

NOTES.

Note on "Syntheses in the Indole Series. Part II." (*J.*, 1946, 461). By JOHN W. BAKER.

THE author's attention has been called to the fact that the reaction of acid chlorides of the type $\text{CO}_2\text{R}\cdot[\text{CH}_2]_n\cdot\text{COCl}$ ($n = 0$ or 1) (cf. also *J.*, 1940, 458) with indolylmagnesium iodide, described in the above communications, had previously been published by Oddo and Albanese (*Gazzetta*, 1927, **57**, 827), who actually prepared ethyl β -keto- β -3-indolylpropionate, identical in m. p. 121° , with the product obtained by the present author. It is regretted that the earlier publication was inadvertently overlooked, and acknowledgment is now made.—THE UNIVERSITY, LEEDS. [Received, January 17th, 1947.]

The Mechanism of Substitution at a Saturated Carbon Atom. By A. G. EVANS, M. G. EVANS, and M. POLANYI.

IN a recent paper by Dostrovsky, Hughes, and Ingold (*J.*, 1946, 173), calculations are made of the effect of steric hindrance on the activation energy of an organic substitution reaction. For the bimolecular reaction $\text{X}^- + \text{R} - \text{X} \longrightarrow \text{X} - \text{R} + \text{X}^-$ the transition state will involve resonance between two structures of equal energy, *viz.*, $\text{X}^- \cdots \text{R} - \text{X}$ and $\text{X} - \text{R} \cdots \text{X}^-$. Any such configuration is a possible transition state. To calculate the interatomic distances of the actual transition state one must find the configuration for which the potential energy is a minimum; the distances involved in the transition state are determined by this condition alone. The work of Polanyi (*Proc. Roy. Soc.*, 1934, *B*, **116**, 203), Ogg and Polanyi (*Trans. Faraday Soc.*, 1935, **31**, 604), and Baughan and Polanyi (*ibid.*, 1941, **37**, 648) has shown how this calculation can be made for symmetrical substitution reactions.

If the negative ion is assumed to be incompressible, then the minimum energy of the transition state is achieved when both the carbon-halogen distances are equal to the sum of the carbon radius and the ionic radius of X^- . This was used by Baughan and Polanyi as a first approximation in the determination of the transition-state configuration. There is no question here of determining the configuration of the transition state without considering the energy as a function of configuration. Steric compressions for the methyl to *tert.*-butyl halide series have been calculated by A. G. Evans and Polanyi (*Nature*, 1942, **149**, 608) using the transition-state distances obtained by Baughan and Polanyi.

Dostrovsky, Hughes, and Ingold (*loc. cit.*) claim to be able to define the configuration of the transition state by a different method. In the case of a symmetrical bimolecular reaction as discussed above they would obtain the transition-state distance by adding the covalent radius of carbon to the mean of the covalent and negative ionic radii of the halogen (p. 176). They point out that this procedure differs from that of Baughan and Polanyi, who take the full negative ionic radius of the halogens, and they suggest that their procedure is more correct since there is only one unit of charge shared between the incoming and outgoing halogen. This seems to indicate a misunderstanding of the approximation used by Baughan and Polanyi. We believe that any proper determination of transition-state distances, however approximate in nature, must necessarily involve a consideration of the dependence of energy upon these distances.

The authors do in fact use the method of Ogg and Polanyi at a later stage to calculate the absolute value of the activation energy. On this occasion they compare the transition-state distances obtained from their own method with those obtained from the correct application of the transition-state method, and a measure of agreement is found. Any such agreement, however, must be regarded as fortuitous.

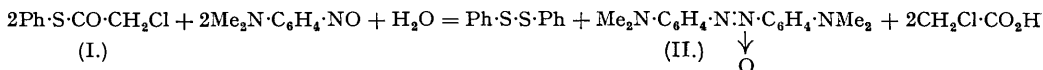
An important point is the conclusion to be drawn about the existence of polar effects in the series methyl to *tert.*-butyl halides. These authors find that in this series the increase in activation energy calculated as due to steric hindrance is about one half of that found experimentally. They conclude from this that about one half of the increase in the bimolecular activation energy along this series is due to the induction effect. In our experience, the type of calculation involved here is not sufficiently exact to warrant such a quantitative conclusion. We feel, therefore, that for the primary to tertiary halide series there is no evidence that the decrease in the bimolecular reaction rate is due to anything other than the increase in steric repulsion energy along this series as postulated by Polanyi, Ogg, and A. G. Evans (*loc. cit.*), Meer and Polanyi (*Z. physikal. Chem.*, 1932, **B**, **19**, 164), and A. G. Evans (*Nature*, 1946, **157**, 438).—UNIVERSITY OF MANCHESTER. [Received, July, 29th, 1946.]

The Preparation and Properties of Thiol-esters. By CHARLES E. DALGLIESH and
FREDERICK G. MANN.

Phenyl chlorothiolacetate, Ph·S·CO·CH₂Cl (I), is readily prepared in 95% yield by the action of chloroacetyl chloride on an ice-cold aqueous alkaline solution of thiophenol. The *p*-tolyl ester can be similarly prepared, and is identical with that obtained by Arndt and Bekir (*Ber.*, 1930, **63**, 2390) who proved its constitution. This method of preparation is similar to Chattaway's method (*J.*, 1931, 2495) of acetylating phenols in alkaline solution with acetic anhydride, and is of interest because it is generally stated (cf. "Organic Chemistry", Gilman, 2nd Edtn., 1944, p. 932) that aliphatic acid chlorides are too readily hydrolysed to be used in aqueous suspension, and react with thiophenols and alkyl thiols only under anhydrous conditions.

Although ω -chloroacetanilide, Ph·NH·CO·CH₂Cl, can be readily cyclised to oxindole, and phenylthioacetyl chloride, Ph·S·CH₂·COCl, to thioindoxyl, (I) cannot be cyclised to thio-oxindole under similar conditions, probably because it enolises. This reaction, if it could be achieved, would be valuable, as Marschalk's preparation (*J. pr. Chem.*, 1913, **88**, 239) of thio-oxindole from oxindole is laborious and wasteful.

(I) reacts with *p*-toluidine to give thiophenol and chloroaceto-*p*-toluidide. It also reacts very readily with *p*-nitrosodimethylaniline to give diphenyl disulphide and 4 : 4'-bis(dimethylamino)azoxybenzene (II) :



The azoxy-compound was also obtained when *p*-tolyl chlorothiolacetate was used, but not with phenyl thiolbenzoate, Ph·S·COPh. Several examples are known of the reaction of nitroso-derivatives with compounds containing the ·CO·CH₂X group (X = halogen) in the presence of pyridine (Krohnke and Borner, *Ber.*, 1936, **69**, 2006; Sanna, *Gazzetta*, 1942, **72**, 363); thus phenacyl bromide and nitrosobenzene give the nitrone, Ph·CO·CH·N·Ph. It is possible therefore that unstable intermediates



of the nitrone type are formed in the course of the above reaction with *p*-nitrosodimethylaniline.

(I) reacts with thiourea to form 2-thiohydantoin, undoubtedly through the intermediate formation of *N*-chloroacetylthiourea.

Experimental.—Thiophenol (25 g.) was dissolved in a solution of sodium hydroxide (13.5 g., 1.5 mols.) in water (40 c.c.) containing crushed ice (150 g.). Chloroacetyl chloride (37 g., 1.5 mols.) was then rapidly added, and the whole vigorously shaken for 5 minutes. The solid *phenyl chlorothiolacetate* (I) (40 g., 95%) was collected, dried, and recrystallised from aqueous alcohol; colourless leaflets, m. p. 45° (Found : C, 51.7; H, 3.9; Cl, 19.5. C₈H₇OClS requires C, 51.5; H, 3.8; Cl, 19.0%).

A similar preparation, using thio-*p*-cresol (27.5 g.), afforded *p*-tolyl chlorothiolacetate (44 g., 98%), m. p. 40° after crystallisation from alcohol. Arndt and Bekir (*loc. cit.*) give m. p. 38°.

The similar use of benzoyl chloride afforded phenyl thiolbenzoate.

When (I) (1.9 g.) and *p*-toluidine (1.1 g., 1 mol.) were gently fused together, thiophenol was readily evolved. The cold residue, recrystallised from alcohol, furnished chloroaceto-*p*-toluidide (1.3 g., 70%), colourless needles, m. p. 161—162° (Found : N, 7.6. Calc. for C₉H₁₀ONCl : N, 7.6%).

A solution of *p*-nitrosodimethylaniline (9 g.) in alcohol (50 c.c.) was added to a solution of (I) (11.4 g.) in alcohol (40 c.c.), and the mixture boiled for 5 minutes and set aside (the reaction occurs, but more slowly, in the cold). The precipitated azoxy-compound (II) (5.5 g., 65%) was collected and recrystallised from benzene; glistening brown needles, m. p. 241° (Found : C, 67.7; H, 6.8. Calc. for C₁₆H₂₀ON₄ :

C, 67.6; H, 7.0%. Consistent values for nitrogen could not be obtained). Previous workers have given m. p.'s ranging between 236° and 244°. The alcoholic filtrate was added to dilute hydrochloric acid (600 c.c.) and extracted with ether; evaporation of the dried extract gave diphenyl disulphide, (5.2 g.), colourless crystals from alcohol, m. p. 60° (Found: C, 66.0; H, 4.7; S, 29.4. Calc. for $C_{12}H_{10}S_2$: C, 66.1; H, 4.6; S, 29.4%).

(I) gave a *monopicrate* which separated from benzene as ruby-red needles, m. p. 144° (decomp.), containing benzene of crystallisation (Found: C, 54.8; H, 4.7; N, 18.0. $C_{16}H_{20}ON_4, C_6H_5O_7N_3, \frac{1}{2}C_6H_6$ requires C, 54.3; H, 4.7; N, 17.8%); heating at 80°/0.1 mm. for 3 hours gave yellow needles of the benzene-free picrate, m. p. unchanged (Found: C, 51.9; H, 4.7; N, 19.2. $C_{16}H_{20}ON_4, C_6H_5O_7N_3$ requires C, 51.5; H, 4.5; N, 19.1%). (II) gave a *distyphnate*, which crystallised from benzene as yellow needles, m. p. 148° (decomp.), which also contained benzene of crystallisation (Found: C, 46.1; H, 3.8; N, 17.4, 17.0. $C_{16}H_{20}ON_4, 2C_6H_5O_8N_3, \frac{1}{2}C_6H_6$ requires C, 45.8; H, 3.6; N, 17.2%). (II) did not apparently form a methiodide.

The identity of (II) was further confirmed by reductive acetylation (cf. Dalglish and Mann, *J.*, 1945, 894). A mixture of (II) (3 g.), acetic acid (30 c.c.), acetic anhydride (30 c.c.), and zinc dust was refluxed for 3.5 hours and filtered; the residue was extracted with boiling acetic acid, and the combined filtrates were poured into water. After concentration and cooling, *p*-dimethylaminoacetanilide, $Me_2N \cdot C_6H_4 \cdot NHAc$, white plates, m. p. 130°, was obtained (Found: N, 15.8. Calc. for $C_{10}H_{14}ON_2$: N, 16.0%). Further concentration gave successive crops of the same compound.

A mixture of (I) (5 g.), thiourea (2.05 g.), alcohol (25 c.c.), and water (5 c.c.) was refluxed for 2 hours, cooled, diluted with water, and basified. The solution deposited 2-thiohydantoin, white needles (1.25 g.), m. p. 228° (decomp.) after recrystallisation from aqueous alcohol. Wheeler, Nicolet, and Johnson (*Amer. Chem. J.*, 1911, **46**, 469) give m. p. 228°. It gave a *picrate*, yellow needles from alcohol, m. p. 195—198° (decomp.) (Found: N, 20.3. $C_6H_4ON_2S, C_6H_5O_7N_3$ requires N, 20.3%).

During preliminary experiments on the action of chloroacetyl chloride on sodium thiophenoxide suspended in organic liquids, one of the products isolated was *phenyl phenylthiothiolacetate*, $Ph \cdot S \cdot CO \cdot CH_2 \cdot S \cdot Ph$, pale brown crystals from alcohol, m. p. 64—65° (Found: C, 64.0; H, 4.5. $C_{14}H_{12}OS_2$ requires C, 64.6; H, 4.6%).—UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [Received, August 17th, 1946.]

4-*p*-Aminostyryl- and 2:6-Di-*p*-aminostyryl-pyridine. By RICHARD ROYER.

A SEARCH of the literature reveals several cases of styrylpyridines where different authors have assigned the same constitution to two substances of widely-differing solubilities and melting points. In each case the analytical figures appear satisfactory, but the higher-melting substance has been prepared in a roundabout way. The present work provides the first direct syntheses of the higher-melting compounds, thus confirming their constitution. It is assumed that the problem is one of geometrical isomerism and that the lower-melting and more soluble forms are probably the *cis*-isomerides. However, repetition of the procedures described for producing the low-melting forms gave only the high-melting compounds.

4-*p*-Nitrostyrylpyridine (4'-Nitro-4-stilbazole).—Baumert (*Ber.*, 1906, **39**, 2971) obtained the low-melting form (m. p. 118—119°) by heating 4-methylpyridine, *p*-nitrobenzaldehyde, and zinc chloride. By the nitration of 4-styrylpyridine, Wagstaff (*J.*, 1934, 276) obtained a substance of m. p. 171° (apparently corrected) to which he assigned this constitution as it gave a 24% yield of *p*-nitrobenzoic acid on oxidation with nitric acid (*d* 1.42). The following is the first direct synthesis of this compound.

4-Methylpyridine (1.9 g.; Eastman's pure), *p*-nitrobenzaldehyde (3.0 g.; 1 mol.), and acetic anhydride (2.0 g.; 1 mol.) were refluxed for 5 hours in a bath at 155—160°. Crystals separated on cooling and were filtered off, washed with acetic acid, then with water, and dried (4.1 g.; m. p. 150—153°). Recrystallisation from ethanol gave Wagstaff's 4-*p*-nitrostyrylpyridine (2.8 g.; 60%), m. p. 167—168° (170—171° corr.).

4-*p*-Aminostyrylpyridine. Baumert (*loc. cit.*) reduced his nitro-compound with stannous chloride and obtained a substance, m. p. 138—139°, readily soluble in ethanol, ether, and chloroform, and analysing for 4-*p*-aminostyrylpyridine. Wagstaff did not reduce his compound.

4-*p*-Nitrostyrylpyridine (2.0 g.; m. p. 167—168°) was added during ten minutes to a solution of hydrated stannous chloride (7.5 g.; 25% excess) in concentrated hydrochloric acid (8 ml.) maintained in a boiling water-bath. Heating was continued for 1½ hours with occasional stirring. The thin paste was poured into 2.5*N*-sodium hydroxide and excess of the latter added until Orange-II paper was reddened. The solid was filtered off, dried, and continuously extracted (Soxhlet) with acetone, giving 1.46 g. (85%) of yellow crystals, m. p. 273—274°. After repeated recrystallisation from ethanol and washing with acetone, the m. p. became steady at 275° (285° corr.). The substance consists of yellow crystals, slightly soluble in methanol, soluble in about 270 parts of boiling (and 600 parts of cold) ethanol and only slightly soluble in boiling benzene, chlorobenzene, chloroform, ether, or acetone (Found: C, 79.6; H, 6.2; N, 14.3%. $C_{12}H_{12}N_2$ requires C, 79.55; H, 6.2; N, 14.3%). It is evident that this is a form of 4-*p*-aminostyrylpyridine, higher-melting and less soluble than that described by Baumert, and that the two amino-compounds differ from one another in much the same way as the isomeric nitro-compounds from which they were derived.

Concentrated hydrochloric acid dissolves the high-melting base to give a faintly yellow solution which becomes quite colourless on dilution to *N*/2 acid and yellow on further dilution (*N*/20 acid), the latter being the colour of the freely soluble monohydrochloride. The pale yellow diazo-solution couples (crimson) with β -naphthol. The base dissolves with an orange colour in glacial (and a deep yellow colour in *N*-) acetic acid; the higher melting form of the similarly constituted 5-*p*-aminostyrylacridine is yellow and gives a violet solution in acetic acid (Sharp, Sutherland, and Wilson, *J.*, 1943, 5).

2:6-Di-*p*-nitrostyrylpyridine.—Werner (*Ber.*, 1903, **36**, 1687) obtained the low-melting form (m. p. 168—169°) by melting together 2:6-dimethylpyridine, *p*-nitrobenzaldehyde, and zinc chloride. By nitrating 2:6-distyrylpyridine, Wagstaff (*loc. cit.*) obtained a compound, m. p. 258° (apparently

corrected), to which he assigned the same constitution on the grounds of the analytical figures and the production of *p*-nitrobenzoic acid in 83% yield on oxidation with nitric acid. The following is the first direct synthesis of this compound.

2 : 6-Dimethylpyridine (5.35 g.; b. p. 142°), *p*-nitrobenzaldehyde (10.6 g.; 2 mol.), and acetic anhydride (30 g.; 6 mol.) were refluxed for 10 hours. The yellow crystals which separated on cooling were filtered off, washed with acetic acid, then with water, and dried at 110°. The yield was 54%, m. p. 251—253°, but only 40% was obtained after 5 hours' refluxing. Repeated recrystallisations from pyridine and from chlorobenzene gave material of constant m. p. 253—254° (262—263° corr.) and agreeing with Wagstaff's description in all other respects. Identical results were obtained with two specimens of pure 2 : 6-dimethylpyridine, one of Australian and one of American origin.

2 : 6-Di-*p*-aminostyrylpyridine.—Werner (*loc. cit.*) reduced his nitro-compound with tin and hydrochloric acid and obtained a substance, m. p. 146°, readily soluble in dilute alcohol and analysing for 2 : 6-di-*p*-aminostyrylpyridine. Wagstaff did not reduce his compound.

2 : 6-Di-*p*-nitrostyrylpyridine (2.0 g.; m. p. 253—254°) was finely powdered, suspended in acetone (50 ml.), and reduced with hydrogen and Raney-nickel catalyst at atmospheric temperature and pressure until the calculated amount had been absorbed (2 hours). After filtration, the solution was concentrated to 20 ml. and treated with water (both liquids at 50°) until crystallisation began (0.72 g.; 44%; m. p. 230—231°). Repeated recrystallisation from dilute acetone raised the m. p. to 233°. The substance consists of golden crystals, sparingly soluble in boiling alcohol, benzene, and ether, moderately soluble in chlorobenzene and chloroform, and readily soluble in pyridine with green fluorescence (Found: C, 80.1; H, 6.1; N, 13.5. $C_{21}H_{19}N_3$ requires C, 80.5; H, 6.1; N, 13.4%). Obviously this is a higher-melting and less soluble 2 : 6-di-*p*-aminostyrylpyridine than that described by Werner.

The new substance does not evolve ammonia on boiling with 5*N*-sodium hydroxide. The hydrochloride is only sparingly soluble in water; the mono-acetate is deep orange and moderately soluble. The yellow diazo-solution couples (crimson) with β -naphthol.

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