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The title compounds were prepared by the condensation of a series of β-keto esters with 2-benzylimidazoline. A mechanism is proposed wherein the dienamine **4** undergoes an intramolecular acylation with the elimination of ethoxide and subsequent hydride shift.

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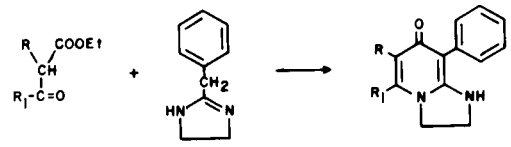
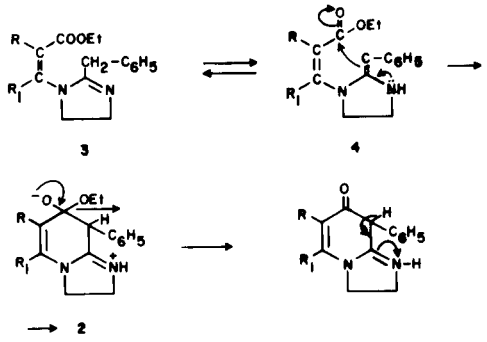
In an attempt to prepare the enamine derived from 2-benzylimidazoline (1) and a series of β-keto esters, an unexpected condensation reaction was observed. Under the usual conditions for enamine formation, *i.e.* heating in benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid, only the substituted imidazopyridones of formula 2 were obtained.



1 2

The reaction procedes *via* the initial formation of the intermediate enamine **3** which tautomerizes to the dienamine **4**. The intramolecular acylation of **4**, (1) accompanied by a loss of ethoxide and a concomitant hydride shift, results in the formation of **2** as shown in Chart I.

CHART I



This reaction can be carried out in the absence of an acid catalyst, albeit in somewhat lower yield, by percolating the refluxing mixture through 4A molecular sieves in a Soxhlet extractor.

The compounds were identified by the usual spectral data (Table II). Of especial interest is the strong carbonyl absorption (1630-1650 cm^{-1}) in the infrared spectra of these compounds. Representative compounds were converted into the 1-methyl derivatives by alkylation (methyl iodide) in the presence of sodium hydride. The 1-methylated compounds showed the typical carbonyl absorption in the ir spectra as well as a sharp singlet in their nmr spectra at approximately δ 2.3. The physical properties of these compounds are listed in Table I.

EXPERIMENTAL

The β-keto esters used in this work were commercial products. In several cases the commercial preparations were mixtures of the ethyl and methyl esters. 1-Benzyl-3-carbethoxy-4-piperidone was liberated from its hydrochloride by aqueous sodium carbonate, extracted into chloroform, dried and used directly without further purification after removal of the solvent. The 2-benzyl-2-imidazoline was liberated from its hydrochloride by a similar procedure.

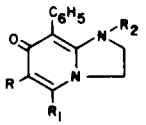
Table II

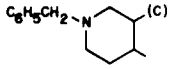
Spectral Data

Compound No.	Ir (C=O) cm^{-1}	δ	Nmr Assignment (a)
1	1630	7.25	(5, Ar-H)
		5.25	(bs, 1, N-H)
2	1640	7.30	(5, Ar-H)
		2.30	(s, 3, N-CH_3)
3	1630	7.28	(5, Ar-H)
		5.85	(bs, 1, NH)
4	1640	7.28	(5, Ar-H)
		5.85	(s, 1, NH)
		5.55	(s, 1, =CH)
		1.88	(s, 3, =C-CH_3)
5	1630	7.25	(5, Ar-H)
		5.70	(s, 1, =CH)
		2.20	(s, 3, N-CH_3)
		1.70	(s, 3, =C-CH_3)
6	1640	7.30	(5, Ar-H)
		4.45	(s, 1, NH)
		2.20	(s, 3, -C-C(CH_3)=C)
		1.90	(s, 3, =C-CH_3)
7	1650	7.00	(10, Ar-H)
		5.47	(s, 1, =CH)
		3.22	(s, 1, NH)
8	1650; 1740	7.35	(5, Ar-H)
		5.82	(s, 1, C=C-H)
		3.25	(s, 2, CH_2-CO)
		1.18	(t, 3, CH_3)
9	1650	7.32	(10, Ar-H)
		4.40	(bs, 1, N-H)
		3.68	(s, 2, CH_2-φ)
		3.50	(bs, 2, N-CH_2-C=C)

(a) s, singlet; bs, broad singlet; t, triplet.

Table I



Compound No.	R	R_1	R_2	M.p. °C (a)	Yield % (b)	Formula	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1			H	179-180	38	$C_{16}H_{16}N_2O$	76.18	6.39	11.10	76.28	6.67	11.14
2			CH_3	181-182	35	$C_{17}H_{18}N_2O$	76.67	6.81	10.52	76.77	6.77	10.45
3			H	240-242	59	$C_{17}H_{18}N_2O$	76.67	6.81	10.52	76.54	6.87	10.66
4	H	CH_3	H	161-162	61	$C_{14}H_{14}N_2O$	74.60	6.19	12.38	74.51	6.34	12.49
5	H	CH_3	CH_3	85-86	33	$C_{15}H_{16}N_2O \cdot H_2O$	69.74	7.02	10.84	69.83	7.37	10.72
6	CH_3	CH_3	H	230-231	11	$C_{15}H_{16}N_2O$	74.97	6.71	11.65	75.13	6.31	11.73
7	H	C_6H_5	H	270 (d)	35	$C_{19}H_{16}N_2O$	79.14	5.59	9.72	79.11	5.30	9.50
8	H	CH_2COOEt	H	142-143	40	$C_{17}H_{18}N_2O_3$	68.45	6.04	9.39	68.24	6.15	9.39
9			H	162-163	20	$C_{23}H_{23}N_3O$	77.50	6.22	11.79	77.71	6.37	11.66

(a) All compounds were recrystallized from ethanol-water. (b) The yields reported do not represent the maximum obtainable since in the majority of cases they are based on single experiments. (c) From 1-benzyl-3-carbethoxy-4-piperidone.

Melting points are uncorrected and were obtained on a Thomas Hoover melting point apparatus. Infrared spectra were recorded using a Perkin Elmer 180 instrument. Nmr spectra were obtained in $CDCl_3$ using TMS as internal standard on a Varian CFT-20 spectrometer. Mass spectra were taken with a Varian Mat CH5 spectrometer.

General Condensation Procedure (Acid Catalyzed).

A mixture of 0.3 mole of β-keto ester, 0.3 mole of 2-benzylimidazoline, 300 ml. of anhydrous benzene and 0.5 g. of toluenesulfonic acid was heated under reflux with stirring for 20-24 hours using a Dean-Stark trap. After cooling the unreacted starting material was filtered off and the filtrate was concentrated *in vacuo* to a small volume. The product was filtered and recrystallized from ethanol-water or benzene.

Condensation Procedure (Molecular Sieves).

Equimolecular mixtures (0.3 mole) of the keto ester and 2-benzylimidazoline in 300 ml. of anhydrous benzene was percolated through 30 g. of 4A molecular sieves contained in a Soxhlet extractor for 24 hours and the product was isolated as described above.

Methylation Procedure.

To a suspension of 0.5 g. (50% sodium hydride) in 25 ml. of benzene was added protionwise 0.01 mole of NH-compound and the mixture was cautiously heated to reflux. After 1½ hours at the boiling point, 1.5 g. of methyl iodide was added and the mixture was heated for 1 hour and allowed to stir overnight at room temperature. Glacial acetic acid (10 ml.) was added followed by 25 ml. of water and extracted into ether (3 X). The combined ether solution was extracted with 10% hydrochloric acid, acid extracts backwashed with ether, basified (sodium hydroxide) and the product allowed to crystallize.

Acknowledgement.

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REFERENCES AND NOTES

(1) For other examples of intramolecular acylation of enamines, see J. Szmuszkovicz, in "Advances in Organic Chemistry", Vol. 4, R. A. Raphael, E. C. Taylor and H. Wynberg, Eds., Interscience Publishers, 1963, p. 1.