

become necessary to prepare additional compounds of the same class. These were prepared and purified and the nitrogen determinations made in the same way as for the others.

Name	Formula	M. p., °C. (cor.)	Nitrogen, % Calcd.	Found
N-Ethylpiperonyl- amide	C ₁₀ H ₁₁ NO ₂	87-88	7.25	7.29
N-Propylpiperonyl- amide	C ₁₁ H ₁₃ NO ₂	86-7	6.76	6.57
N-Amylpiperonyl- amide	C ₁₁ H ₁₇ NO ₂	104-5	5.95	5.84
N-(<i>m</i> -Chlorophenyl)- piperonylamide	C ₁₄ H ₁₃ ClNO ₂	110.5-112.5	5.08	4.94
N-(<i>o</i> -Bromophenyl)- piperonylamide	C ₁₄ H ₁₃ BrNO ₂	109.5-110	4.37	4.35
N-(<i>m</i> -Bromophenyl)- piperonylamide	C ₁₄ H ₁₃ BrNO ₂	116-117	4.37	4.30
N-(<i>p</i> -Bromophenyl)- piperonylamide	C ₁₄ H ₁₃ BrNO ₂	222-222.5	4.37	4.34

BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE

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WASHINGTON, D. C.

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RECEIVED JANUARY 19, 1944

N¹-Acetyl-N⁴-benzoyl-sulfanilamide

N¹-Acetyl-N⁴-benzoyl-sulfanilamide, the simplest N¹-acyl-N⁴-aracylsulfanilamide, has been prepared both by acetylation of N⁴-benzoyl-sulfanilamide and by benzoylation of N¹-acetyl-sulfanilamide.

Acetylation of N⁴-Benzoyl-sulfanilamide.—A solution of N⁴-benzoyl-sulfanilamide (m. p. 285-286^o) (1.4 g.) in acetic anhydride (11 ml.) and anhydrous pyridine (6 ml.) was refluxed in a boiling water-bath for one hour, and then

(1) Miller, Rock and Moore, *THIS JOURNAL*, **61**, 1199 (1939), reported the m. p. as 280^o.

cooled. The solid was collected and dried; it weighed 1.14 g. (70%), m. p. 261-263^o. The N¹-acetyl-N⁴-benzoyl-sulfanilamide was recrystallized from ethanol; it formed needles melting at 262-263^o. *Anal.* Calcd. for C₁₅H₁₄O₄N₂S: N, 8.80; neut. equiv., 318. Found: N, 9.01; neut. equiv., 317.

Benzoylation of N¹-Acetyl-sulfanilamide.—To a solution of 0.21 g. of N¹-acetyl-sulfanilamide² (m. p. 181-182^o) in 2 ml. of pyridine, five drops of benzoyl chloride was added. The solution was refluxed in a boiling water-bath for one hour. It was then diluted with water and acidified, whereupon 0.29 g. of N¹-acetyl-N⁴-benzoyl-sulfanilamide, m. p. 255-257^o, precipitated. After crystallization from ethanol, it melted at 261-262^o alone or when mixed with the product obtained by the first method.

The N¹,N⁴-dibenzoyl-sulfanilamide has also been prepared by refluxing either sulfanilamide or N⁴-benzoyl-sulfanilamide with excess of benzoyl chloride in the presence of pyridine for one hour. The mixture was then diluted with about ten times its volume of ethanol and allowed to stand in the icebox. The solid was recrystallized from ethanol in which it is only slightly soluble. The m. p. of the pure product was found to be 260^o (with decomposition).³ Yields in both cases were 70%. *Anal.* Calcd. for C₂₀H₁₆O₄N₂S: N, 7.37. Found: N, 7.57.

Thanks are due to Dr. T. S. Ma, University of Chicago, for the micro-analyses.

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RECEIVED JANUARY 11, 1944

(2) Crossley, Northey and Hultquist, *ibid.*, **61**, 2591 (1939); Huang, Lo and Chu, *J. Chinese Chem. Soc.*, **9**, 63 (1942).

(3) The m. p. of N¹,N⁴-dibenzoyl-sulfanilamide has been reported as 268-270^o by Dewing, Gray, Platt and Stephenson, *J. Chem. Soc.*, 239 (1942), and as 252^o (dec.) by Siehenmann and Schnitzer, *THIS JOURNAL*, **65**, 2126 (1943).

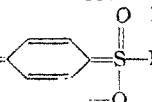
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COMMUNICATIONS TO THE EDITOR

STRUCTURE AND ACTIVITY OF SULFANILAMIDES

Sir:

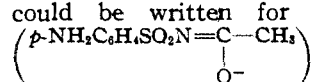
In a recent paper, Kumler and Daniels¹ have suggested that the activity of sulfonamides may be correlated with the contribution of the reso-

nance form, H₂N⁺= (1) to the struc-

ture of the molecule. To account for the fact that the sulfonamide anion seems to be the active form of the drug, they have postulated that the contribution of the resonance structure with the separation of charge is greater in the anion than in the undissociated molecule. *A priori*, one would be inclined to the contrary conclusion, and we believe the spectral evidence² confirms this interpretation.

High intensity ultraviolet absorption spectra are due to transitions from the neutral ground

state of the molecule to an ionic excited state.³ An increase in the number or contribution of ionic resonance structures stabilizes the excited state, *i. e.*, decreases its energy relative to that of the ground state, and hence shifts the maximum of the absorption toward larger wave lengths. Consequently, the fact that the maximum absorption of sulfanilamide in neutral solution is at 2600 Å., whereas that in basic solution is at 2500 Å., indicates that ionic resonance forms contribute *less* to the anion than they do to the undissociated molecule.

The Kumler and Daniels theory also does not explain the low activity of sulfanilylurea and 3-sulfanilamido-1,2,4-triazole. Resonance structures similar to those written for these molecules could be written for N¹-acetylsulfanilamide, () for sulfadiazine,

(1) Kumler and Daniels, *THIS JOURNAL*, **65**, 2190 (1943).

(2) Kumler and Strait, *ibid.*, **65**, 2349 (1943).

(3) Mulliken, *J. Chem. Phys.*, **7**, 20 (1939); **7**, 121 (1939); **7**, 339 (1939); O'Shaughnessy and Rodebush, *THIS JOURNAL*, **62**, 2906 (1940).