perature for the reaction is about 245°, but it was found advantageous to work close to a reflux temperature (270–275°). When evolution of hydrogen sulfide ceased, the mixture was cooled to 140°, and about 5 ml. of hot xylene was added for each gram of *p*-toluic acid. The solution was refluxed 30 minutes, filtered hot, and the cake washed with hot xylene. Evaporation of the xylene yielded any unreacted *p*-toluic acid and sulfur and some of the acids of higher molecular weight. The toluic acid could be distilled off and reused. The filter cake was extracted with hot dioxane, which dissolves more than 20 g. of higher polymer acids per 100 ml. The remaining cake consisted largely of 4,4'-stilbenedicarboxylic acid, with a small amount of an unidentified, yellow polymeric acid. The stilbenedicarboxylic acid was dissolved in a slight excess of boiling aqueous KOH, allowing about 4 g. of stilbenedicarboxylic acid per 100 ml. of solution, and the potassium salt of the stilbenedicarboxylic acid crystallized from the solution. The free acid was precipitated from the hot salt solution by addition of an excess of HCl and digestion of the hot solution to ensure the absence of the insoluble half-acid salt and to coagulate the otherwise colloidal precipitate. Purification of 4,4'-stilbenedicarboxylic acid can also be effected through the ammonium or guanidine salts.

TABLE I

REACTION OF *p*-TOLUIC ACID WITH SULFUR

Run	Reactants, mole Toluic	S	*p*-Toluic acid purity, %	*T*, °C.	Hr.	*p*-Toluic acid reacted, %	SDCA[a] Yield, %
1	1.0	0.5	97.8	260	4.5	51.7	60.6
2	1.0	0.05	92.6	260	4.0	5.7	70.6
3	1.0	1.0	Pure	271	2.0	79.5	57.3
4	1.0	0.5	97.8	275–280	3.0	55.0	53.6

[a] SDCA = 4,4'-stilbenedicarboxylic acid, yield based on *p*-toluic acid reacted.

4,4'-Stilbenedicarboxylic Acid.—Repeated recrystallization of the potassium salt of stilbenedicarboxylic acid gives a white, sulfur-free product. The free acid, m.p. 460° (sealed tube), has a neutral equivalent of 134.1. Permanganate oxidation gave terephthalic acid almost quantitatively. The acid chloride was prepared by reaction of thionyl chloride in the presence of pyridine, m.p. 228–232°. The diethyl ester, b.p. 195–203° (0.1–0.09 mm.), m.p. 129.9–130.0°, was prepared from the acid chloride. Previous workers report for the acid chloride, m.p. 223–224°[2] and 227–228°.[6] For the diethyl ester, a m.p. of 130–131° is reported.[1] The absorption spectrum of an aqueous solution of the potassium salt shows broad peaks at 3425, 3275 3150 and approximately 2300 Å. The configuration of the spectrum closely resembles the spectra of *p*-toluic acid and dimethyl terephthalate, but is displaced to longer wave lengths. It closely resembles published spectra[7,8] of *trans*-*p,p'*-stilbene derivatives but not those of *cis*-stilbene derivatives. The acid and its solution show intense blue fluorescence when irradiated with ultraviolet light of the appropriate wave length, which is not a characteristic of *cis*-stilbene.[7] Irradiation of stilbenedicarboxylic acid with 2537 Å. light causes a change in the spectrum similar to *trans* to *cis* isomerization of stilbene. Hence, the available evidence points to the conclusion that the product is the *trans* isomer of 4,4'-stilbenedicarboxylic acid.

The solubility of 4,4'-stilbenedicarboxylic acid in most neutral solvents is less than 20 mg./100 ml. It is moderately soluble in dimethyl formamide, acetic anhydride and molten toluic acid, and somewhat soluble in ethylene glycol and diethylene glycol. Solubility in boiling sulfolane is about 2.5 g./100 ml., and the acid can be recrystallized from this solvent.

Tetra-(*p*-carboxyphenyl)-thiophene.—The dioxane-soluble, xylene-insoluble products could not be crystallized from dioxane. A brown to orange, finely divided solid was obtained by pouring the solution slowly into a large excess of xylene or water. Sulfur analyses of this crude material gave values varying from 5.10 to 5.41%, compared to 5.67% for tetra-(*p*-carboxyphenyl)-thiophene. Oxidation of the compound with permanganate gave terephthalic acid. The molecular weight of the crude compound, determined ebulliometrically in acetone, was 520 ± 30 (theoretical for tetra-(*p*-carboxyphenyl)-thiophene, 564.62). As sulfur reacts with stilbene and its analogs to form thiophene derivatives[3-5] it seems probable that the main by-product is impure tetra-(*p*-carboxyphenyl)-thiophene, which has not yet been isolated in pure form due to contamination with low polymers of the type reported by Thayer and Corson.[4]

3,3'-Stilbenedicarboxylic Acid.—Refluxing 104 g. (0.765 mole) of *m*-toluic acid with 12.2 g. (0.383 mole) of sulfur at 262–267° until evolution of hydrogen sulfide ceased (5 hours), followed by extraction with two 150-ml. portions of hot xylene and washing with acetone gave 5.0 g. of dimer acid cake. Evaporation of the xylene, and extraction of the solid with 250 ml. of acetone containing 25 ml. of water, followed by xylene extraction to remove sulfur, gave an additional gram of dimer acid. Crystallization of the ammonium salt, acidification and digestion with hydrochloric acid gave 4.5 g. of acid, neutral equivalent 135.6 (theory 134.1). Oxidation with permanganate gave isophthalic acid.

The dimethyl ester was formed by refluxing 2 g. of acid with 50 ml. of methanol and 5 ml. of concentrated sulfuric acid. The ester was dissolved by addition of chloroform, the solution washed with water and sodium carbonate solution, and the ester crystallized twice from mixed chloroform and methanol to give 1.0 g. of ester, m.p. 145.5–146°.

Anal. Calcd. for $C_{18}H_{16}O_4$: C, 72.95; H, 5.44; sapn. equiv., 148.15. Found: C, 72.65; H, 5.35; sapn. equiv., 147.7.

Purified 3,3'-stilbenedicarboxylic acid, prepared by saponifying the dimethyl ester and precipitating the free acid, melted at 352–354°. Titration with 0.1 *N* permanganate solution in boiling 0.05 *N* sodium hydroxide solution to give an end-point stable for more than 30 seconds took 95% of the theoretical permanganate.

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.63; H, 4.51. Found: C, 71.53; H, 4.60.

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(6) G. P. Hager and H. A. Shonle, THIS JOURNAL, **68**, 2167 (1946).

(7) G. N. Lewis, T. T. Magel and D. Lipkin, *ibid.*, **62**, 2973 (1940).

(8) M. Calvin and R. E. Buckles, *ibid.*, **62**, 3324 (1940).

The Dielectric Properties of Supercooled Liquids[1]

BY G. N. ROBERTS[2]

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Viscosity measurements on phenyl ether[3] indicate the existence of a structural change occurring in the supercooled liquid at the melting point; the points obtained by plotting log η against $1/T$, where η is the viscosity at absolute temperature T, fall into two groups corresponding to measurements made above and below the melting point, the points of each group lying on a straight line but the line for the supercooled liquid being steeper than that for the liquid above the melting point. A similar effect has been observed for *m*-chloronitrobenzene, menthol and salol[4] and Greenwood and Martin[5] have observed corresponding discontinuities at the

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(1) This note represents part of the work submitted by Dr. G. N. Roberts to the University of London in fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Frick Chemical Laboratory, Princeton University, Princeton, N. J.

(3) C. Dodd and Hu Pak Mi, *Proc. Phys. Soc. (London)*, **B62**, 454 (1949).

(4) Hu Pak Mi, Thesis, University of London, 1950.

(5) N. N. Greenwood and R. L. Martin, *J. Chem. Soc.*, 1795 (1951).

melting points while examining the conductivities of a number of ionic complexes formed from boron trifluoride. Preliminary measurements on phenyl ether, menthol, salol and azoxybenzene[6] have revealed discontinuities in the temperature variation of the static dielectric constant ϵ_0 of these substances and this note reports further measurements carried out on both polar and non-polar liquids.

Experimental

Measurements of the static dielectric constant ϵ_0 were carried out using an oscillator loosely coupled to a parallel resonance circuit which had the test cell containing the specimen liquid and the variable condensers C_m and C_p which could be adjusted to tune the circuit to resonance. Resonance was indicated by a maximum reading on a valve voltmeter. The oscillator was crystal controlled at a frequency of 80.86 kc./s. C_m was a low-loss micrometer air condenser similar to that described by Ward and Pratt.[7] It had a linear response up to a capacitance value of 8 $\mu\mu$F., corresponding to 2500 scale divisions. C_p consisted of a low-loss air condenser variable between 10–50 $\mu\mu$F. The test cell was of the concentric cylinder type, of low-loss and small stray capacitance. The cell was immersed in a constant temperature bath maintained to within 0.01° for tests above room temperature and to within 0.05° for tests below this temperature. For the empty cell, the capacitance of that portion of the cell normally containing the dielectric was 9.9 $\mu\mu$F. and the stray capacitance 3.02 $\mu\mu$F. The variation of the empty cell capacitance with temperature was approximately linear, changing by only 0.0331 $\mu\mu$F. for a temperature change of 40°.

Experimental Results

(a) **Polar Liquids.**—In Fig, 1, micrometer condenser settings for resonance and values of ϵ_0 deduced from these settings are shown plotted against temperature for liquid methyl *n*-nonyl ketone. The line drawn through the experimental points is the quadratic calculated by the method of least squares to fit best the points corresponding to the liquid above its melting point (12.1°). The points for the supercooled liquid also lie on a line which is, however, inclined to the line for the normal liquid. This discontinuity is brought out more strikingly by the inset to the graph, where deviations of *all* points from the quadratic for the liquid above the melting point are plotted against temperature. Above the melting point the deviations are small and both positive and negative about the zero line, but in the supercooled region the deviations are all positive and increase progressively as the temperature is lowered. A similar discontinuity in the ϵ_0–temperature curve has been observed for *p*-bromotoluene (m.p. 27.5°). It may be mentioned that repeated measurements on salol carried out at the Frick Chemical Laboratory, Princeton University, using a heterodyne beat apparatus[8] and also an impedance bridge,[9] gave results similar to those previously reported.[5]

(b) **Non-polar Liquids.**—Attempts to supercool benzene (m.p. 5.5°) and cyclohexane (m.p. 6.4°) were unsuccessful. The symmetry of the molecules of these substances probably enables them to set into crystal lattices with little rearrangement or re-orientation when the temperature is lowered below their respective melting points. On the other hand, moderately asymmetrical molecules have been shown to supercool readily.[10] Suitable liquids, therefore, appeared to be those with molecules whose attached groups caused sufficient asymmetry to prevent premature crystallization but whose arrangement of groups was such as to make the whole molecule effectively non-polar.

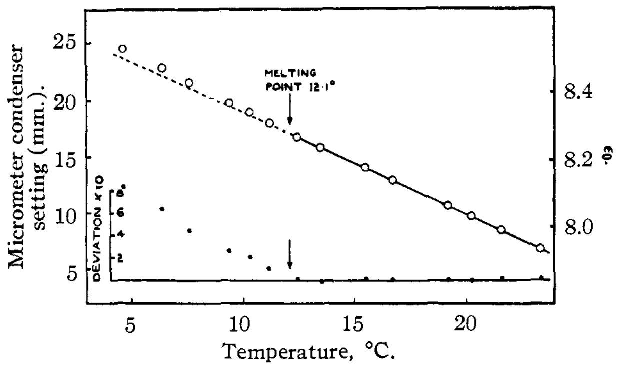

Fig. 1.—Micrometer condenser setting and ϵ_0 *vs.* temperature for methyl *n*-nonyl ketone.

TABLE I

	M.p., °C.	Dipole moment, $\mu \times 10^{18}$ Literature	This work
Diphenylmethane	25.5	0.30, 0.23, 0.37, 0	<0.3
p-Xylene	13.2	0.06, 0.12, 0	< .2
Bibenzyl	50.7	0.36, 0.02, 0	< .3

Table I lists the dipole moments given in the literature[11,12] for the three liquids tested, together with the moments estimated from measurement of ϵ'' over a range of temperature at 3 cm. wave length using a H_{01} cavity resonator. The very small moment observed for *p*-xylene is probably due to impurity. In Fig, 2, the micrometer condenser setting for resonance is plotted against temperature for both normal and supercooled diphenylmethane and the inset to the graph shows the deviations of all points from the best quadratic through the points in the normal region. Over the whole temperature range these deviations are small

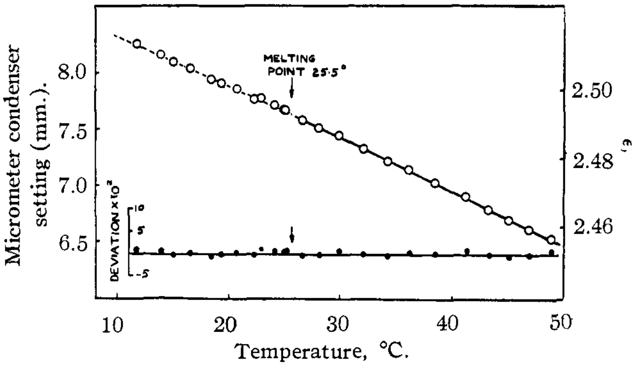

Fig. 2.—Micrometer condenser setting and ϵ_0 *vs.* temperature for diphenylmethane.

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[6] C. Dodd and G. N. Roberts, *Proc. Phys. Soc.* (*London*), **B63**, 814 (1950).

[7] W, Ward and E. Pratt, *J. Sci. Instruments*, **16**, 192 (1939).

[8] L. M. Kushner and C. P. Smyth, THIS JOURNAL, **71**, 1401 (1949).

[9] C. P. Smyth and C. S. Hitchcock, *ibid.*, **54**, 4631 (1932); **55**, 1830 (1933).

[10] W. O. Baker and C. P. Smyth, *ibid.*, **61**, 2063 (1939).

[11] Table of Dipole Moments, *Trans. Faraday Soc.*, **30**, 1193 (1934).

[12] C. P. Smyth, "Dielectric Constant and Molecular Structure," Chemical Catalog Co. (Reinhold Publ. Corp.), New York, N. Y., 1931

and unsystematic. Similar results have been obtained for *p*-xylene and bibenzyl.

Discussion

For the six polar liquids so far tested, a significant discontinuity in the slope of the static dielectric constant–temperature curve has been found in the neighborhood of the melting point in each case. On the other hand, no such effect has been observed with any non-polar or slightly polar liquids, suggesting that the *magnitude* of the change in slope may be related—at least in a qualitative way—to the permanent dipole moment. In Table II are listed the differences in slope between the lines for the normal and supercooled liquids, together with the respective dipole moments and values of ϵ_0 at the melting point. Examination of the table does reveal a qualitative relationship between the change in slope $d\epsilon_0/dT$ and the dipole moment for the four liquids of smallest dipole moment. This relationship does not hold, however, for azoxybenzene and salol, and one reason for this disagreement may be the existence of dipolar interaction or association which would be expected to have a strong influence on any process that might occur at the melting point. Thus it seems more legitimate to compare the magnitude of the change in slope (change in $d\epsilon_0/dT$) with ϵ_0 itself, since ϵ_0 is a macroscopic measure of the polarization produced in the pure liquid, which includes the effects of dipolar interaction. If n^2 is regarded as the contribution toward the dielectric constant from electronic and atomic polarization, n being the index of refraction, then $(\epsilon_0 - n^2)$ is that part arising only from the orientation of permanent molecular dipoles. In Fig. 3, change in $d\epsilon_0/dT$ is shown plotted against $(\epsilon_0 - n^2)$ for each liquid tested and now the points are seen to lie reasonably well on a line through the origin.

TABLE II

	Change in slope $d\epsilon_0/dT$	Dipole moment, $\mu \times 10^{18}$	ϵ_0	$\epsilon_0 - n^2$
Azoxybenzene	0.0010	3.39	5.2	2.4
Salol	.0019	3.15	6.4	3.6
Methyl *n*-nonyl ketone	.0036	2.69	8.3	6.3
p-Bromotoluene	.0031	1.90	6.0	3.6
Menthol	.0009	1.58	4.0	1.8
Phenyl ether	.0006	1.15	3.6	1.1
Diphenylmethane	.0	<0.3	2.49	0.01
Bibenzyl	.0	< .3	2.42	.05
p-Xylene	.0	< .2	2.23	.00

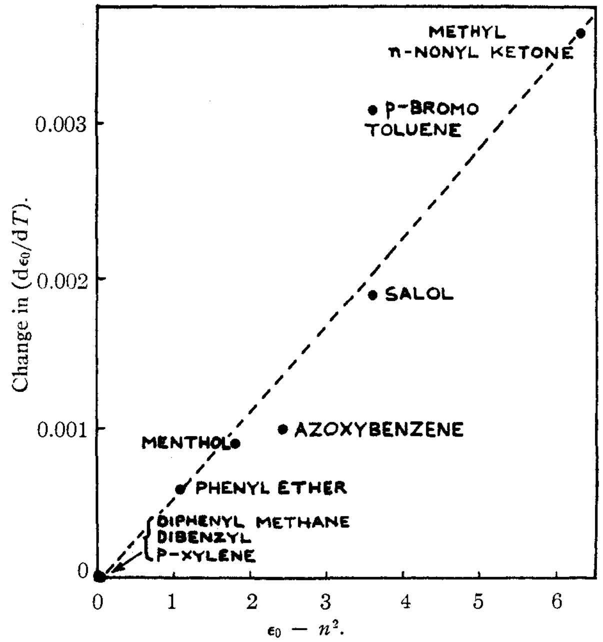

Fig. 3.—Correlation of change in $d\epsilon_0/dT$ with $(\epsilon_0 - n^2)$.

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N-Trifluoroacetyl Derivatives of Carcinogenic Amines[1]

BY EUGENE SAWICKI AND F. E. RAY

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N-Acetyl derivatives of 2-aminofluorene,[2] 2,7-diaminofluorene,[3] 2-naphthylamine,[4] 4-aminobiphenyl,[5] 3-aminodibenzofuran[6] and 3-aminodibenzothiophene[7] have been shown to have carcinogenic properties. The free amines, 2-anthramine,[7] benzidine[8] and 2',3-dimethyl-4-aminoazobenzene,[9] have also been shown to be active.

In the fluorene series it has been shown that 2-aminofluorene is carcinogenic in the rat.[10] The carcinogenic N-acetyl derivative is easily hydrolyzed *in vivo*.[11] On the other hand, 2-benzoylaminofluorene has little activity[12] and cannot be hydrolyzed readily.[13] Similarly the non-carcinogenic[12] 2-*p*-tosylaminofluorene is stated to be very slightly hydrolyzed *in vivo*.[14] On the basis of these facts it is probable that the free amines or their metabolites are the primary carcinogens. To test this hypothesis the N-trifluoroacetyl derivatives have been prepared. According to this hypothesis if the trifluoroacetyl derivatives cannot be hydrolyzed *in vivo*, then they should be non-carcinogenic. If these groups are hydrolyzed, then the compounds should be carcinogenic

The physical properties and yields of the compounds are given in Table I.

General Procedure.—To 0.01 mole of the amine (or 0.005 mole of the diamine) in 20 ml. of hot benzene was carefully added through a reflux condenser 0.01 mole of tri-

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[1] The work described in this paper was supported by a grant from the Sloan-Kettering Institute for Cancer Research.

[2] R. Wilson, F. DeEds and A. Cox, *Cancer Research*, **7**, 453 (1947).

[3] H. P. Morris and C. Dubnik, *ibid.*, **10**, 233 (1950).

[4] G. Bonser, *J. Path. Bact.*, **55**, 1 (1943).

[5] R. Melby, R. Brown and R. Sandin, THIS JOURNAL, **72**, 1032 (1950).

[6] E. Miller, J. Miller, R. Sandin and R. Brown, *Cancer Research*, **9**, 504 (1949).

[7] F. Bielschowsky, *Brit. J. Exper. Pathology*, **27**, 54 (1946).

[8] S. Spitz, W. Maguigan and K. Dobriner, *Cancer*, **3**, 789 (1950).

[9] H. Crabtree, *Brit. J. Cancer*, **3**, 387 (1949).

[10] H. P. Morris, C. S. Dubnik and J. M. Johnson, *J. Nat. Cancer Inst.*, **10**, 1201 (1950).

[11] H. P. Morris, J. H. Weisburger and E. K. Weisburger, *Cancer Research*, **10**, 620 (1950).

[12] H. P. Morris, private communication.

[13] H. R. Gutmann and J. H. Peters, *Cancer Research*, in press.

[14] F. E. Ray and M. F. Argus, *ibid.*, **11**, 783 (1951).