

THE ACTION OF CERTAIN FORMAMIDINES
ON THE PYRAZOLONS.

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and the faculty of the Graduate School
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Dept. of Chemistry

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These pyrazolons react with equal moles of formamidines to form another pyrazolon and an aniline, the methylene hydrogen of the pyrazolon being attacked.

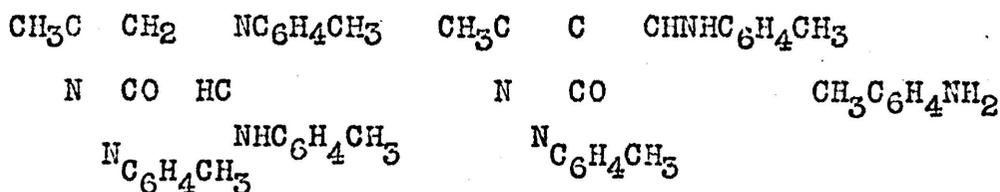


The amine is separated from the pyrazolon by acidifying the solution. If the amine is not a solid -- in which case it is easily recognized by its melting point -- it is treated with benzoyl chloride in alkaline solution; the resulting benzoyl derivative is easily recrystallized from hot alcohol and identified by its melting point. A series of such pyrazolons were prepared, and the reactions of one of them studied in detail.

4 - m - toluido-methylene - I p-tolyl - 3 methyl -
5 pyrazolon.

This was prepared by heating 5 grams of I-p-tolyl-3 methyl-5 pyrazolon with 6 grams (molar quantities) of di-m tolyl formamidine on an oil bath at 150° for 20 minutes. The mass cooled into a mixture of brown-yellow crystals in a dark, heavy liquid. This was acidified with HCl and boiled, leaving the crystals which were filtered off and recrystallized several times from a little alcohol. Sandy golden-yellow crystals resulted, melting at 121° - 20; the yield was 4.8 grams, 59.3% of theory. The filtrate

was made alkaline and treated with benzoyl chloride; the resulting benztoluide was recrystallized from a little hot alcohol, giving 3.6 g. of white crystals melting at 124°.^I



Analysis:² .2294 gms. gave 28.9 cc. at 20° and 725.6 mm.
.2280 gms. gave 27.65 cc, at 21° and 727.3 mm.

Found	Theory for C ₁₉ H ₁₉ O ₃
13.85%	13.77%
13.30%	

4 - O - toluido methylene - I p Tolyl - 3methyl -
5 pyrazolon.

This reaction was repeated with di-o-tolyl formamide and I-p tolyl - 3 methyl - 5 pyrazolon. After acidifying the product and filtering, the yellow residue was recrystallized repeatedly with considerable alcohol. Yellow crystals were obtained which melted at 176.5° and gave a yield of 78%. The filtrate was benzoylated;

^I M.P. Meta benz m-toluide, 124°, B-

2. Since the Kjeldahl method will not for some reason apply when there are two nitrogen atoms in the same ring, the combustion process was used in all analyses. The nitrogen was collected over KOH solution in a nitrometer, and measured.

the white crystals resulting melted at 143°. *(The product resulting from heating - O-toluidine and benzoyl chloride melted at 142.5°).

Analysis: .2417 gms. gave 30.3 cc. at 23° and 727.2 mm.

.2245 gms. gave 28.4 cc. at 24° and 726.7 mm.

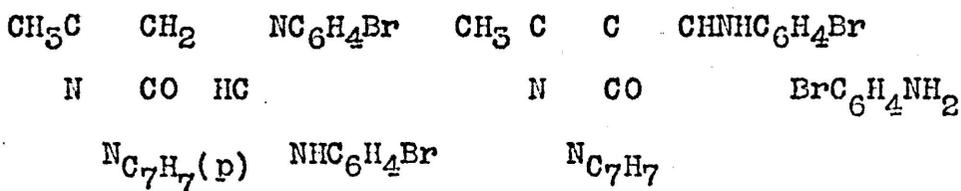
Found	Theory for C ₁₉ H ₁₉ ON ₃
13.86%	13.77%
13.69	

4-p bromanilido methylene - I p tolyl - 3 methyl -
5 pyrazolon, and Methenyl bis methyl p - tolyl pyrazolon.

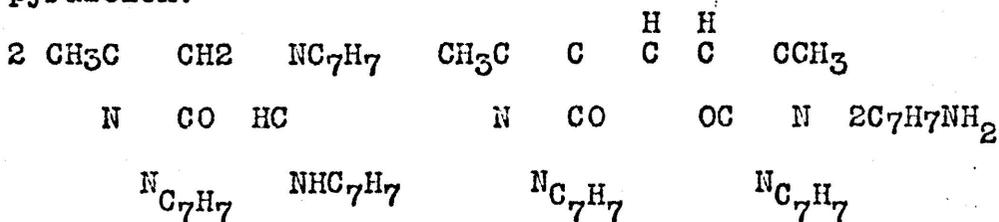
Doctor Dains heated di - p - brom di - phenyl formamidine with 3 - methyl - I p tolyl pyrazolon. I dissolved part of the product in alcohol slightly acidified. The residue was recrystallized from alcohol, giving yellow crystals, M.P. 196-7°, the pyrazolon expected. Something else was present, however, as another portion of the remainder on recrystallization from chloroform deposited first 1.4 grams of bright orange crystals; melting at 249°. Later deposits were a mixture of the two. The filtrate was treated with benzoyl chloride; the resulting glistening white crystals of benz p - brom anilide melted at 203°. **

* Benz o - toluid, 131° B. 21, 2553; 27, 2422.

** Benz p. brom anilid, 202° B. 8, 564; 32, 3581; 58, 2545.



The orange compound was identified by heating two moles of p-tolyl-methyl pyrazolon with one mole of di-m tolyl formamidine. A red solid formed on cooling. The base was separated out with water and HCl; the benztoluide formed with benzoyl cholride melted at 125-5° * The residue was recrystallized from chloroform and gave orange crystals, M. P. 249°. The mixture with the orange compound of the previous experiment melted at 248°, proving their identity as Methenyl bis methyl-p-tolyl pyrazolon.



Analysis: .2049 gms. substance gave 27.8 cc. nitrogen at 24.5° and 732.3 mm. 14.77%

.1928 gms. substance gave 25.9 cc. nitrogen at 23° and 735.3 mm. 14.78%

Found Theory for $\text{C}_{23}\text{H}_{21}\text{O}_2\text{N}_4$

14.77% 14.47%

14.78

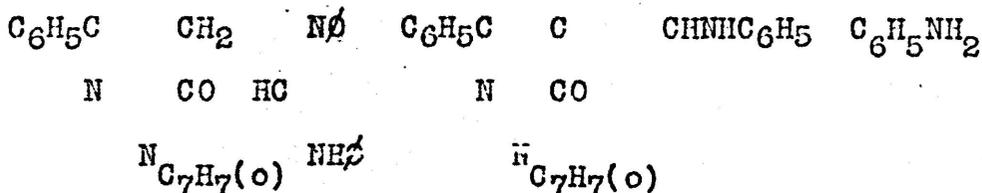
* Benz - m toluid, M.P. 124°.

4 - anilido - methylene - I o-tolyl - 3 phenyl -
5 pyrazolon

In preparing this product I - tolyl 3 phenyl pyrazolon was made by condensing molar quantities of o - tolyl hydrazine and benzoyl acetic ethyl ester. The result, on recrystallization from gasoline,



was a brown-white solid, M.P. 188°. Molar quantities of this pyrazolon and of di - phenyl formamidine were heated on an oil bath for 20 - 30 minutes at 150°. After the basic product was dissolved out with HCl, the residue was recrystallized from alcohol; lemon-yellow needles melting at 167-8° in 85.7% yield were obtained. A treatment of the filtrate yielded benzanilide, M.P. 160 - 161.5°. *



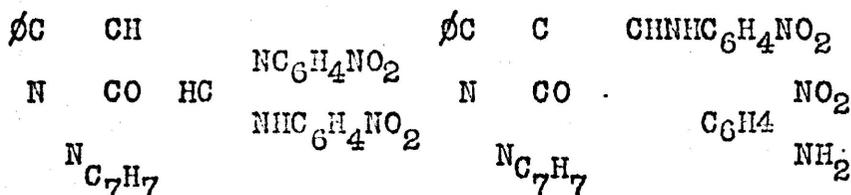
Analysis: .2532 g. gave 27.35 cc. at 22.3° and 729.5 mm.
.2434 g. gave 26.3 cc. at 21.5° and 729.2 mm.

Found	Theory for C ₂₃ H ₁₉ ON ₃
11.82%	11.90%
11.91	

* M.P. benzanilide 161 - 3°

4 - p - nitro anilido methylene, I o tolyl, - 3 phenyl,
5 pyrazolon

This was obtained by heating one mole of di - p - nitro - di - phenyl formamidine with one mole of phenyl tolyl pyrazolon at 170° for ten minutes. After the base was extracted with HCl, the residue was recrystallized from much boiling alcohol, yielding lemon-yellow crystals, M.P. 168.5°; yield 65%. The filtrate was concentrated and filtered again. This filtrate was made

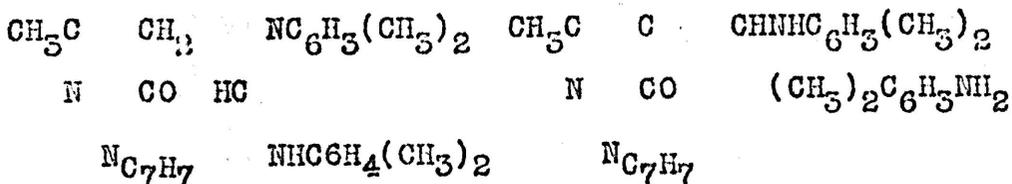


alkaline, when the yellow p - nitro - aniline came down; M.P. 147° *perfect yellow needles.

4 - m xylydine methylene, I - phenyl, 3 - methyl,
5 - pyrazolon

Di meta xylyl formamidine was heated with methyl phenyl pyrazolon for fifteen minutes at 110 - 125°. The brown solid product was acidified with HCl, and washed with alcohol to dissolve the base. The residue was recrystallized from much hot alcohol (it is very soluble in chloroform), forming golden yellow crystals, M.P. 171-3°; yield, 70%.

* M.P. p - nitroaniline 147°



With benzoyl chloride, the basic filtrate gave white crystals melting at 124° . * As this was far from the expected result the entire process was repeated. This time the filtrate yielded a white benzoyl product whose M.P. was $189 - 192^\circ$.* The yellow pyrazolon melted at 169° , but the mixture with the first product melted at 171° ; yield on second trial, 87.6%.

Analysis: .2299 g. gave 28.6 cc. at 24° and 735 mm.

.1945 g. gave 24.8 cc. at 24° and 739.6 mm.

Found Theory for $\text{C}_{19}\text{H}_{19}\text{ON}_3$

13.65% 13.77

14.05

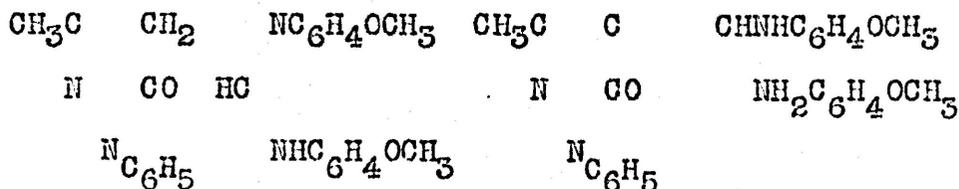
4 - p - methoxyanilido methylene, 1 - phenyl,

3 - methyl, 5 - pyrazolon

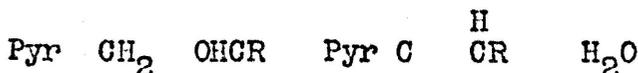
This was made by heating di - p - anisyl formamide with methyl-phenyl pyrazolon at 124° for two minutes, and allowing to cool in bath. Moist green crystals formed on standing. The mixture was treated with acid, and the residue recrystallized from hot alcohol. Golden brown needles resulted, M.P. 178° , a small quantity being obtained pure. Some methyl phenyl pyrazolon, M.P. 127° , was also obtained in this reac-

* M.P. benz m - xylydide (1,2,4,) 192° , B. 10, 1710

tion; it had evidently been unchanged, and came down in the acid filtrate. The benzanisidid obtained from the filtrate formed over two grams of shiny, colorless crystals, M.P. 156 - 156.5°.*



At the beginning of the work a series of pyrazolon compounds were prepared by heating together methyl phenyl pyrazolon and various aromatic aldehydes. Here, again, the methylene hydrogen of the pyrazolon was the point of attack. The general reaction occurring followed this equation:



This was mainly repetition of the work of others.

4 Benzal, - I phenyl, - 3 - Methyl, pyrazolon

The first of this series was obtained by heating molar quantities of methyl - phenyl pyrazolon and benzaldehyde at 140 - 160° on an oil bath. After some hours of cooling the mixture solidified. Deep red crystals were secured by recrystallizing from glacial acetic acid (or alcohol), M.P. 105 - 6°; **yield, 62.5%.

* M.P. benz anisidid 154.5°, B. 39, 3806.

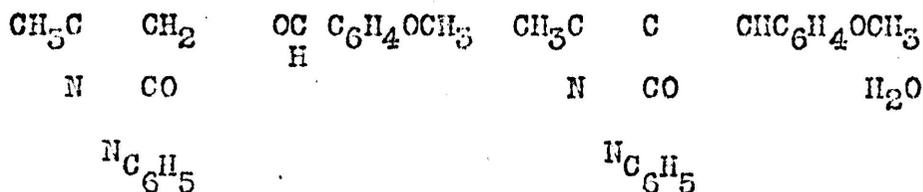
** M.P. benzal pyrazolon, 106-7°

heated some of the white form turned red again.

Analytical work confirmed the suspicion that this was only an isomeric form of the piperonal pyrazolon.

4 - Anisal, 1 - phenyl, 3 methyl pyrazolon

This was gotten by mixing equimolecular quantities of methyl phenyl pyrazolon and anisaldehyde at 140-160°. Fluffy red crystals recrystallized from hot alcohol, M.P. 126.5 - 127°; yield, 87.2%.



Analysis: .2209 g. gave 18.05 cc. at 24° and 735 mm.

.2093 g. gave 17.65 cc. at 25.3° and 735.2 mm.

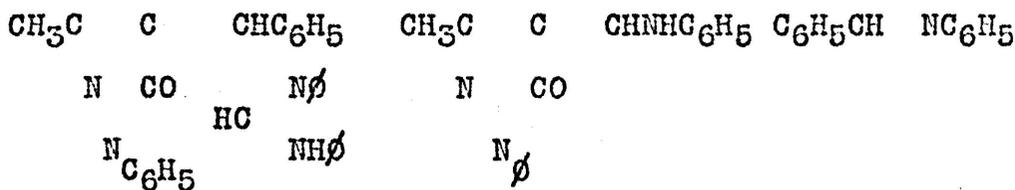
The persistence of the red color in this type of compound is very interesting, and would seem to be a fit subject for further investigation.

4 - Anilido - methylene, 3 methyl, 1 - phenyl
pyrazolon

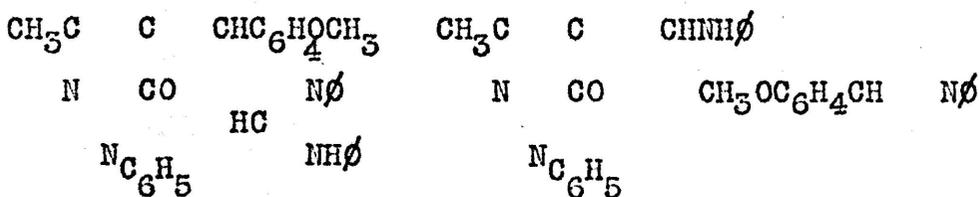
The rest of the work was on the preparation and properties of this substance. The first method of preparation was the interaction of the aldehyde pyrazolons made above, with di - phenyl formamidine.

Molar quantities of benzal - pyrazolon and di phenyl formamidine were heated at 140 - 165° for fifteen minutes. From the brown red solid, which appeared on

cooling, there was obtained by fractional crystallization from alcohol brown yellow crystals of the anilido pyrazolon, melting at 152°. Though the odor of benzal aniline was very apparent in the solution, efforts to recrystallize it from alcohol or ether failed.

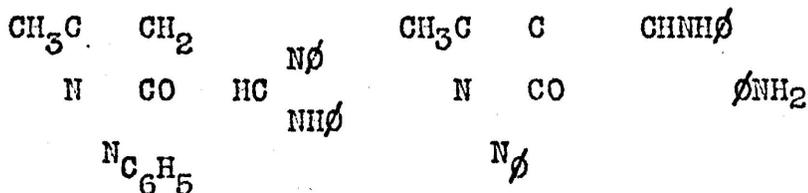


Anisal pyrazolon was heated with di - phenyl formamidine on the oil bath at 150 - 170°. The resulting product was dissolved in gasoline. A dark oil came down on adding HCl. This solidified and was recrystallized slowly from alcohol, giving yellow crystals, M.P. 152°. The mixture of these with anilido - pyrazolon also melts at 152°.



White piperonal - pyrazolon was heated with di - phenyl formamidine (2 moles) at 180°, allowing to cool. The product was recrystallized from alcohol, after acidifying with HCl; yellow crystals were finally obtained, M. P. 154°. Some red piperonal mono pyrazolon was observed, but could not be isolated. There was a strong odor of aniline present.

Anilido methylene methyl phenyl pyrazolon is most conveniently made by heating together molar quantities of di phenyl formamidine and methyl phenyl pyrazolon at 140 - 150° for 15 - 20 minutes. The brown mass which formed on cooling was boiled with dilute HCl, dissolving out the base. The residue was recrystallized from much boiling alcohol; yellow crystals melting at 153 - 153.5°. On benzoylating the filtrate (6.9 grams) considerable white benzanilid was formed, M.P. 162°. *



The yield obtained was 90.0%.

ACTION WITH HCl

Five grams of this anilido methylene methyl phenyl pyrazolon were boiled with a little alcohol and 10 cc. of HCl on a hot plate, with reflux condenser, for 4 - 5 hours. The next day a quantity of brown needles were apparent. These were filtered off, and washed with boiling alcohol, in which they were comparatively insoluble. The residue melted at 178.5°; yield, 1.5 grams.

* M.P. Benzanilide 161- 3°.

melting at 161° ,* showing the presence of aniline.

Heating under pressure with sealed tube at 150° for two hours gave a black solution, not investigated fully. There seemed, however, to be complete decomposition, not even the odor of aniline being apparent.

ACTION WITH KOH

Five grams of the anilido pyrazolon were boiled with 7.5 grams KOH in alcohol, on a water bath with reflux condenser for two hours, a reddish liquid resulting. On acidifying, cooling and adding water, the yellow original product settled out; M.P. on recrystallization, 148° . No trace of aniline in the filtrate.

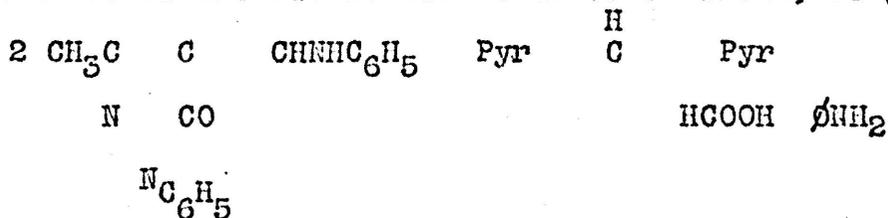
Boiling for 6 - 8 hours with KOH in alcohol was then tried. On cooling, a mass of fine, silky crystals appeared. These were filtered off, but as they were easily soluble in both alcohol and water, could not be purified. They were dried in a dessicator and analyzed for potassium by treating with H_2SO_4 , and weighing as K_2SO_4 ; but no accurate results could be obtained without washing the crystals. In the light of later work, prolonged boiling with alcoholic potash should be tried again.

The effect of metallic sodium was next tried. Four grams of the pyrazolon were placed in 50 cc. absolute alcohol and half a gram of sodium was added, the

* M.P. Benzanilide, $161-163^{\circ}$.

solid quickly dissolving. Some methyl iodide was added and the mixture heated 7 - 8 hours on hot plate. When poured into water, however, yellow crystals of the original separated out; M.P. 153°. Evidently unchanged.

Finally 5 grams of the pyrazolon were heated with 10 grams KOH in 20 cc. water, for several days. A crystalline mass was left, which dissolved in water. On adding acid, a yellowish mass came down; filtered off and recrystallized, this proved to be the original; M.P. 153°. From the filtrate there slowly came down a brown substance. When recrystallized, it melted at 179°; evidently the bis pyrazolon obtained with HCl, as a mixture of the two melted at 178.5°. Yield, .3 grams.



A strong odor of aniline was present.

BROMINATION

I treated some anilido pyrazolon with a molar quantity of bromine. A granular red-brown powder separated out, M.P. 159-161°; yield, 79.2%. Some bromine analyses seem to indicate that this is a tri bromide, but much work on the analysis and reactions of this compound remains to be done.

A later treatment of 5 grams with 3 grams bromine (both dissolved in chloroform) gave canary yellow crystals, M.P. about 200°.

NITRATION

To ten grams of the yellow powder, dissolved in concentrated H_2SO_4 and cooled, I added 5 grams of HNO_3 slowly. After some time, I poured the mixture into cold water, when brown-yellow crystals were formed at once. These were insoluble in hot alcohol, chloroform and gasoline. It was recrystallized from much hot pyridine; brown-yellow crystals, which did not melt at 250°; it is also soluble in hot nitrobenzene. The filtrate residue would not give an aniline test with bleaching powder, but on boiling, gave the odor of phenol. *

This nitro compound was untouched by boiling with HCl in alcohol for 6 - 8 hours. High pressure was tried and three grams sealed in a tube with 5 cc. HCl and heated to 150° for 4 - 5 hours. On unsealing, the odor of an aromatic nitro compound was apparent. Some yellow residue remained after treating with boiling water. As this did not melt at 250°, it was probably the original; yield, 1.7 grams. On my concentrating the filtrate and making it alkaline, brown crystals

* Aniline HNO_2 Diazo (D) Phenol

It had no sharp melting point, but decomposed up to 188° . It could not be analyzed by titration with standard alkali, and it failed to give a precipitate with AgNO_3 . Time did not permit of trying other methods.

This research has touched but briefly on some of the reactions of the methylene grouping of some pyrazolons and formamidines. Inasmuch as a large series of products similar to anilido methylene methyl phenyl pyrazolon are possible, this would seem an interesting field for investigation and comparison.

In conclusion I wish to express my appreciation of the kindly oversight and suggestions of Doctor F. B. Dains, under whose general direction the research has been conducted.

Respectfully submitted,