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ATTEMPTED REFORMATSKII REACTION OF BENZONITRILE, 1,4-DIKETO-3,6-DIPHENYLPYRROLO[3,4-C]PYRROLE. A LACTAM ANALOGUE OF PENTALENE.

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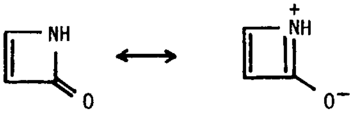
Some time ago we became interested in the synthesis of derivatives of 2-azetinone (1), a lactam analogue of the "antiaromatic" hydrocarbon, cyclobutadiene. It seemed possible that a



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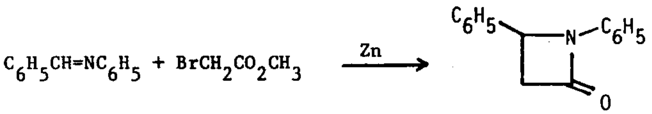
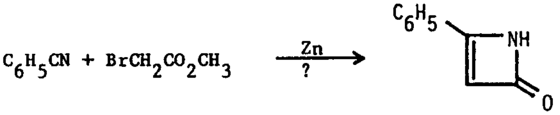
modification of the Reformatskii reaction, already used for the synthesis of 2-azetidinones, or β-lactams,[1] might yield 2-azetinones as well, as shown in equations (1) and (2).



$C_6H_5CH{=}NC_6H_5 + BrCH_2CO_2CH_3 \xrightarrow{Zn}$ (1)

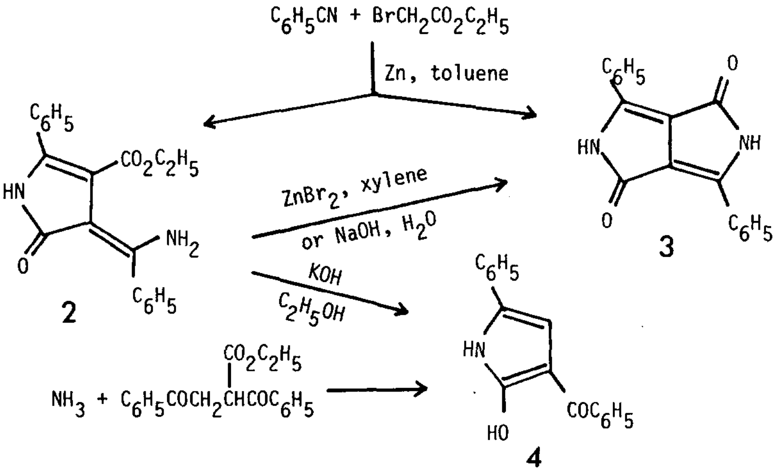


$C_6H_5CN + BrCH_2CO_2CH_3 \xrightarrow[?]{Zn}$ (2)

The proposed reaction failed to produce any azetinones, which have since been synthesized by other methods[2] (although not yet unsubstituted on nitrogen), but the results were of sufficient interest to warrant presentation.

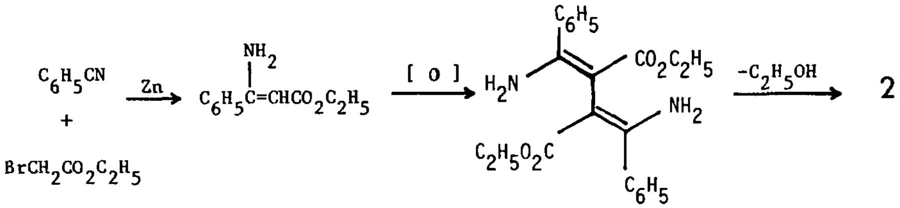
When a solution of benzonitrile and ethylbromoacetate in toluene was heated under reflux for several hours with activated zinc-copper couple, the color changed from yellow, to green, to brown, to red. A deep yellow, crystalline compound, $C_{20}H_{18}N_2O_3$,[3] mp 233° was isolated from the toulene solution, and a highly insoluble, brilliant red, crystalline compound, $C_{18}H_{12}O_2N_2$,[3] mp > 350°, was isolated from the insoluble residue by extraction with hot DMSO or DMF. The red compound alone could be obtained in higher yield by conducting the reaction in boiling xylene. The formal loss of the elements of ethanol between the molecular formulas of the yellow and red compounds was actualized in the preparation of the red compound from the yellow compound with zinc bromide in boiling xylene, or with 5% aqueous sodium hydroxide. This conversion is easily understood in terms of the structures **2** and **3** derived for the yellow and red products, respectively, on the basis of spectroscopic data and the chemical conversions given in Chart 1. Thus, although a derivative of azetidine was not formed in this Reformatskii reaction, a lactam analogue, **3**, of the 8 π electron fused ring hydrocarbon pentalene was obtained.

Chart 1



The key structural information was provided by hydrolysis of the yellow lactam **2** with potassium hydroxide in boiling ethanol. Work up of the reaction mixture yielded the known golden 3-benzoyl-2-hydroxy-5-phenylpyrrole (**4**), mp 229-230°, identified by comparison with an authentic sample.[4] The infrared spectrum of pyrrole **4** had a curious array of peaks of descending absorbance at 1655, 1630, 1605, 1575, and 1540 cm^{-1}, in accord with the highly conjugated carbonyl system.

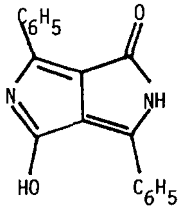
The formation of pyrrole **4** establishes the presence of only monosubstituted benzene rings in its yellow precursor. Furthermore the transformation is readily interpreted in terms of hydrolysis and decarboxylation of the structure **2** proposed for the yellow compound. In formal mechanistic terms, structure **2** is easily derivable by oxidative dimerization of the expected Reformatskii product[5] from benzonitrile and ethylbromoacetate, either free, as illustrated, or as a metal complex.



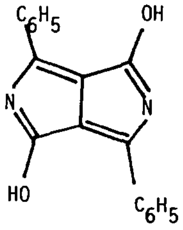
The infrared spectrum of the yellow product is entirely consistent with the proposed structure with strong peaks at 3230 cm^{-1} (hydrogen bonded amine), 1685 cm^{-1} (conjugated ester), 1640 cm^{-1} (highly conjugated γ-lactam), and 1535 cm^{-1} (NH deformation?). Cyclization of **2** to give lactam **3** is unexceptional.

The spectroscopic data for red lactam **3** were curious. The infrared spectrum showed carbonyl absorption at 1655 cm^{-1} --an unusually low frequency for the lactam carbonyl. The strongly hydrogen bonded NH appeared as a broad peak from 3000 to 2500 cm^{-1}, and additional absorption appeared at 1630, 1605, and 1540 cm^{-1}. The ultraviolet spectrum in dimethylsulfoxide solution gave multiple absorption at 300, 320, 467, and 475 nm. Addition of a few drops of dilute ethanolic sodium hydroxide to the solution resulted in the formation of an intense fuchsia color.

It is particularly difficult in this case to distinguish among the several tautomers of **3**, including **3a** and **3b**. Structure **3** is chosen simply by analogy to the pyridones, although the others could also be consistent with the spectroscopic data.



3a



3b

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