2-phenyl-4H-1-imidazolin-4-one (2a) Typical Procedure.- A mixture of **1a** (13.95 g, 0.05 mol) and hydrazine hydrate (85%, 2.50 g, 0.05 mol) in pyridine (10 mL) was heated under reflux for 1.5-2.0 hrs. The solvent was distilled off under vacuum (10mm/Hg) and the oily residue was diluted with water, neutralized with dil. hydrochloric acid to remove traces of pyridine and allowed to stand for some time at room temperature. The resulting solid (13.30 g) was dried and purified by column chromatography on silica gel using petroleum ether:ethyl acetate (5:1) as an eluent to give 8.05 g (55%) of **2a** as a bright yellow powder, mp. 207-208°, IR (Nujol): 3300 (-NH_2), 1690 (amide CO) cm^{-1}. MS (*m/z*): 293 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.51-6.18 (m, 10H, aromatic H), 4.43 (br s, 2H, -NH_2), 3.96 (s, 3H, -OCH_3).

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.62; H, 5.11; N, 14.33. Found: C, 69.45; H, 4.95; N, 14.45

Compound **2b** was obtained in a similar way (Table).

1,3-*bis*(2-Methoxyphenyl)-6-chloro-5-formyl-2-thiouracil (4a).- Dimethylformamide (5.80 g, 0.08 mol) was added dropwise to an ice cold solution of phosphorus oxychloride (22.90 g, 0.15 mol) with constant stirring. After the addition was complete 1,3-*bis*-(2-methoxyphenyl)-2-thiobarbituric acid (**3a**, 2.10 g, 0.006 mol) was added and the reaction mixture was refluxed for 45-55 min. The reaction mixture was cooled and added slowly to a beaker containing 200 mL of ice cold water with stirring. The resulting solid was collected, washed with water, dried and recrystallized from benzene:petroleum ether to give 1.97 g (82%) of **4a**. Compounds **4b-e** were obtained in a similar manner.

1,3-*bis*-(2-Methoxyphenyl)-6-chloro-5-[5-(4-methoxybenzylidene)-4-oxo-2-phenyl-4H-1-imidazolin-3-iminomethyl]-4-oxo-1,2,3,4-tetrahydro-2-thioxopyrimidine (5a). Typical Procedure.- A mixture of **2a** (1.46 g, 0.005 mol) and **4a** (2.01 g, 0.005 mol) in ethanol (25 mL) containing a few drops of glacial acetic acid was refluxed on a steam bath for 30-35 min. The reaction mixture was concentrated and the solid thus obtained was collected, dried and recrystallized from chloroform:methanol to give 2.70 g (80%) of **5a** as yellow powder. Compounds **5b-c** were obtained in 80-85% yield in a similar way. Data for **5a-e** are given in the table.

Acknowledgement.- Thanks are due to University Grants Commission for financial assistance.

REFERENCES

† Present Address: Manipur University, Canchipur, Imphal-795003, Manipur, India.

1. O. P. Shvaika and G. P. Klimisha, *Dopov. Akad. Nauk Ukr. RSR. Ser B*, **32**, 350 (1970); *Chem.*

Abstr., **73**, 35334W (1970).

2. K. Nalepa, *Monatsh. Chem.*, **98**, 1230 (1967).
3. D. S. Iyengar, K. K. Prasad and R. V. Venkataraman, *Australian J. Chem.*, **27**, 2439 (1974).
4. E. L. Maghraby, M. A. A. Abou and El-Ela Hussan, *J. Indian Chem. Soc.*, **59**, 867 (1982).
5. A. M. Islam, A. M. Khalil and E. L. Houseni, *Australian J. Chem.*, **26**, 1701 (1973).
6. J. Barluenga, N. Gomez, F. Palacios and V. Gotor, *Synthesis*, **7**, 563 (1981).
7. A. F. M. Elkaschef, M. E. A. Megeid and M. A. Salah, *Acta Chim. (Budapest)*, **80**, 119 (1974); *Chem. Abstr.*, **80**, 95819h (1974).
8. S. Senda, K. Hirota, G. N. Yang and M. Shiraishi, *Yakugaku Zasshi*, **91**, 1372 (1971).
9. C. N. O'Callaghan and M. L. Conalty, *Proc. R. Ir. Acad.*, **B19**, 214 (1983).
10. O. Goldberg, A. Luini and I. V. Teichberg, *J. Med. Chem.*, **26**, 39 (1983).
11. A. Boltazzi, *Quar. Rev. Chem. Soc.*, **9**, 150 (1955).
12. I. N. D. Dass and P. K. Dutt, *Proc. Indian Acad. Sci.*, **8A**, 145 (1938).

****

IMPROVED PREPARATION OF 18-HYDROXYPROGESTERONE

Submitted by (05/18/92)

M. O. Violeta Benedetti and Gerardo Burton*

Departamento de Quimica Organica
Facultad de Ciencias Exactas y Naturales
Universidad de Buenos Aires, Pabellon 2, Ciudad Universitaria
(1428) Buenos Aires, ARGENTINA

Previous methods used for the preparation of 18-hydroxyprogesterone hemiacetal (**1**) involved multi-step procedures (usually five to seven) and gave low yields of the desired product.[1] Slaunwhite and Solo[1] obtained a 19% yield of **1** in five steps starting from pregnenolone acetate, this being the best yield described in the literature. All these procedures, which involve either the hypoiodite reaction ($Pb(OAc)_4/I_2$) or the Barton reaction (photolysis of a C-20 nitrite) for functionalization of the C-18 angular methyl group, limit the functional groups that may be present in the precursor molecule.