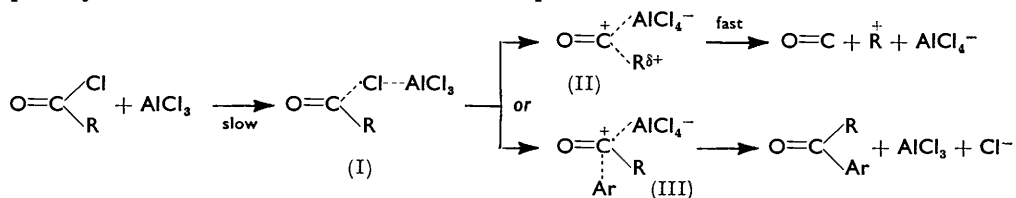


113. *The Reaction between Aromatic Compounds and Derivatives of Tertiary Acids. Part X.* Elimination of Carbon Monoxide from Some Highly Alkylated Acetyl Chlorides.*

By MICHAEL E. GRUNDY, WEI-HWA HSÜ, and EUGENE ROTHSTEIN.

The replacement of methyl by ethyl in pivaloyl chloride increases the rate of the aluminium-catalysed elimination of carbon monoxide three- to four-fold for each replacement. *tert.*-Butylmethylneopentylacetyl chloride reacts over 300 times as fast as pivaloyl chloride. This increase is probably associated with the inductive effect of alkyl. It is possible that steric effects are largely responsible for the relative amounts of ketone and hydrocarbon which are formed when anisole is the solvent. In general, the kinetics of the above reactions closely resemble those of pivaloyl chloride.

INVESTIGATION of the kinetics of the catalysed elimination of carbon monoxide from derivatives of tertiary acids has hitherto been concerned with those of pivalic acid.¹⁻³ The rate-determining step is the production of a dipolar ion between the catalyst and the acid derivative followed, in the normal case, by the fast elimination of carbon monoxide or alternatively, by the formation of a ketone, the latter reaction occurring only when a specially reactive aromatic nucleus, such as is present in anisole, is available:



* Part IX, *J.*, 1956, 4561.

¹ Rothstein and Saville, *J.*, 1949, 1954.

² Grundy, Hsü, and Rothstein, *J.*, 1956, 4558.

³ *Idem*, *J.*, 1956, 4561.

The initial reaction requires separation of halogen (it is not suggested that the chlorocarbonyl group separates as such) and it is evident that electron-releasing groups should accelerate it irrespective of the relative stabilities of entities (II) and (III). Hyperconjugation with an α -alkyl group cannot affect the formation of the complex (I) but might lower the energy of (II) compared with (III), *i.e.*, increase the proportion of carbon

monoxide relative to ketone: $O=C\overset{\curvearrowright}{-}CR_2\overset{\curvearrowright}{-}CH_2-H$ but this would not be observable kinetically because it is not for this reaction the rate-determining stage. H. C. Brown and his collaborators⁴ believe that first-order solvolysis of highly branched alkyl halides results from the tendency of the strained tetrahedral carbon atom to assume the less strained form of a planar carbonium ion. Such steric effects though they may influence ketone formation, cannot operate on the halogen atom in acid chlorides and consequently it appears reasonable to infer that the principal factor in the detachment of halogen from the chlorocarbonyl group must be inductive.

The change in reaction rate when a methyl group in pivalic acid is replaced by ethyl and by other groups has been studied. The reaction constant is increased 3–4-fold for each such replacement and over 300-fold when two methyl groups are substituted by *tert.*-butyl and by *neopentyl* groups, respectively. These relative rates are set out in Table 1, but owing to the widely differing reaction rates for differing alkylation, it has been necessary to measure them at two concentrations. The third column combines the results of the first two, an arithmetical average being taken for the figure for diethylmethyl- relative to ethyldimethyl-acetyl chlorides.

TABLE 1. Relative reaction rates for the decomposition of alkylated acetyl chlorides, $RR'R''COCl$, in benzene (Pe = *neopentyl*).

R	R'	R''	AlCl ₃ (mole/l.)		Rel. rates
			0.05	0.025	
Me	Me	Me	0.265	—	1
Et	Me	Me	1	1	3.8
Et	Et	Me	4.74	5.42	19.3
Et	Et	Et	—	19.28	73.3
Bu	Pe	Me*	—	84.78	322

* Unpublished work with W. Bleazard. Details of experiments with this acid chloride will be given in a separate communication.

Comparison of these results with those obtained⁵ by the solvolysis of tertiary alkyl halides at 25° (CMe₃Cl, 1; CEtMe₂Cl, 1.63; CEtMeCl, 2.53; CEt₃Cl, 3.0; CMe₂PeCl, 20) suggests that electron accession to carbonyl carbon not only promotes the separation of chlorine directly, but also decreases the mesomerism inherent in the chlorocarbonyl group,

$\overset{\curvearrowright}{Cl}-\overset{\curvearrowright}{C}R=O \longleftrightarrow \overset{\curvearrowright}{Cl}=\overset{\curvearrowright}{C}R-\overset{\curvearrowright}{O}$. Consequently chlorine is less tightly attached to carbon and the unshared p electrons are more strongly directed for bond formation with the catalyst. Moreover as the chlorine electrons leave vacant the p orbitals on carbon, those of the σ -carbon-carbon bond by which carbonyl is attached to the remainder of the molecule tend to uncouple and to occupy the vacated orbitals, liberating additional energy. This may be appreciable because, according to Pauling,⁶ about one third of the resonance energy of carbon monoxide can be attributed to the triplet state which in this case would be consequential on the suggested electronic rearrangement. Even so, the relative rate of decomposition of *tert.*-butylmethyl*neopentyl*acetyl chloride seems unexpectedly high; it seems desirable, however, to postpone further discussion of this point until a more detailed examination of the reaction has been completed.

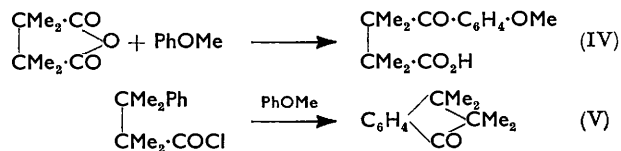
Steric effects as a factor in determining the proportions of ketone and hydrocarbon have

⁴ See for instance, Brown and Moritani, *J. Amer. Chem. Soc.*, 1955, **77**, 3623.

⁵ Hughes, Ingold, and Shiner, *J.*, 1953, 3827.

⁶ Pauling, "The Nature of the Chemical Bond," Cornell University Press, 2nd Edn., 1945, p. 135.

already been mentioned. The ease of cyclisation of tertiary phenylpropionyl and phenylbutyryl halides was taken by Rothstein and Saville ⁷ as an indication that proximity of the reacting groups was especially important in this respect. They also noted ⁸ that tetramethylsuccinic anhydride yields exclusively the ketone (IV) with anisole but on the other hand one of us observed that in this solvent $\alpha\alpha\beta\beta$ -tetramethyl- β -phenylpropionyl chloride affords only the cyclic ketone (V): ⁹



In neither case is any carbon monoxide eliminated and it is probable that if cyclisation were inhibited by the insertion of a *p*-nitro-group (as with *p*-nitrophenylpivaloyl chloride ⁷) the open-chain *p*-methoxyphenyl 2 : 2 : 3 : 3-tetramethyl-3-phenylpropyl ketone would result. Alkylated phenyl groups are less nucleophilic than *p*-methoxyphenyl and therefore in these cases anisole is sterically prevented from closely approaching the chlorocarbonyl group. Alkylation in the β -position is important in this connection because 64% of open-chain ketone is formed from $\alpha\alpha$ -dimethyl- β -phenylpropionyl chloride.⁹

The relevance of the foregoing to the present work is that it has now been found that triethylacetyl chloride and anisole afford a small proportion of triethyl-*p*-methoxyphenylmethane in addition to the main product of triethylmethyl *p*-methoxyphenyl ketone whilst *tert.*-butylmethylneopentylacetyl chloride and anisole yield only the hydrocarbon. It is not yet known whether rearrangement occurs with the latter: it does not appear to do so with the triethyl derivative. Non-production of ketone in the above experiment has made it possible to ascertain whether the use of anisole as a solvent influences the rate of elimination of carbon monoxide. The implicit assumption made in Part IX that solvent effects were not responsible for the diminution of this rate with increasing concentrations of anisole has been confirmed accordingly by carrying out the reaction between *tert.*-butylmethylneopentylacetyl chloride (0.025 mole/l.), and aluminium chloride (0.0125 mole/l.) in pure benzene, in a solution of anisole in benzene (0.025 mole/l.) and in pure anisole. The rate-constants were 0.0584, 0.0556, and 0.0587 min.⁻¹, respectively.

Only the estimations of carbon monoxide were used for the calculation of the rate-constants in Table I. The titration method (Part VIII ²) was unreliable for these rapid reactions, but was of service in indicating that the connection between rate-constant and concentrations of reactants was analogous to that already found for pivaloyl chloride. This is discussed in the kinetic section.

EXPERIMENTAL

Preparation of Materials.— $\alpha\alpha$ -Dimethylbutyric acid (*ethyl*dimethylacetic acid). This was obtained in 40% yield, b. p. 92.5°/20 mm., by passing carbon dioxide into ethereal 1 : 1-dimethylpropylmagnesium chloride.¹⁰ The acid chloride (yield 90%; b. p. 132°) was prepared from the acid and 50% excess of thionyl chloride at room temperature.

3-Methylpentane-3-carboxylic acid (*diethyl*methylacetic acid). Ethylmagnesium bromide and either ethyl methyl ketone ¹¹ or ethyl acetate ¹² furnished 3-hydroxy-3-methylpentane in 80% and 65% yields, respectively. Gaseous hydrogen chloride ¹³ below 0° converted this into the corresponding chloro-derivative (yield 83%), b. p. 37°/140 mm. (Found: C, 60.3; H, 10.5; Cl, 29.0. Calc. for C₁₆H₁₃Cl: C, 59.8; H, 10.8; Cl, 29.5%). Saturation of the

⁷ Rothstein and Saville, *J.*, 1949, 1946.

⁸ *Idem*, *ibid.*, p. 1950.

⁹ Rothstein, *J.*, 1951, 1459.

¹⁰ Gilman and Zoellner, *Rec. Trav. chim.*, 1928, **47**, 1058.

¹¹ Whitmore and Lewis, *J. Amer. Chem. Soc.*, 1942, **64**, 2964.

¹² Wilcox and Brunel, *ibid.*, 1916, **38**, 1838.

¹³ Schreiners, *J. prakt. Chem.*, 1910, **82**, 295.

corresponding Grignard reagent with carbon dioxide afforded 3-methylpentane-3-carboxylic acid (yield, 40%), b. p. 108°/13 mm. The acid chloride (b. p. 54°/19 mm.) was prepared by using thionyl chloride (90% yield).

3-Ethylpentane-3-carboxylic acid (triethylacetic acid). Several methods for the synthesis of this acid were attempted. That from tetraethylethylene glycol¹⁴ was unsatisfactory because of the poor yield (25%) of starting material obtained by the reduction of diethyl ketone. Isomerisation of the glycol to 4:4-diethylhexan-3-one (yield, 45%) was carried out with ice-cold concentrated sulphuric acid, and the ketone was oxidised by boiling nitric acid to triethylacetic acid (yield, 60%).

The hydrolysis of diethylbutyronitrile, obtained by the alkylation of acetonitrile,¹⁵ was inconvenient because a mixture of butyro- (29%), ethylbutyro- (21%), and diethylbutyronitriles (11%) was obtained; further alkylation of the first two nitriles was extremely difficult.

The synthesis finally adopted followed that devised by Doering and Wilberg¹⁶ for the preparation of other tertiary acids from alkylated acetoacetic esters.

A solution of ethyl diethylacetoacetate (60 g.) in alcohol (50 c.c.) was mixed with Raney nickel (3 g.) and reduced at 110° for 10 hr. under 60—90 atm. pressure. Fractionation from unchanged ester (20 g.) afforded *ethyl α -diethyl- β -hydroxybutyrate* (40 g.; 66%), b. p. 97°/9 mm. (Found: C, 63.7; H, 10.6. $C_{10}H_{20}O_3$ requires C, 63.9; H, 10.6%), $d_4^{18.4}$ 0.9731, $n_D^{17.4}$ 1.4425.

The above hydroxy-ester (32 g.) was gradually added to a stirred suspension of phosphorus pentoxide (37 g.) in dry benzene (30 c.c.). The solvent was distilled off and the residue extracted first with benzene and then with alcohol. The combined extracts and distillate yielded *ethyl diethylvinylacetate* (20 g.; 71%), b. p. 76°/16 mm. (Found: C, 70.5; H, 10.4. $C_{10}H_{18}O_2$ requires C, 70.6; H, 10.6%), $d_4^{17.2}$ 0.8900, $n_D^{17.5}$ 1.4332. Hydrogenation of this ester (13.4 g.) in alcohol (40 c.c.) with Raney nickel (1.2 g.) for 3 hr. at 2—3 atm. yielded ethyl triethylacetate (12 g.; 89%), b. p. 63°/18 mm. (Found: C, 70.0; H, 11.6. Calc. for $C_{10}H_{20}O_2$: C, 69.8; H, 11.6%), d_4^{16} 0.8837, $n_D^{17.2}$ 1.4200. Hydrolysis with methanolic potassium hydroxide afforded the acid (93%), b. p. 119°/14 mm. (Found: C, 66.8; H, 10.9. Calc. for $C_8H_{16}O_2$: C, 66.6; H, 11.2%). Excess (50%) of thionyl chloride at room temperature furnished the acid chloride (87%), b. p. 62°/12 mm. (Found: C, 59.5; H, 9.2; Cl, 21.9. Calc. for $C_8H_{15}OCl$: C, 59.5; H, 9.5; Cl, 21.1%).

Friedel-Crafts Condensations with 3-Ethylpentane-3-carbonyl Chloride.—(1) *In benzene at 0°.* The product obtained by stirring the acid chloride (10 g.), aluminium chloride (10 g.), and benzene (60 c.c.) at 0° consisted mainly of 3-ethyl-3-phenylpentane (2.86 g.), two unidentified unsaturated hydrocarbons (1.1 g. in all), b. p. 142—148°/2 mm. and b. p. 150—170°/2 mm., severally, and much non-volatile tar.

(2) *In benzene at 20—22°.* A solution of aluminium chloride (16.75 g., 0.125 mole) in nitrobenzene (100 c.c.) was added to a stirred solution of the acid chloride (20.1 g., 0.125 mole) in benzene (800 c.c.). The liquid was left overnight at room temp. and then decomposed by ice and dilute acid. The product (26.8 g.), b. p. 90—92°/9 mm., was heated on a steam-bath and stirred with equal volumes (1550 c.c.) of 15% titanous chloride and concentrated hydrochloric acid. The yield of nitrobenzene-free 3-ethyl-3-phenylpentane, b. p. 97°/9 mm., was 12 g. (54.5%). The previously recorded¹⁷ b. p. was 107.5°/20 mm. (Found: C, 88.2; H, 11.5. Calc. for $C_{13}H_{20}$: C, 88.6; H, 11.4%). The infrared absorption curve showed the absence of a carbonyl group and had a number of low-intensity bands between 2000 and 1660 cm^{-1} , the most prominent being at 1961, 1876, 1805, 1754, and 1704 cm^{-1} . The absence of high-intensity peaks in the 1250—1200 cm^{-1} region characteristic of quaternary carbon appears to be typical of highly alkylated benzenes. Frequencies and approximate extinction coefficients measured in 0.05 molar solutions in carbon tetrachloride, a 0.8 mm. cell being used with quartz windows for the 3000 cm^{-1} region, are given in Table 2 and are compared with those of *n*-butylbenzene. The latter (one methyl group) shows the expected differences from ethylphenylpentane (three methyl groups) and also from 3-ethyl-3-*p*-methoxybenzoylpentane (see below).

(3) *In anisole.* The reaction was carried out as with benzene but nitrobenzene was not used. A small quantity of 3-ethyl-3-*p*-methoxyphenylpentane, b. p. 142—143°/15 mm., 88—92°/0.30 mm., was isolated (Found: C, 81.6; H, 10.7%; *M*, 204. $C_{14}H_{22}O$ requires C, 81.6; H, 10.7%; *M*, 206). The main product (90% yield) was 3-ethyl-3-*p*-methoxybenzoylpentane, b. p.

¹⁴ Meerwein, *Annalen*, 1919, **419**, 153.

¹⁵ Ziegler and Ohlinger, *ibid.*, 1932, **495**, 84; Schuerch and Huntress, *J. Amer. Chem. Soc.*, 1948, **70**, 2824.

¹⁶ Doering and Wiberg, *ibid.*, 1950, **72**, 2608.

¹⁷ Huston, Fox, and Binder, *J. Org. Chem.*, 1938, **3**, 251.

TABLE 2. C-H Stretching frequencies for 1-phenylbutane, 3-ethyl-3-phenylpentane, and 3-ethyl-3-p-methoxybenzoylpentane.

Assignment ¹⁸	<i>n</i> -BuPh		CEt ₃ Ph		CEt ₃ ·CO·C ₆ H ₄ ·OMe	
	cm. ⁻¹	ε	cm. ⁻¹	ε	cm. ⁻¹	ε
Ph	3086	29	3088	29	3081	20
Ph	3063	35	3062	36	3070	20
Ph	3027	53	3028	36	3042	22
Me	2956	104	2964	127	2972	199
Me (?)	—	—	—	—	2944	157
CH ₂	2928	123	2933	102	2882	99
Me	2871	53	2874	69	2868	58
CH ₂	2858	61	—	—	2841	54

129°/0.13 mm. (Found: C, 77.0; H, 9.4. C₁₅H₂₂O₂ requires C, 76.9; H, 9.4%). Strong infrared carbonyl absorption was shown at 1672 cm.⁻¹ and intense peaks at 1258 and 1238 cm.⁻¹ due to quaternary C-C skeletal vibrations also appeared in the infrared spectrum.

Kinetic Measurements (cf. Part VIII).—(1) *Carbon monoxide method*. The increase in reaction rate in passing from one homologue to the next was about four-fold so that although the variation of the individual "runs" was of the order of 10%, the overall aspects of the results are quite clear. Some individual measurements are given in Table 3 together with the derived first-order constants. The values in parentheses indicate the percentage of the reaction used for the calculation. Table 4 gives the complete results, the constants being the mean of 3 or 4 determinations. In all cases, equal concentrations of acid chloride and catalyst were employed.

TABLE 3. Carbon monoxide (mole/l.) evolved from acid chlorides RR'R''C·COCl.

[AlCl ₃] (mole/l.):	0.050		0.025		<i>t</i> (min.)	Bu ^t MePe
	R, R', R'': EtMeMe	EtEtMe	EtEtMe	EtEtEt		
<i>t</i> (min.)						
6	0.0030	0.0101	0.0022	0.0044	2	0.0019
12	0.0061	0.0210	0.0040	0.0115	4	0.0102
18	0.0087	0.0278	0.0057	0.0149	6	0.0169
24	0.0111	0.0326	0.0070	0.0171	8	0.0196
30	0.0134	0.0359	0.0090	0.0185	10	0.0210
36	0.0152	0.0383	0.0102	0.0195	12	0.0215
42	0.0169	0.0400	0.0113	0.0202	—	—
48	0.0184	0.0413	0.0121	0.0206	—	—
54	0.0197	0.0421	0.0128	—	—	—
60	0.0210	0.0426	0.0135	—	—	—
66	0.0220	0.0430	0.0141	—	—	—
10 ² <i>k</i> ₁ (min. ⁻¹)	0.82(42)	4.49(65)	1.32(46)	5.44(59)	—	25.45(78)

TABLE 4. First-order constants for acid chlorides RR'R''C·COCl.

R, R', R'': MeMeMe *	EtMeMe		EtEtMe		EtEtEt		Bu ^t MePe
[AlCl ₃], mole/l.	0.05	0.05	0.025	0.05	0.025	0.025	0.0167
10 ² <i>k</i> ₁ (mean), min. ⁻¹ ...	0.223	0.840	0.272	3.98	1.475	5.231	3.55
							23.060

* Part IX.

(2) *Acid titration method*. These measurements with large excesses of acid chloride were not very accurate because of the large volumes of carbon monoxide evolved in the initial stages of the reaction, and since repetition of individual "runs" was impracticable, the values of the reaction constants were only approximate. Nevertheless the following conclusions could be made: (a) aluminium chloride is unaltered by the main reaction and can catalyse the decomposition of more than ten times its molecular proportion of acid chloride. (b) Side-reactions (e.g., the formation of the ketone, CR₂=CH·CO·CR₂Me) deactivate the catalyst as the reaction progresses ¹⁹ and this deactivation decreases as the molecular proportion of the acid halide decreases; when this proportion is small [e.g., the reaction between triethylacetyl chloride (0.08 mole/l.) and aluminium chloride (0.025 mole/l.)] there is no deactivation. (c) Although in most cases it was not possible to measure the initial rates of the reactions, comparison with the corresponding carbon monoxide determinations at equivalent points of the reactions showed

¹⁸ Fox and Martin, *Proc. Roy. Soc.*, 1938, *A*, **167**, 257; 1940, *A*, **175**, 208.¹⁹ Grundy, Hsi, and Rothstein, *J.*, 1952, 4136.

TABLE 5. Progress of reaction for (A) ethyldimethyl- and (B) diethylmethyl-acetyl chlorides.

		[AlCl ₃] = 0.05 mole/l.						
A, Time (min.)	0	3.2	10.6	24.5	61.4	115	181	301
Reaction (%)	17.5	25.4	28.9	34.6	48.6	62.9	72.4	79.7
B, Time (min.)	0	2.5	6.4	12.0	21.6	37.6	73.6	180.5
Reaction (%)	43.8	45.7	47.6	61.6	75.5	80.6	91.1	94.0

TABLE 6. Initial and total reactions, and some first-order constants for ethyldimethyl-, diethylmethyl-, and (C) triethylacetyl-chlorides.

[AlCl ₃], mole/l.	Reaction before 1st titration (%)			Total reaction (%)			10 ² k ₁ (min. ⁻¹)			n _A †
	A	B	C	A	B	C	A	B	C	
0.0315	4	23	—	60	96	—	0.375	2.2	—	—
0.05	17	44	—	80	94	—	0.680	—	—	1.28
0.05 *	13	34	—	63	81	—	0.442	—	—	—
0.063	13	45	81.5	94	97	100	1.34	—	—	1.84
0.126	37	85	—	97	98	—	4.24	—	—	1.75
0.025 †	—	—	9	—	—	94	—	—	5.44	—

* [Acid chloride] = 0.630 mole/l.

† [CET₃·COCl] = 0.08 mole/l.

‡ Order (for A) with respect to catalyst.

that the time-concentration curves were nearly identical in slope. (d) For ethyldimethylacetyl chloride the order with respect to catalyst approaches 2 (as for pivaloyl chloride) and it is probable that this is also true for the other acid halides. The reaction rates are comparable for constant concentrations of the catalyst only; consequently the exact dependence of rate on the latter cannot be accurately derived from the available data and therefore no attempt has been made to obtain the third-order constants, involving both the catalyst and the acid chloride. The next two tables give some of the details obtained by the titration method. Initial concentrations were [CETMe₂·COCl] = [CET₂Me·COCl] = [CET₃·COCl] = 0.315 mole/l., unless otherwise indicated. These halides are labelled A, B, and C, respectively.

THE UNIVERSITY, LEEDS.

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