

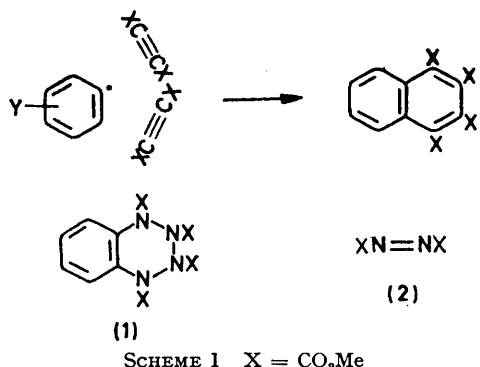
Reaction of Phenyl Radicals with Dialkyl Azodiformates: Formation of, and Nuclear Magnetic Resonance Studies of Conformational Restrictions in, Tetra-alkyl 1,4-Diphenyltetra-azane-1,2,3,4-tetracarboxylates

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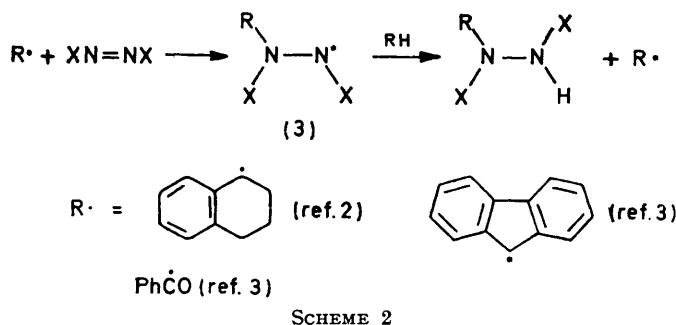
Dialkyl azodiformates ($\text{RO}_2\text{C}\cdot\text{N}=\text{N}\cdot\text{CO}_2\text{R}$; $\text{R} = \text{Me}, \text{Et}, \text{or Bu}^t$) do not undergo annelation reactions with phenyl radicals from benzoyl peroxide, to give tetrahydrobenzotetrazines. Instead they give good yields (up to 69%) of the novel, very stable tetra-alkyl 1,4-diphenyltetra-azane-1,2,3,4-tetracarboxylates (4), formed by addition of phenyl radicals to give hydrazyls $\text{PhN}(\text{CO}_2\text{R})\cdot\text{N}(\text{CO}_2\text{R})\cdot$ which then dimerise. Reaction of dimethyl azodiformate with triphenyl(phenylazo)methane gives dimethyl *N*-phenyl-*N'*-triphenylmethylhydrazodiformate (9; $\text{R} = \text{Me}$). Variable-temperature n.m.r. studies of the latter and of the tetra-azanes (4) show that considerable barriers to rotation about $\text{N}-\text{CO}_2\text{Et}$ bonds exist in these compounds.

Oxidation of diethyl *N*-phenylhydrazodiformate (10) by lead tetra-acetate does not give the tetra-azane (4; $\text{R} = \text{Et}$) but instead proceeds *via* a novel deformylation to give ethyl phenylazoformate ($\text{PhN}=\text{NCO}_2\text{Et}$).

In the preceding paper¹ we showed that aryl radicals, generated from dibenzoyl peroxide, react with dimethyl acetylenedicarboxylate to give naphthalenetetracarboxylates. It was of considerable interest to see whether a corresponding annelation to give the unknown tetrahydrobenzotetrazine system (1) occurred on reaction of dibenzoyl peroxide with dialkyl azodiformates (2) (Scheme 1).



We were encouraged in this because several examples of the addition of radicals ($\text{R}\cdot$) to azodiformates in the

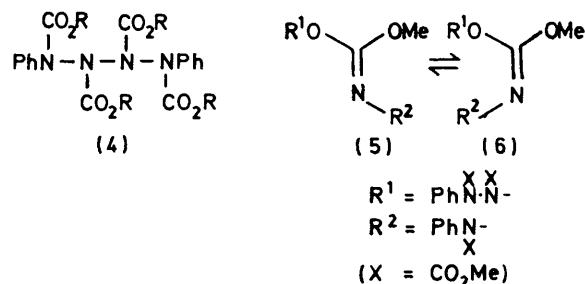


presence of hydrogen donors had been reported.^{2,3} In all cases the reaction proceeds as shown in Scheme 2, and

¹ B. D. Baigrie, J. I. G. Cadogan, and J. T. Sharp, preceding paper.

² K. Alder, F. Pascher, and A. Schmitz, *Ber.*, 1943, **76**, 27; L. Horner and W. Naumann, *Annalen*, 1954, **587**, 81.

there is ample additional evidence³⁻⁵ of the ease with which azodiformates undergo radical addition reactions. Since the pattern of these reactions suggested that radical addition to give a hydrazyl (3) occurs readily, but that hydrogen abstraction (Scheme 2) is also favoured, it was clear that annelation to give (1) would be more likely in the absence of hydrogen donors. Accordingly we allowed dibenzoyl peroxide to decompose in an excess of dimethyl azodiformate at 80°. Annelation did not occur and instead we isolated the novel tetramethyl 1,4-diphenyltetra-azane-1,2,3,4-tetracarboxylate (4; $\text{R} = \text{Me}$) (69%). Similar reactions occurred with diethyl and di-*t*-butyl azodiformates.



Structure of Tetra-alkyl 1,4-Diphenyltetra-azane-1,2,3,4-tetracarboxylates (4).—The product from dimethyl azodiformate, for example, had elemental analysis and molecular weight (high resolution mass spectrometry) which suggested a dimeric form of the 1:1 adduct of phenyl radicals and the azodiformate. This was in accord with the tetra-azane structure (4; $\text{R} = \text{Me}$) but at first sight the ¹H n.m.r. spectrum was puzzling (Figure 1). As expected, there were two methyl singlets at τ 6.2 and 6.8; both were very broad, possibly indicating a number of almost equivalent absorptions under each signal. The integral tracings of the respective methyl signals gave a ratio of 2:1. A variable-temperature study of the n.m.r. spectrum gave the maximum

³ R. Huisgen and H. Pohl, *Chem. Ber.*, 1960, **93**, 527.

⁴ K. Alder and T. Noble, *Ber.*, 1943, **76**, 54.

⁵ A. Shah and M. V. George, *Tetrahedron*, 1971, **27**, 1291.

ratio as 2 : 1 at all temperatures between -60 and 80° ; between 80 and 140° the ratio converged to unity, reaching a minimum of 1.2 : 1 at 140° and all temperatures up to 200° (Table). At no stage did the signals coalesce, although the separation decreased from 54 Hz at 28° to 30 Hz at 200° .

Since the product appeared to be isomerically pure these n.m.r. data pointed to an equilibrium mixture of

give a hydrazyl radical ion at m/e 223 (100%) which then underwent two common skeletal rearrangements as shown. The prediction of metastable peaks at m/e 144 and 121 for the respective rearrangements was borne out.

Exactly comparable and consistent data were obtained for the products (4; R = Et or Bu^t) of reaction of dibenzoyl peroxide with diethyl and di-*t*-butyl azodiformates [see Table for (4; X = CO₂Et)].

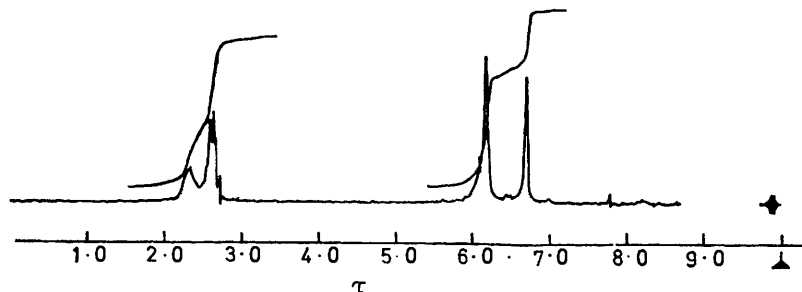


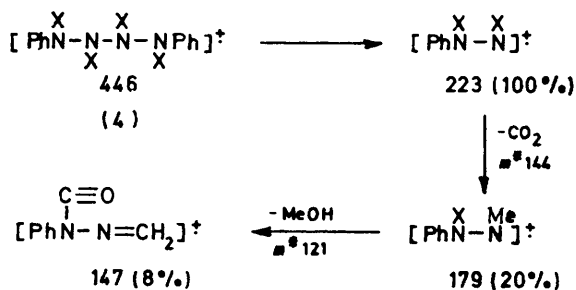
FIGURE 1 ^1H N.m.r. spectrum of (4; R = Me) at 28°

preferred conformers of (4) rather than a mixture of isomers such as (5) and (6). This was supported by ^{13}C n.m.r. spectroscopy; four different carbonyl absorptions were observed at 155.4, 155.3, 155.2, and 153.5

Variation of the ratios of methyl absorptions in tetra-azanes (4; R = Me or Et) with temperature

Temp. (°C)	Solvent	Ratio of methyl singlets in (4; X = CO ₂ Me)	Ratio of methyl triplets in (4; X = CO ₂ Et)
-60	CDCl ₃	2 : 1	3 : 2
-20	CDCl ₃	2 : 1	3 : 2
0	CDCl ₃	2 : 1	3 : 2
28	CDCl ₃	2 : 1	3 : 2
60	CDCl ₃	12 : 7	4 : 3
80	Ph ₂ O	2 : 1	5 : 4
120	Ph ₂ O	3 : 2	1 : 1 : 1
140	Ph ₂ O	1 : 2 : 1	1 : 1 : 1
160	Ph ₂ O	1 : 2 : 1	1 : 1 : 1

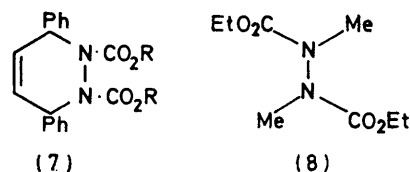
p.p.m., and four different methyl absorptions were observed at 54.6, 54.3, 53.8, and 53.3 p.p.m.; two distinct aromatic nitrogen-bearing carbon atoms were also observed. Finally, detailed analysis of the mass



SCHEME 3 X = CO₂Me

spectrum confirmed that the compound had structure (4) (Scheme 3). The product fragmented as expected to

The apparent anomalies posed by the ^1H n.m.r. spectra of compounds (4; R = Me, Et, or Bu^t) can be successfully rationalised in terms of these compounds existing in solution as mixtures of conformers, as a result of hindered rotation about the N-CO₂R bonds. Examples of this are rare but not unknown. The first to be reported for the system N-CO₂R (R = Me or Et) was the observation⁶ of conformational isomerism in the tetrahydropyridazines (7), and low-temperature ^1H n.m.r. observations⁷ in the system (8), closely related to ours,



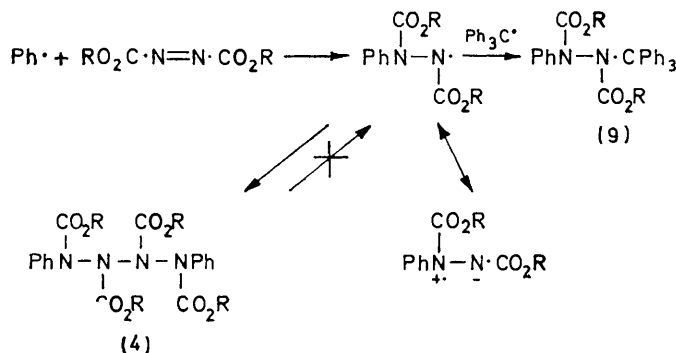
are compatible with equilibrium between some or all of the possible *trans*-coplanar conformations. In our case, the number of possible conformations is even greater, leading to a correspondingly more complex ^1H n.m.r. spectrum.

Mode of Formation of the Tetra-azanes (4).—There seems little doubt that these novel tetra-azanes (4) are formed by attack of phenyl radicals on the azo-ester with subsequent dimerisation of the long-lived hydrazyl radical (3; X = CO₂R) (Scheme 4). That this dimerisation step was favoured was demonstrated when dilution of the respective reaction mixtures with benzene still gave the tetra-azanes in comparable yields together with bi-phenyl. It is known that hydrazyl radicals such as 1-acyl-1,2-diphenylhydrazyl dimerise to give the corres-

⁶ J. C. Breliere and J. M. Lehn, *Chem. Comm.*, 1965, 426.

⁷ B. Price, I. O. Sutherland, and F. G. Williamson, *Tetrahedron*, 1966, 3477.

ponding tetra-azanes,⁸ although most of these easily undergo reversible dissociation. The tetra-azanes (4)

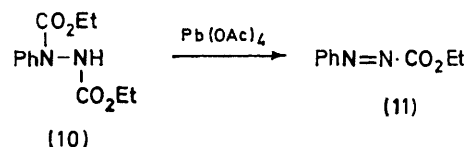


SCHEME 4

were remarkably stable, showing no tendency to dissociate even at 200°. In accord with Scheme 4, decomposition of *N*-nitrosoacetanilide, an alternative source of

position of triphenyl(phenylazo)methane in dimethyl azodiformate gave dimethyl *N*-phenyl-*N'*-triphenylmethylhydrazodiformate (9; R = Me) (11%), indicating the intermediacy of the hydrazyl radical, subsequently trapped by the long-lived triphenylmethyl radical (Scheme 4). This triphenylmethylhydrazine (9; R = Me) provided a further example of an equilibrating mixture of conformers: a variable-temperature ¹H n.m.r. study showed that the mixture could be frozen at low temperatures (Figure 2A) but equilibrated rapidly at higher temperatures (Figure 2B–F).

Attempts to synthesise the tetra-azane (4; R = Et) by first producing the hydrazyl radical (3; X = CO₂Et) by oxidation of diethyl *N*-phenylhydrazodiformate (10) failed. Compound (10) did not react with lead dioxide in benzene, *N*-bromosuccinimide, or di-*t*-butyl peroxide in *t*-butylbenzene. Reaction with lead tetra-acetate gave ethyl phenylazoformate (11) (Scheme 5).



SCHEME 5

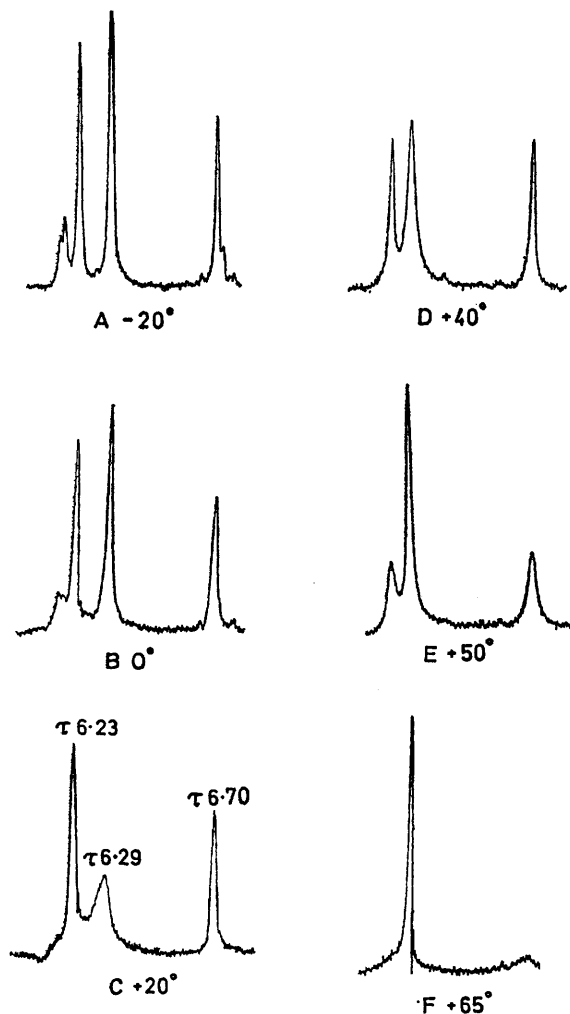


FIGURE 2 Methyl signals of (9; R = Me) at various temperatures

phenyl radicals, in diethyl azodiformate gave the corresponding tetra-azane (4; R = Et). Further, decom-

EXPERIMENTAL

Reactions of Diethyl Azodiformate with Dibenzoyl Peroxide.—Dibenzoyl peroxide (1.21 g, 5 mmol) was allowed to decompose at 80°, under nitrogen, in diethyl azodiformate (8.7 g, 50 mmol). After 12 h, the excess of solvent was distilled off and the residue, an amorphous sticky solid (3.0 g), was examined by t.l.c. (alumina; dichloromethane). Only one component was observed. The residue was dissolved in boiling methanol, and on cooling the product crystallised as lustrous plates (1.50 g, 60 mol per 100 mol of peroxide), m.p. 137.5–138° (Found: C, 57.3; H, 5.8; N, 11.0%; *M*⁺, 502.207545. C₂₄H₃₀N₄O₈ requires C, 57.4; H, 6.0; N, 11.2%; *M*, 502.206370), of tetraethyl 1,4-diphenyltetra-azane-1,2,3,4-tetracarboxylate, *m/e* 502, 251 (13%), and 179.082351 (100%) (C₉H₁₁N₂O₂), τ (CDCl₃) 2.20–2.60br (4H, m, aromatic), 2.60–2.73br (6H, m, aromatic), 5.60–6.50 [8H, 2 vbr quartets, 4 × (O₂CH₂)], and 8.60–8.88 and 9.20–9.42 (12H, 2 br triplets, 4 × OCH₂CH₃) (the integral tracings for the two ester triplets gave a ratio of 3 : 2, as did the tracings for the two ester quartets; no change in the spectrum was observed after shaking the deuteriochloroform solution with a solution of sodium dithionite in D₂O); δ_C (CDCl₃) 154.9 (C=O), 153.0 (C=O), 140.3 (C-N, aromatic), 128.3–128.0 (C-H, aromatic), 63.3 and 62.9 (2 × OCH₂), and 14.5 and 13.5 p.p.m. (OCH₂CH₃), ν_{max} (Nujol) 1730 cm⁻¹ (C=O), λ_{max} 207 nm (log ϵ 3.98). High speed liquid chromatography (h.s.l.c.) (Spherisorb A, 20 μ ; CH₂Cl₂) indicated a single product with a retention time of 4.6 min.

The reaction was repeated with benzene as solvent. Dibenzoyl peroxide (1.21 g, 5 mmol) was decomposed in a solution of diethyl azodiformate (5.22 g, 30 mmol) in benzene (7.8 g, 100 mmol) at the b.p. The mixture was cooled and kept at 10° for 48 h. The precipitate was filtered off;

⁸ A. R. Forrester, J. M. Hay, and R. H. Thomson, 'Organic Chemistry of Stable Free Radicals,' Academic Press, London, 1968.

recrystallisation from methanol afforded a product (1.04 g, 40 mol per 100 mol of peroxide) identical with that obtained above. The filtrate was evaporated and the residue (2.7 g) was chromatographed on a dry alumina column to give biphenyl (0.15 g, 20 mol per 100 mol of peroxide), m.p. and mixed m.p. 70°.

Reactions of Dimethyl Azodiformate.—(i) *With dibenzoyl peroxide.* Dibenzoyl peroxide (1.21 g, 5 mmol) was allowed to decompose in dimethyl azodiformate (7.3 g, 50 mmol), stirred under nitrogen at 80°. After 12 h, the excess of solvent was distilled off and the residue, a sticky orange gum (4.5 g), was recrystallised from benzene-cyclohexane (1 : 3) to give, as a colourless solid (1.55 g, 69 mol per 100 mol of peroxide), m.p. 225°, *tetramethyl 1,4-diphenyltetra-azane-1,2,3,4-tetracarboxylate* (Found: C, 53.6; H, 5.1; N, 12.6. $C_{20}H_{22}N_4O_8$ requires C, 53.8; H, 4.9; N, 12.6%), *m/e* 282 (M^+ , 10%), 223 (100%), and 179 (15%), τ (CDCl₃) 2.20—2.50br (4H, m, aromatic), 2.50—2.75br (6H, m, aromatic), and 6.23 and 6.79 (12H, 2 br singlets, 4 × CO₂CH₃) (integral tracings for the two methyl singlets gave a ratio of 2 : 1), δ_G (CDCl₃-0.05M-chromium acetylacetonate) 155.4, 155.3, 155.2, and 153.5 (4 × C=O), 140.1 and 140.0 (2 × C-N, aromatic), 128.4—127.1 (C-H, aromatic), and 54.6, 54.3, 53.8, and 53.4 p.p.m. (4 × OCH₃), ν_{max} (Nujol) 1730 cm⁻¹ (C=O). H.s.l.c. (Spherisorb A, 20 μ ; CH₂Cl₂) indicated a single product with retention time 7 min.

The reaction was repeated with (a) benzene (7.8 g, 100 mmol) and (b) *t*-butylbenzene (13.4 g, 100 mmol) as solvent. In both cases the above product was obtained in yields of 56 and 27 mol per 100 mol of peroxide, respectively.

(ii) *With N-nitrosoacetanilide.* *N*-Nitrosoacetanilide (0.83 g, 5 mmol) was allowed to decompose in dimethyl azodiformate (3.65 g, 25 mmol) stirred under nitrogen in an ice-bath. The solution was gradually allowed to reach room temperature and then stirred for 12 h. The excess of solvent was distilled off and the black tarry residue was boiled with methanol. The hot solution was filtered and the brown powder obtained was recrystallised from benzene-cyclohexane (1 : 3) to give a cream-coloured solid (0.12 g, 11%), identical with the product obtained from dibenzoyl peroxide.

(iii) *With triphenyl(phenylazo)methane.* Triphenyl(phenylazo)methane (3.48 g, 10 mmol) was allowed to decompose in a solution of dimethyl azodiformate (5.84 g, 40 mmol) in benzene (7.8 g, 100 mmol) at the b.p. The dark residue obtained (5.6 g) after removal of solvents was chromatographed on alumina (350 g) to give triphenylmethane (0.03 g, 1%), m.p. and mixed m.p. 93°, and a yellow solid which when recrystallised from benzene gave, as a white, amorphous powder (0.5 g, 11%) which sublimed with-

out melting, *dimethyl N-phenyl-N'-triphenylmethylhydrazodiformate* (9; R = Me) (Found: C, 74.8; H, 5.8; N, 5.9. $C_{29}H_{26}N_2O_4$ requires C, 74.7; H, 5.6; N, 6.0%), *m/e* 466 (M^+) and 243 (100%), ν_{max} (Nujol) 1725 and 1710 cm⁻¹ (C=O), τ (CDCl₃) 2.82 (18H, s, aromatic), 3.26—3.53br (2H, m, aromatic), and 6.23, 6.29, and 6.70 (6H, 2 br singlets and a sharp singlet, 2 × CO₂CH₃), δ_G (CDCl₃) 157.4, 156.4, 156.0, and 155.3 (4 × C=O), 143.1, 142.4, 141.9, and 141.2 (4 × C, aromatic), 130.8—125.7 (C-H, aromatic), 53.5 and 52.5 (2 × OCH₃), and 80.8 p.p.m. (CPh₃).

Reaction of Di-t-butyl Azodiformate with Dibenzoyl Peroxide.—Dibenzoyl peroxide (1.21 g, 5 mmol) was decomposed under nitrogen in a solution of di-*t*-butyl azodiformate (3.45 g, 15 mmol) in benzene (7.8 g, 100 mmol) at the b.p. After 12 h, standard work-up gave biphenyl (20 mol per 100 mol of peroxide; m.p. and mixed m.p. 69°) together with di-*t*-butyl hydrazodiformate (0.16 g, 14 mol per 100 mol of peroxide), m.p. and mixed m.p. 124—125°, i.r. spectrum identical with that of an authentic specimen. In addition chromatography gave an oily solid (0.34 g) which afforded *di-t-butyl 1,4-diphenyltetra-azane-1,2,3,4-tetracarboxylate*, m.p. 127° (0.18 g, 6 mol per 100 mol of peroxide) as colourless needles (from cyclohexane) (Found: M^+ , 614.330839. $C_{32}H_{34}N_4O_8$ requires M , 614.331542), τ (CDCl₃) 2.1—2.6vbr (4H, m, aromatic), 2.6—2.9br (6H, m, aromatic), and 8.5 and 8.6 (2 br singlets) and 8.95 (br singlet) (36H, 4 × CO₂C₆H₅) (the integral tracings for the two sets of br singlets gave a ratio of 1.8 : 1), ν_{max} (Nujol) 1740 and 1725 cm⁻¹ (C=O).

Reaction of Diethyl N-Phenylhydrazodiformate with Lead Tetra-acetate.—To a stirred solution of the hydrazodiformate (0.5 g, 2 mmol), m.p. 56—58° (lit.,⁹ 58—59°) and potassium carbonate (1 g) in benzene (20 ml) at room temperature was added lead tetra-acetate (0.9 g, 2 mmol). The solution, which turned orange immediately, was stirred for 1 h, then filtered. Evaporation left a dark oil (0.5 g) which was distilled to give a dark red viscous liquid (0.28 g, 78%), b.p. 55° at 0.05 mmHg (lit.,¹⁰ 130—132 at 24 mmHg), identified as ethyl phenylazoformate by comparison with an authentic sample; τ (CDCl₃) 1.95—2.30 (2H, m, aromatic), 2.35—2.65 (3H, m, aromatic), and 5.30—5.70 (2H, q) and 8.40—8.55 (3H, t) (CO₂C₂H₅).

Attempted oxidations with di-*t*-butyl peroxide in *t*-butylbenzene at 120° or lead dioxide in benzene led to quantitative or near quantitative recoveries of starting material.

[4/2334 Received, 8th November, 1974]

⁹ H. Rupe and H. Gebhardt, *Ber.*, 1899, **32**, 10.

¹⁰ M. Busch and O. Limpach, *Ber.*, 1911, **44**, 1573.