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PEROXYESTER REACTION OF DIMETHYLFORMAMIDE [1a-c]

David J. Rawlinson* and Byron M. Humke
Chemistry Department, Western Illinois University, Macomb, Illinois 61455

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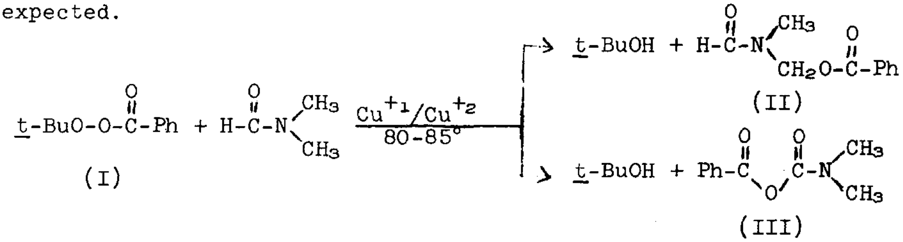
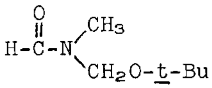
As part of a study of the radical reactions of amides, we have investigated the copper-ion catalyzed thermal reaction (Kharasch-Sosnovsky peroxyester reaction[2a]) of t-butyl peroxybenzoate (I) with dimethylformamide (DMF). The peroxyester reaction generally results in introduction of an acyloxy group in place of hydrogen [2a,b], and such acyloxylation of DMF at the N-methyl group to give N-benzoyloxymethyl-N-methylformamide (II) in 35% yield has been reported[3]. In view of the reactivity in radical reactions of formamide derivatives[4a-c], it is surprising that no product of acyloxylation of the formyl group was reported[3]. At least initially, production of the mixed carboxylic-carbamic anhydride III would be expected.



Our reaction conditions resembled those of previous workers[3]. Peroxyester I (0.4 mole) was added dropwise over 2hr to a refluxing mixture of benzene (200 ml), DMF (1.0 mole) and the metal salt under nitrogen. Refluxing was continued until peroxyester was undetectable by ir and gas evolution was complete. Our results (Table 1) show yields of up to 20%[5] of ester-amide II, together with roughly equal amounts of dimethylbenzamide and CO_2 in 43-69% yield. Smaller amounts ($<$5%yield) of N-t-butoxymethyl-N-methylformamide (IV)[6], and N-benzoyloxymethyl-N-methylbenzamide (V) were also isolated. Compound V (mp 59.5-60.5°) was independently synthesized by the peroxyester reaction of I with dimethylbenzamide (43% yield); analysis calc for V C 71.38 H 5.61 N 5.20, found C 71.63 H 5.55 N 5.15; $\nu_{c=o}$ at 1720 and 1660cm^{-1}; nmr (CCl_4) at 7.2-8.2 δ (m,10H), 5.54 δ (s,2H), 3.11 δ (s,3H).



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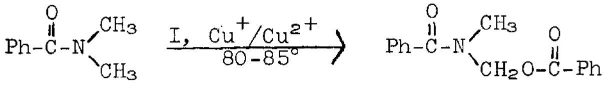


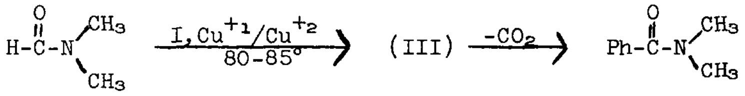
(V)

TABLE 1.[a] REACTION OF t-BUTYL PEROXYBENZOATE (I) WITH DMF AT 80-85°

Metal Salt	Dimethylbenzamide (% yield)[b]	Ester-amide II (% yield)[c]	Benzoic acid (% yield)[d]	CO_2 (% yield)	Reaction time
CuCl(2.0g)	50	6	4	69	8hr
CuCl(0.2g)	62	8[e]	4	68	12hr
CuCl(0.2g)[f]	57	20	0	66	14hr
CuCl(0.02g)	50	14	2	54	17hr
CuCl(0.002g)	43	12	0	55	27hr
$FeCl_2.4H_2O$(2.0g)	17	5	27	49	47hr
none	~1	~4	21	33	6day

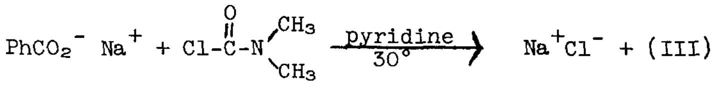
[a] Conditions specified in text. [b] Estimated by gc; identity established, after distillation, by bp, ir, nmr gc and mixture mp. [c] As isolated by distillation. Comparison of bp, refractive index, ir and nmr with authentic material was satisfactory. [d] Extracted with aqueous base. [e] Isolation by column chromatography on alumina. [f] DMF (200 ml) is reactant and solvent.

The unexpected formation of considerable yields of a phenylation product, dimethylbenzamide, in the peroxyester reaction of DMF seems best rationalized through decomposition of mixed anhydride III resulting from acyloxylation of the formyl group. Until recently[7], such carboxylic-carbamic anhydrides have been thought to be unstable[8a,b], one mode of decomposition being decarboxylation to yield the corresponding amide[9a-d].



$$\mathrm{H{-}\overset{\overset{O}{\|}}{C}{-}N(CH_3)_2} \xrightarrow[80\text{-}85^{\circ}]{\mathrm{I,\,Cu^{+1}/Cu^{+2}}} \mathrm{(III)} \xrightarrow{-\mathrm{CO_2}} \mathrm{Ph{-}\overset{\overset{O}{\|}}{C}{-}N(CH_3)_2}$$

Compound III was prepared independently by adding dimethylcarbamoyl chloride (0.2 mole) to a stirred suspension of dry sodium benzoate (0.2 mole) in pyridine (100 ml) with moderate cooling below 30°. After 45 min at room temperature the mixture was filtered. Evaporation on a rotary evaporator at room temperature yielded a liquid (45g). A wash procedure with 10% aqueous $NaHCO_3$ yielded a liquid (21.6g); analysis calc for III C 62.2 H 5.74 N 7.25, found C 62.70 H 5.85 N 7.54; $\nu_{C=O}$ at 1730 and 1770cm^{-1}; nmr (CCl_4) 7.2-8.2δ(m,5H), 2.97δ and 2.92δ (two singlets, 6H, non-equivalent N-CH_3 groups).



$$\mathrm{PhCO_2^-\ Na^+ + Cl{-}\overset{\overset{O}{\|}}{C}{-}N(CH_3)_2} \xrightarrow[30^{\circ}]{\text{pyridine}} \mathrm{Na^+Cl^-} + \mathrm{(III)}$$

Our method for making such mixed anhydrides may have wider scope than another recently published method which was unsuccessful for III[7].

We find that compound III is unstable under the conditions of the peroxyester reaction, thus lending indirect support to the role of III in the reaction. In refluxing benzene in the presence of equimolar amounts of <u>t</u>-butanol or DMF or traces of CuCl, anhydride III rapidly loses CO_2 to form dimethylbenzamide in almost quantitative yield Surprisingly, however, the purified III is stable for weeks at room temperature or when a solution in benzene alone was refluxed for 24 hr.

During the course of this work, concerned mainly with delineating the products of the peroxyester reaction of DMF, some novel directing effects by metal ions in a similar system (DMF, pyridines) were reported[10]. In our system, the reactions in the presence of iron (II) chloride or in the absence of metal salt are slow and give a variety of products in low yield, so that comparison with the copper-salt catalysis is not meaningful. Inspection of the yields of CO_2 or dimethylbenzamide[5] indicate that there is no dramatic change in product ratio dimethylbenzamide:ester amide II over a range of four powers of ten in the concentration of copper salt.

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1a) Supported in part by the Research Council, Western Illinois University, b) analyses by Micro-tek labs. Inc., Skokie, Ill., c) dimethylcarbamoyl chloride donated by Chemetron Corp.

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