

between solid and liquid phases.³ Since k cannot be negative, the limiting value of K_f' must be smaller than K_f . The unexpected behavior of camphor therefore cannot be caused by solid solution.

Since the theory cannot be satisfied, it seems that the experimental data must be at fault somewhere. The experimental values involved in the calculation of the ideal constant, K_f , are the melting point and the heat of fusion. The melting point, though somewhat uncertain, can hardly be so incorrect, especially as an absolute temperature, as to account for an almost 50% change in K_f . The fusion heat seems to have been measured with great care, and it similarly does not seem possible for it to be wrong by such a factor; Frandsen reports it as 10.74 ± 0.40 cal., and his data seem to justify this estimate.

There are, however, two points in Frandsen's report which indicate that the camphor under observation near its melting point was not absolutely pure; it appears that it may have been slightly impure at the outset or that it underwent some slight decomposition at temperatures at or near its melting point. Thus: (1) the cooling curve for the determination of the melting point shows a degree of rounding-off hardly consistent with purity; and (2) the agreement in the duplicate determinations of heat content for liquid camphor was not very close. Incidentally, the above suggestions about the impurity or the instability of the camphor used are made by Frandsen himself.

Now, while a slight degree of impurity or instability would hardly affect the measured melting point and heat of fusion to the extent here in question, it is possible to account, on such a basis, for the apparently anomalous molecular freezing point depressions reported by Meldrum. Even with initially pure camphor, it may be that the melting, mixing and grinding required in the preparation of the binary mixtures for melting point determinations, caused in each case a small and approximately constant extent of decomposition of the camphor. If this decomposition amounts to m' moles of foreign species per 1000 g. of camphor, then the true molecular depression would be $K_f = \Delta T_f / (m + m')$. If m' is very small, its neglect would have a negligible effect on K_f measured in high concentration, but would cause the apparent K_f' to rise higher and higher as the concentration decreases.

It is sufficient to assume m' equal to only 0.005, in Meldrum's experiments, to derive a molecular depression approximately constant throughout, within the probable experimental error (as shown in Fig. 1), and with an average value of 39.2° per mole, which is sufficiently close to the calculated limiting or ideal value. The constancy is even better than it seems, when it is remembered that

(3) Thus in Glasstone, "Text-Book of Physical Chemistry," D. Van Nostrand Co., New York, 1940, p. 641.

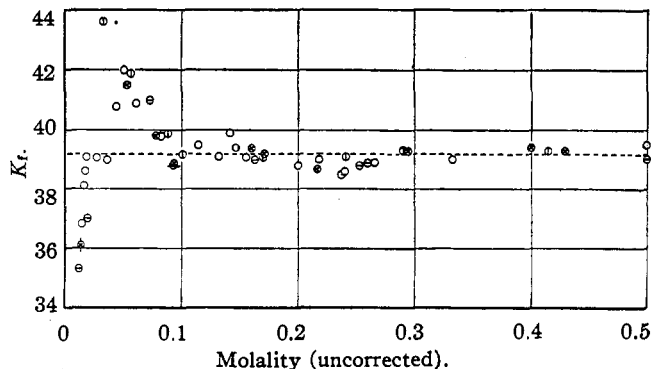


Fig. 1—Solute key: O, naphthalene; ⊙, *p*-bromodiphenyl; ⊖, phenylacetic acid; ⊗, ethylacetanilide.

the points at lowest concentration are likely to be experimentally the most uncertain (as pointed out by Meldrum himself). Since the temperatures in Meldrum's experiments seem to have been measured to a precision of only 0.05° , ΔT is probably dependable only within 0.05 to 0.10° . It follows then that at small values of m , even relatively large variations in the value of the ratio $\Delta T/m$ must be considered insignificant; for example, ± 2 or 3 at $m = 0.05$, and as high as ± 8 at m (uncorrected) = 0.012 . It is significant that the values of K_f now calculated from all the measurements with $\Delta T > 3^\circ$, lie, with one exception, within one unit of the mean, 39.2 , the average deviation being only 0.3 unit.

It should be pointed out that, depending on the molecular weight of the impurity, this value of m' would represent about 0.02 to 0.06% (for molecular weights of 50 to 150) by weight of the camphor used. Such contamination or decomposition would hardly be detectable in the melting point or in the heat of fusion of the substance, but would have the actual effect on the determination of K_f at very low concentrations which was observed by Meldrum.

We have here, in other words, another and very sensitive method for the determination of the purity (or the stability) of a substance. In the absence of solid solution, the molecular depression of the freezing point should approach the value calculated from its melting point and heat of fusion, in limiting dilution.

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NEW COMPOUNDS

N-Substituted Piperonylamides

In a previous communication¹ several new N-substituted piperonylamides have been recorded. Since then, it has

(1) Gertler and Haller, *THIS JOURNAL*, **64**, 1741 (1942).

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	85-7	5.76	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

AGRICULTURAL RESEARCH ADMINISTRATION

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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.

NATIONAL RESEARCH INSTITUTE OF CHEMISTRY

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CHIEN-PEN LO⁴

LUCY JU-YUNG CHU

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(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 Siebenmann 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 resonance form, H₂N=C₆H₄-S(=O)₂NR (1) to the structure 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, (*p*-NH₂C₆H₄SO₂N=C(CH₃)), for sulfadiazine,

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

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

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